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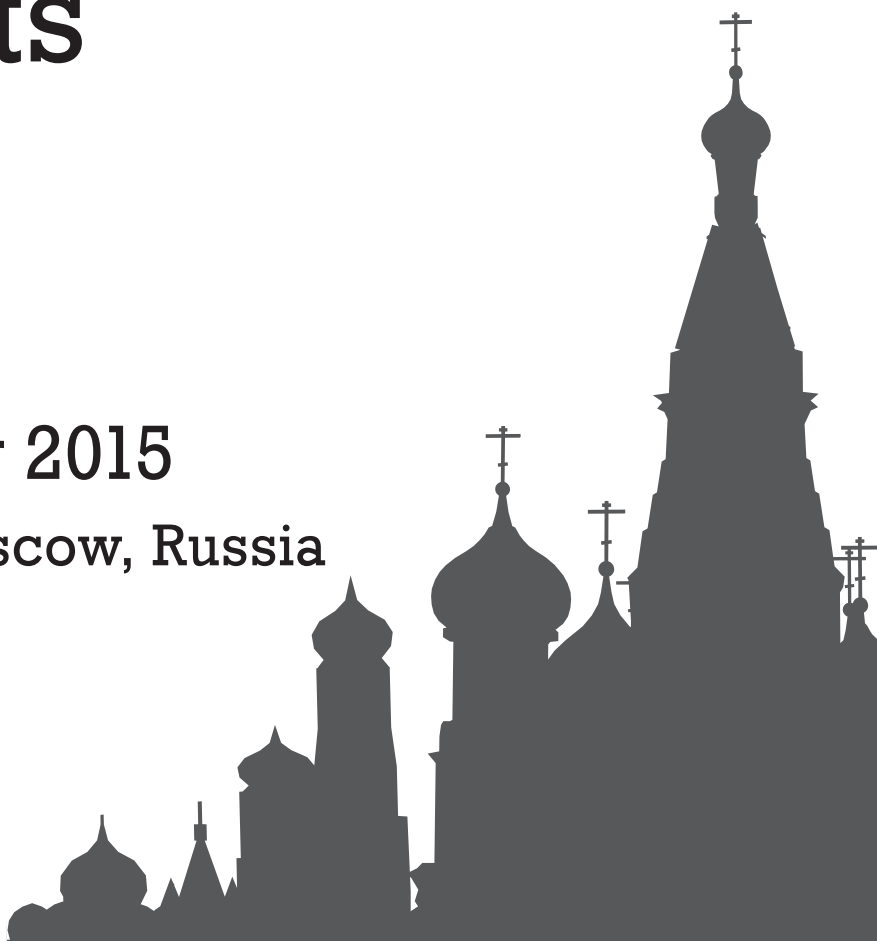
# 14<sup>th</sup> European Congress of Internal Medicine

«Internal Medicine without borders»

## Abstracts

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## Quality of anticoagulation with warfarin in patients with atrial fibrillation and venous thromboembolism

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**Objectives:** Warfarin is an affordable and effective anticoagulant drug that uses in practical medicine more than 60 years. The use of warfarin is allowed to prevent 64% of strokes in patients with atrial fibrillation (AF). Time in therapeutic range (TTR) is impartial way to find the effectiveness of warfarin using. There is a lot of information about TTR in Europe but lack in Russian Federation. We decided to estimate effectiveness of warfarin anticoagulation therapy in our clinic.

**Methods:** In our retrospective study were included 72 patients (48 men and 24 women) with AF (60 patients) and venous thromboembolism (VTE) (12 patients). All patients took warfarin and checked INR at least one time monthly or more frequently over 2014 year. Mean age of patients was 77.4±4.8 years. TTR observation period was 326±31 days. TTR was counted by means of Rosendaal technique.

**Results:** Mean TTR was 53.4±22.4% or 173.8±73.5 days. Patients with TTR value more than 60% were 44.4% (32 (24 men and 8 women)). Correlation analysis showed absence of correlation between TTR value and patient's age and sex. There was negative correlation between TTR and hospitalization – 33.3% vs. 11.1% ( $r=-0.350$ ,  $p=0.003$ ).

**Conclusions:** Our small retrospective study provides insights into the anticoagulation therapy in patients with AF and VTE in our clinic. We reveal that quality of anticoagulation therapy was poor, but patient with TTR value less than 60% had a higher risk of hospitalization. Further study with a large number of patients will clear the quality of anticoagulation therapy in Russian Federation.

## Atrial septal defect diagnosis in a patient with right-sided heart failure

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**Introduction:** Atrial septal defect (ASD) is a congenital malformation characterized by a communication between the atrial chambers of the heart. Overall, openings between the atrial chambers account for about 6 to 8% of all congenitally

malformed hearts. As a group, such defects are detected in 1:1500 live births, with a female-to-male ratio of 2-4:1. The estimated prevalence in the general population is 1 in 25,000.

**Case report:** We report a case of a 61 years old women, Caucasian, with known history of permanent atrial fibrillation, Raynaud phenomenon, chronic lower limb venous insufficiency and obesity. The patient presented with a 1 year history of heart failure NYHA class II–III with a right-sided heart failure symptoms. The transthoracic echocardiogram by color Doppler examination revealed atrial septal defect with left-right shunt and suggested pulmonary hypertension confirmed with right heart catheterization (mean pulmonary artery pressure of 37 mmHg, total pulmonary resistance 4,47 Wood Units). The patient was proposed for transcatheter closure of interatrial septal defect with self expanding Amplatzer occluder.

**Discussion:** We report that pulmonary hypertension (PH) in the context of ASD is a cause of right-sided heart failure. We emphasize the important role of transthoracic echocardiogram in the diagnosis of PH and that transesophageal echocardiogram should be included in the workup of PH for diagnostic and therapeutic evaluation.

## MitraClip insertion for severe mitral regurgitation – a case report

Anjo C.<sup>2</sup>, Satendra M.<sup>1</sup>, Victor A.R.<sup>1</sup>, Longo S.<sup>1</sup>, Parente M.L.<sup>1</sup>, Duarte F.<sup>2</sup>, Pinto S.<sup>2</sup>, Narciso S.<sup>2</sup>, Vieira R.<sup>1</sup>, Figueiredo H.<sup>1</sup>, Lopes S.<sup>1</sup>, Bento B.<sup>1</sup>, Lousada N.<sup>1</sup>, Palma R.R.<sup>1</sup>

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**Introduction:** Percutaneous mitral valve repair (MVR) using the MitraClip system is a promising technique for the treatment of mitral regurgitation (MR) which involves mechanical edge-to-edge coaptation of the mitral leaflets, it's indicated in patient with severe systolic dysfunction.

**Case report:** We report a case of a 76 years old man, Caucasian, with known history of hypertensive cardiopathy, heart failure NYHA class III, essential hypertension, type II diabetes mellitus, chronic obstructive pulmonary disease and status post colorectal cancer resection. The patient presented with a 20 year history of heart failure with progressive deterioration, especially in the last year. He was admitted to the hospital with decompensated heart failure in the context of the progression of MR. In the transthoracic echocardiogram, he presented a severe mitral regurgitation (IV/IV) with a 28% ejection fraction. Coronarography with no evidence of lesions. Levosimendan was performed with clinical and laboratorial improvement. The patient was proposed for MitraClip insertion in the context of severe mitral regurgitation. After the MitraClip insertion, the patient had clinical and functional improvement, perioperative transesophageal echocardiogram presented with low regurgitation (I/IV) with a transvalvular gradient of <2 mmHg. Follow up after one week



from the procedure revealed clinical improvement from NYHA class III to II.

**Discussion:** We report the presence of MR with progressive deterioration diagnosed by transthoracic echocardiogram and the use of levosimendan in making a bridge for surgery with clinical and functional improvement. We further report the use of percutaneous mitral valve repair with MitraClip system with excellent results confirmed by transesophageal echocardiogram.

### **Risk factors association in cardiac pacemaker infection: 4 year follow-up**

Anjo C.<sup>2</sup>, Satendra M.<sup>1</sup>, Victor A.R.<sup>1</sup>, Longo S.<sup>1</sup>, Parente M.L.<sup>1</sup>, Duarte F.<sup>2</sup>, Pinto S.<sup>2</sup>, Narciso S.<sup>2</sup>, Vieira R.<sup>1</sup>, Figueiredo H.<sup>1</sup>, Lopes S.<sup>1</sup>, Bento B.<sup>1</sup>, Lousada N.<sup>1</sup>, Palma R.R.<sup>1</sup>

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**Objectives:** Infectious complications after cardiac pacemaker (CPM) implantation are increasing over time and are associated with substantial mortality and healthcare costs. The aim of this study was to establish the incidence and determine if there was a relation between risk factors and CPM infection.

**Methods:** We conducted a descriptive analysis of 17 patients (79.1±6.1 years old, 94.1% male) selected from a universe of 1247 patients with CPM implantation from January 2011 to December 2014, in a 4 year follow-up. To investigate risk factors associated with infectious complications, we conducted a 1:2 matched case-control study of patients with infectious complications and controls without infectious complications who had the same implantation period, related by age and gender to the infectious complications group. A multivariate analysis was used with statistical significance  $p < 0.05$ .

**Results:** Among 1247 patients, 17 (1.4% per year) had a confirmed device-related infection, all presented with pocket infection. Mean duration from the time of implantation to infection was 7.1±2.7 years in late-onset infection and 73±57 days in early-onset infection. In a multivariate analysis, diabetes (OR 1.157; 95% CI 0.318–4.212;  $p=0.049$ ) or neoplasm (OR 1.029; 95% CI 0.213–4.973;  $p=0.001$ ) were an independent risk factor for cardiac pacemaker infectious complications. No correlation was found between CPM infection and history of asthma or heart failure.

**Conclusions:** At our study infection was a rare complication of CPM implantation. We observed that risk factors as diabetes or neoplasm are associated with cardiac pacemaker infections in our group of patients. A closer monitor in the follow-up period is recommended in this particular group.

### **Five years of endocarditis in a tertiary hospital in Portugal**

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**Objective:** The current medical advances and prophylactic measures have led to a shift in the paradigm of infective

endocarditis, with an increase of mean age, due to more frequent invasive medical procedures which have caused a change in the most common infectious agents.

**Methods:** The authors conducted a retrospective descriptive study by reviewing the medical records of all patients with infective endocarditis admitted to the internal medicine wards in the past 5 years, namely the diagnosis, whether there was an identification of the infectious agent, the antibiotic treatment performed and the outcome.

**Results:** In the past 5 years, 16 patients were discharged with the diagnosis of infective endocarditis. They were mostly male ( $n=11$ , 69%), with a mean age of 59.4 years. Only 2 patients had prosthetic valves (in the aortic position) and 2 patients had a device-related endocarditis (a cardioverter-defibrillator and a dialysis catheter). Most patients were admitted due to a febrile syndrome ( $n=14$ , 87.5%), 1 presented with congestive heart failure symptoms and another with altered mental status. Only 5 of these patients had a heart murmur, which increased the suspicion of infective endocarditis. Blood cultures were obtained from all patients, but a bacterial agent was only identified in 50% – the most frequent agents were methicillin-resistant *Staphylococcus aureus* ( $n=3$ ) and *Streptococci* ( $n=3$ ). All patients had a transthoracic and, subsequently, a transesophageal echocardiogram to confirm the diagnosis. The most frequently affected valve was the mitral valve ( $n=7$ ), followed by the aortic and the tricuspid valves. All patients were started on broad-spectrum empirical antibiotic therapy according to guidelines – 2 patients were transferred to a specialized cardiology unit for valve surgery, 2 patients died and the remaining patients were successfully treated.

**Conclusion:** The diagnosis of infective endocarditis may be difficult and one must bear this possibility in mind when addressing a patient with fever of unknown origin. Echocardiography has confirmed itself as one of the diagnostic pillars and the cultural exams remain crucial to the identification of the infectious agent and adjustment of adequate antibiotic treatment.

### **Management of heart failure in an intermediate care unit**

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**Objectives:** Over the last years, intermediate care units (ICU) have become increasingly important to internal medicine wards, allowing the management of patients who need more care but do not really need the degree of monitoring of an intensive care unit. As life expectancy grows, more elderly patients are hospitalized with decompensation of chronic diseases, with cardiovascular pathology as a leading cause. We aimed to analyze the demographic and clinical characteristics of the patients admitted to our ICU with acute exacerbation of cardiac disease. **Methods:** We conducted a retrospective observational study of consecutive patients with heart failure admitted to our ICU during the year of 2014. Clinical and demographic data were collected by medical record review.

**Results:** 50 admissions due to heart failure (49 patients), 22,7% of all ICU admissions. The average age was 80 years

(41–92). 54% were women. The average length of stay in the ICU was 10 days with a total hospital stay of 26 days; 18% had been admitted for exacerbation of heart failure in the previous 6 months and 34,9% were admitted in the 6 following months for the same reason. 19 patients were admitted through the emergency department, 17 from an internal medicine ward and 8 from intensive care units. 14 required non-invasive ventilation for an average of 6,9 days. Cardiac decompensation was related with cardiac arrhythmias in 6 patients, pneumonia in 10 and exacerbation of chronic obstructive pulmonary disease in 9. 5 patients were admitted with sepsis/septic shock; 5 needed inotropic therapy (4 days on average). The ICU worked as a “step down unit” in 4 patients. The most frequent co-morbidities were hypertension, atrial fibrillation, chronic kidney disease and diabetes. 5 patients were transferred to intensive care units, 31 to internal medicine wards. 11 patients developed nosocomial infections during the ICU stay. Occurred 7 deaths (14%), 5 related to the expected progression of the cardiac disease.

**Conclusions:** The current study supports a positive effect of ICUs on efficiency and cost outcomes. Our results show that the existence of ICUs in internal medicine departments allows better management and outcome for patients presenting with cardiac failure by providing intensive monitoring and differentiated care to unstable patients.

### **Prediction of vascular events in remote period in patients after myocardial revascularization and myocardial infarction**

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**Objective:** To analyze the frequency of cardiovascular events (CE), as well as forecasting the timing of their development in patients (pts) in the long term after myocardial infarction (MI, Group 1, 63 pts), coronary artery bypass grafting (CABG, Group 2, 59 pts) and endovascular prosthesis (EVP, Group 3, 35 pts).

**Material and methods:** 157 patients (mean age 52.9±0.7 years, 96.2% – male) were observed from 2003 to 2015. Among the patients after CABG, the intervention against the background of acute MI was conducted in 16 pts, on the background of stable coronary artery disease (CAD) in 25 patients, 18 – had a history of MI. In the group with EEC intervention was carried out against a background of acute MI in 26 pts, 2 pts on the background of ischemic heart disease (IHD), 7 pts had a history of MI.

**Results:** At the time of the study we were notified about the death of 1 patient with a history of MI, who had undergone CABG with the implantation of 4 stents and died after 71 months (5.9 years) due to stroke. When forecasting the timing of CE in 50% of pts, the maximum duration observed for the group 1, treated conservatively and amounted to more than 144 months (12 years). For patients of groups 2 and 3 forecast was more than 141 months (11.8 years, p=0.1082). During the

observation period: MI happened in 2 patients, stroke – in 3 pts, CABG in 4 cases and stents implantation in 2 cases. When comparing the frequency of CE and the average actual length of terms to their development between the groups of MI and CABG (p=0.109), and MI and EVP (p=0.451), no significant differences were obtained. Significantly different average time to development of vascular complications in patients after CABG and EEC (120.6±1.7 and 110.9±3.3 months, p=0.011), as well as in the group after CABG on a background of IHD compared with MI pts (p=0.047). CE were observed significantly less compared with pts after MI (p=0.024).

**Conclusions:** Projected timing of vascular events in 50% of patients after MI, CABG, or EEC did not differ significantly. There were no differences between pts with unknown quantities after MI and CABG, and pts with MI and EVP. Average time to the development of CE was significantly higher in pts after CABG than after EVP (p=0.011), as well as in the group after CABG on a background of CAD than after MI (p=0.047).

### **The importance of non valvular atrial fibrillation detection in elderly patients on primary health care**

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**Objectives:** Atrial fibrillation is the most common arrhythmia in clinical practice, accounting for approximately one third of admissions resulting from cardiac rhythm disturbances. The rising prevalence of chronic heart diseases and more frequent diagnosis as a result of increased monitoring. In the last 20 years, atrial fibrillation has become one of the most important public health problems and a significant cause of increasing health care costs, given that atrial fibrillation is associated with significant morbidity associated to cerebral stroke. We aimed to detect atrial fibrillation in elderly than 65 years old asymptomatic patients with risk factors.

**Material and methods:** A transversal descriptive study has done in 430 elderly than 65 years old patients (two groups: Group I – from 65 to 74 years and Group II – elder than 74 years old) that has been studied for health control, from January to December of 2014 in Villaviciosa de Córdoba Health Primary Center. Sex, age, body mass index, cardiovascular risk factors, analytics (blood count, glycemia, cholesterol, triglycerides, uric acid, creatinine, thyroid hormones, sodium and potassium levels) and electrocardiogram have been accomplished to know the elderly population health and detect some health problems included atrial fibrillation. Echocardiography was done in all the patients with atrial fibrillation diagnosis.

**Results:** Women 47%, men 53%. Group I – 45% and Group II – 55%. Normal sinus rhythm was revealed in 66%, atrial fibrillation – in 18%. Known atrial fibrillation – 84%, atrial fibrillation diagnosed at screening – 16%, atrial fibrillation diagnosed in Group I – 14% and in Group II – 20%. First-degree heart block – 10%, other changes – 6%. Hypertension diagnosed in 66% (atrial fibrillation associated – 97%), dyslipidemia – in 41% (atrial fibrillation associated – 47%), heart failure diagnosed in

22% (atrial fibrillation associated –44%), diabetes – 18% (atrial fibrillation associated – 22%).

**Conclusions:** Practicing an electrocardiogram in elder than 65 years is useful to detect asymptomatic atrial fibrillation in order to prevent further diseases, and start anticoagulant treatment. Hypertension in elder than 65 years is associated with atrial fibrillation. Health Control in Primary Care may be useful to atrial fibrillation diagnosis in elderly patients with risk factors associated.

### Investigation of the relationship between galectin-3 and aortic pulse wave velocity in newly diagnosed type 2 diabetic patients

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**Objectives:** Galectin-3 is a family of soluble beta-galactoside binding lectins that play important regulatory roles in inflammation, fibrosis and associated with cardiac failure. Coronary artery disease is one of the most common causes of heart failure. Aortic pulse wave velocity (PWV) is the best indicator of atherosclerosis. Systemic galectin-3 levels was decreased in type 2 diabetes mellitus (T2DM) but no determined in newly diagnosed T2DM. We investigated relationship between aortic PWV and galectin-3 levels in newly diagnosed T2DM patients.

**Material and methods:** A total of 83 patients were enrolled to the study including 48 of patients group without cardiac failure and 35 of healthy group. Serum galectin-3 and pro-BNP levels were measured using the enzyme-linked immunosorbent assay method in newly diagnosed T2DM patients. All patients aortic PWV were measured and HOMA-IR were calculated.

**Results:** The mean serum galectin-3, PWV, HOMA-IR levels were patients group (999,8±490,7 pg/ml, 9,67±1,86 m/s, 5,44±3,1) and healthy group (1217,8±515,7 pg/ml, 8,41±1,37 m/s, 2,22±1,21), respectively. Galectin-3 levels were lower in newly diagnosed T2DM patients, but there were no significant difference between two groups (p=0.059). HOMA-IR and PWV levels were higher in patients (p<0.001, p=0.001) respectively. There was no correlation between serum galectin 3, PWV and HOMA-IR in both group (r=-0.137, p=0.219, r=-0.109, p=0.331) respectively.

**Conclusions:** Previous studies suggest that a low serum galectin-3 level is associated with hyperinsulinemia, insulin resistance in T2DM. We detected low galectin-3 levels and high PWV, HOMA-IR in newly diagnosed T2DM patients. Low levels of galectin-3 may be associated with the function of beta cells and insulin resistance rather than arterial stiffness but new studies in large populations are needed to confirm these findings.

### The effect of aspirin resistance on graft occlusion after coronary artery bypass grafting

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**Objectives:** Coronary artery bypass grafting (CABG) surgery affects the cardiac morbidity and mortality positively in selected patient groups. This positive effect is based on the short and long term graft patency. The most common drug that is used for secondary prevention after coronary artery bypass surgery is aspirin. In this study the relation between aspirin resistance and bypass graft patency was investigated in patients with the history of coronary artery bypass grafting surgery who undergo coronary angiography.

**Methods:** 50 patients (37 men, 13 women, mean age 64,5±7,4) who had taken 100 mg or more aspirin regularly for at least 4 weeks and underwent coronary angiography were included. Impedance aggregometry of complete blood was used to determine aspirin resistance and graft patency was compared with frequency of aspirin resistance. Blood samples were taken after 12 hours of fasting from the antecubital vein just before the angiography.

**Results:** When all grafts were evaluated at least one graft of 22 patients was found to be occluded. Aspirin resistance was found in 32% (n=7) of these patients. The total number of grafts included was 130. The number of saphenous grafts was 84 and that of left internal mammary artery (LIMA) was 46. In aspirin resistance group 11 of 34 grafts (32%) and in aspirin sensitive group 18 of 96 grafts (19%) were found to be occluded and the difference was statistically significant (p=0,044). Also mean platelet volume was significantly higher in aspirin resistance group.

**Conclusions:** Aspirin resistance was found to be an important factor causing bypass graft occlusion. We believe that in patients with coronary artery bypass grafting the response of aspirin treatment should be evaluated with impedance aggregometry method and the treatments of these patients should be modified according to these results by giving ticlopidin or clopidogrel treatment in case of aspirin resistance.

### Potential benefit of heart rate reduction in hypertensive patients with short-term atrial fibrillation and arterial stiffness

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**Background:** Heart rate (HR) and blood pressure (BP) are positively associated with arterial stiffness and left atrial (LA) dysfunction. Atrial fibrillation (AF) is related with worse BP control and rapid HR. Influence of HR and BP on the relationship between AF and arterial stiffness may be not always univocally reported. Objective: To determine whether the difference in terms of increased pulse wave velocity (PWV) can be observed in the

influence of HR at rest and central BP in patients with short-term AF.

**Methods:** Study included 51 pts with mild-to-moderate AH and paroxysmal short-standing AF, mean age  $66 \pm 9,3$  years (40% male): 32 pts with  $PWV < 10$  m/s (G1) and 19 pts with increased  $PWV \geq 10$  mm/s (G2) ( $p < 0,0001$ ). Applanation tonometry and TTE with Doppler technique were performed. LA structural and functional abnormalities were defined as LA indexed volume (LAVI)  $> 29$  ml/m<sup>2</sup>, LA emptying fraction (LA EF)  $< 45\%$  and LA expansion index (LA Exp Inx)  $< 90\%$ .

**Results:** PWV was lower in G1 to compare with G2 group [9,2 (7,5; 9,5) vs 12,7 (10,5; 15,1) m/s respectively,  $p < 0,0001$ ]. Central systolic and pulse pressure, as well as HR were significantly lower in G1 group ( $p < 0,05$  for all cases). Proportion of pts who had AF recurrence was higher in G2 group than in G1 [18 (95%) vs 18 (56%) pts, respectively,  $p = 0,009$ ], as well as the AF episodes frequency during 3 months was [1 (1;1) vs 0,5 (0;1,5), respectively,  $p = 0,021$ ]. Regarding echocardiographic parameters in G2 group LAVI and E/e' were significantly higher ( $p = 0,019$  and  $p = 0,007$ , respectively). In G1 group HR at rest was significantly correlated with LA EF and Exp Inx ( $r = -0,42$  and  $r = -0,51$ ,  $p < 0,05$ ), while LAVI had inverse correlation with central diastolic BP ( $r = -0,52$ ,  $p < 0,05$ ). In G2 group LAVI was significantly correlated with central pulse pressure (PP) ( $r = 0,48$ ), PP amplification ( $r = -0,35$ ), PTIs ( $r = 0,53$ ) and PWV ( $r = 0,55$ ). There was correlation between Tr and LA EF, Tr and Exp Inx ( $r = -0,48$  in both cases,  $p < 0,05$ ) in G2 group. AF episodes frequency had positive correlation with mean systolic and diastolic central BP ( $r = 0,56$  and  $r = 0,45$ , respectively,  $p < 0,05$ ).

**Conclusions:** In hypertensive pts with paroxysmal short-standing AF and  $PWV < 10$  m/s HR reduction could be suggestive of a more potential benefit in protective effect for LA function and decrease of frequency of AF episodes than in pts with increased PWV. Central BP was correlated with LA structure and function.

## Comparative influence of metoprolol and diltiazem on central hemodynamics in hypertensive patients with atrial fibrillation

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**Background:** Aortic stiffness has been shown to contribute to adverse left atrial remodeling leading to higher atrial fibrillation (AF) recurrence in various patient groups including hypertensive AF patients. Data for the effects of diltiazem on arterial stiffness are limited.

**Objective:** To compare the effects of metoprolol (M) and diltiazem (D) on arterial stiffness in hypertensive patients with short-standing AF.

**Methods:** Study included 55 pts (mean age  $66 \pm 9,3$  years, 40% male) with mild-to-moderate arterial hypertension and paroxysmal short-standing AF without any associated diseases. Mean frequency of AF recurrence was 2 (1; 4) episodes per year. Clinical characteristics of M group patients ( $n = 31$ ) and D group patients ( $n = 24$ ) were similar. Applanation tonometry, echocardiography were performed before and 3 months after treatment.

**Results:** All baseline hemodynamic parameter were similar in both groups. Heart rate (HR) was significantly decreased in both groups [from 71 (66; 77) to 55 (49; 62) bpm in M group,  $p < 0,001$ ; from 73 (66; 77) to 62 (62; 62) bpm in D group,  $p < 0,001$ ]. SBP decreased significantly in both groups [from 140 (125; 147) to 121 (115; 138) mmHg in M group,  $p < 0,001$ ; from 140 (120; 150) to 120 (110; 136) mmHg in D group,  $p = 0,012$ ], but changes in cSBP were significant only in D group ( $p = 0,012$ ). DBP decreased in both groups insignificant. Both medications decreased central DBP by 11 ( $p = 0,048$ ) in M group and by 6 mmHg ( $p = 0,21$ ) in D group, that resulted in a significant difference between groups ( $p = 0,03$ ) at the end of the study. There were no changes in Aix-HR75 and Tr in both groups. Systolic pressure-time integral (PTIs) was significantly decreased by 170 mmHg $\times$ s ( $p = 0,004$ ) in M group and diastolic pressure-time integral (PTId) was decreased by 215 mmHg $\times$ s ( $p < 0,001$ ) in D group. Bidirectional change in PWV was observed in M group [from 9,5 (7,5; 12,5) to 9,2 (7,5; 10,5) m/s,  $p = 0,457$ ] and D group [9,4 (6,6; 11,3) to 9,5 (9,4; 12,9) m/s,  $p = 0,21$ ]. However during follow-up period AF recurrence was similar in both groups: 18 (58%) in M group and 18 (75%) pts in D group ( $p = 0,305$ ).

**Conclusions:** Both metoprolol and diltiazem significantly decreased HR and SBP but only metoprolol greater reduced central DBP than diltiazem that could have resulted in difference in this measurement between groups. Frequency of AF recurrence under metoprolol and diltiazem treatment was comparable.

## Severe idiopathic pulmonary hypertension – case presentation

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**Introduction:** Idiopathic pulmonary hypertension, even in today's advanced medicine, remains one of the rare diseases with a poorly understood pathophysiology. As such, diagnosing it is a lengthy process and the prognosis is usually poor, despite continuous research for new treatment options.

**Case report:** We present the case of a 19 years old patient admitted for minimal-effort dyspnea and tiredness which appeared the week before. The clinical examination showed perioral cyanosis and SaO<sub>2</sub> 88%, and the ECG and echocardiogram show the diagnosis to be severe pulmonary hypertension (sPAP 100 mmHg), with dilation and significant right ventricle dysfunction and right-to-left interatrial shunt. Possible etiologies of secondary pulmonary hypertension were excluded subsequently. Cardiac catheterization confirmed the diagnosis – severe idiopathic pulmonary hypertension with mPAP 74 mmHg and patent foramen ovale. Treatment was started with a combination of phosphodiesterase inhibitor and endothelin antagonist, with significant improvement of symptoms and clinical parameters. After 4 months there was an increase in the values of liver enzymes, probably as an adverse effect of bosentan, therefore continuing the therapy on maximum doses requires thorough follow-ups.

**Discussion:** The severity of the disease, the relatively sudden onset of symptoms and also the treatment obstacles lend themselves for discussion. Both the sex and the age

of the patient are unusual for the diagnosis of idiopathic pulmonary hypertension. The vasoreactivity test for calcium blockers could not be performed for technical reasons; if the patient happened to be a responder (5–10% of the cases), the prognosis would improve. Treatment with prostanoids, proven to reduce symptoms, should be initiated, but the drug is not available in Romania and the bureaucratic process of acquiring it is very slow. To summarize, we believe the noteworthy aspects regarding this patient are the insidious and severe presentation of the disease and also the obstacles in treatment. The readily available pharmacological agents have an uncertain effect over the survival rate, even in optimal combinations. The indication for heart-lung transplant, in case of insufficient response to drug therapy, will probably be considered. The notable absence of prostanoids from the therapeutic arsenal available in Romania and of the surgical solution—cast another unwanted shadow over the already poor prognosis of this case.

### Effects of amlodipine on cardiac and renal hemodynamic in patients with ankylosing spondylitis with the presence of arterial hypertension

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**Objective:** To investigate the effect of calcium antagonist amlodipine on the state of intracardiac and renal hemodynamic in patients with ankylosing spondylitis (AS) with the presence of arterial hypertension (AH).

**Material and methods:** The study involved 30 male patients with a documented diagnosis of AS and the presence of AH Stage I and II. All patients AS with the presence of AH in addition to basic therapy, with the purpose of correction of blood pressure (BP), received amlodipine (Norvasc, Pfizer, USA) at a daily dose of 5–10 mg, course for 8 weeks. At baseline and after a period of observation all studied Doppler echocardiography was performed and renal vascular Doppler ultrasound. We calculate the following indices of diastolic filling: E, m/s – maximum speed of early diastolic filling; A, m/s – maximum speed of atrial diastolic filling; E/A – ratio of velocities E/A; DT, ms – the time delay in the flow early filling phase, IVRT, ms – isovolumic relaxation time. To study the renal hemodynamic parameters using Doppler ultrasound renal vascular pulsed blood flow velocity spectrum was determined: the maximum speed in systole – Vs (cm/sec), the minimum velocity in diastole – Vd (cm/sec), the parameter vascular resistance – RI (subscript resistivity). Measurements were made in segmental, interlobar and arcuate arteries of the kidneys.

**Results:** As a result of amlodipine in patients AS with the presence of AH recorded improved speed and time parameters of diastolic function of the left (LV) and right (RV) ventricular compared with baseline: ELV and ERV increase ( $p < 0,001$ ), and the ratio E/A and E/BPH ( $p < 0,001$ ), a decrease LVA ( $p < 0,001$ ) and BPH ( $p < 0,01$ ), DT LV ( $p < 0,001$ ) and IVRT LV ( $p < 0,001$ ), DT RV ( $p < 0,01$ ) and IVRT RV ( $p < 0,05$ ). According to the ultrasonic Doppler blood

vessels of the kidneys, an increase in high-speed performance in segmental: Vs ( $p < 0,01$ ), Vd ( $p < 0,05$ ), interlobar: Vs ( $p < 0,001$ ), Vd ( $p < 0,001$ ) and arc: Vs ( $p < 0,001$ ), Vd ( $p < 0,001$ ) arteries compared to baseline values. The index of vascular resistance decreased with the same degree of confidence ( $p < 0,01$ ) in all studied areas.

**Conclusion:** Treatment with amlodipine in patients with AS with the presence of hypertension AH improves the speed and timing of diastolic function of the left and right ventricles, and also has a beneficial effect on renal hemodynamic, which manifests an increase in blood flow velocity parameters in the renal arteries and decreased vascular resistance.

### Self-reported sleep characteristics and cardiovascular diseases: data from the cohort population study ESSE-RF (Russia)

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**Objective:** To evaluate the association of duration and quality of sleep with cardiovascular diseases in different regions of the Russian Federation.

**Methods and material:** Participants of the cohort study Epidemiology of cardiovascular disease in various regions of the Russian Federation – ESSE-RF (Russian) population aged 25–65 years from 13 regions of the Russian Federation were interviewed about average duration of sleep, difficulty falling asleep, and maintaining sleep, sleepiness, snoring and apnea during sleep.

**Results:** The data was obtained from 21,969 participants, mean age 49 (25–65) years, including 8385 males and 13584 females. The prevalence of hypertension was 37.7%, coronary artery disease 2%, myocardial infarction 10.5%, stroke 2%. For short-sleepers prevalence of hypertension was 1.2 (95% CI: 1.1; 1.3)  $\chi^2=25$ ,  $p < 0,001$ , coronary heart disease 1.3 (95% CI 1.1; 1.7)  $\chi^2=8.6$ ,  $p < 0,01$ ; myocardial infarction 1.5 (95% CI 1.3; 1.6)  $\chi^2=63$ ,  $p < 0,001$ ; stroke 1.1 (95% CI 0.9; 1.4)  $\chi^2=1.2$ ,  $p > 0,05$ . Subjects with frequent difficulties falling asleep had 1.3 (95% CI 1.2; 1.4)  $\chi^2=40$ ,  $p < 0,001$  prevalence for hypertension; 1.7 (95% CI 1.4; 2.1)  $\chi^2=27.7$ ,  $p < 0,001$  for CAD; 2.3 (95% CI 2.1; 2.6)  $\chi^2=289$ ,  $p < 0,001$  for myocardial infarction and 1.7 (95% CI 1.4; 2.1)  $\chi^2=25$ ,  $p < 0,001$  for stroke. The relative risk for insomnia with difficulties maintaining sleep in hypertension was 1.5 (95% CI 1.4; 1.6)  $\chi^2=91$ ,  $p < 0,001$ ; CAD 2.3 (95% CI 1.9; 2.9)  $\chi^2=68$ ,  $p < 0,001$ ; myocardial infarction 2.7 (95% CI 2.4; 2.8)  $\chi^2=377$ ,  $p < 0,001$ ; stroke 2.2 (95% CI 1.7; 2.7)  $\chi^2=50$ ,  $p < 0,001$ .

**Conclusions:** As short sleep duration and indicators of the quality of sleep is associated with an increased risk of occurrence of obesity and cardiovascular disease. Symptoms of insomnia difficulties falling asleep and staying asleep more important than sleep duration when assessing the risk of CVD.

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## Predicting new-onset atrial fibrillation after coronary artery bypass surgery

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**Background:** High frequency and complications of atrial fibrillation in the early period after cardiac surgery encourage researchers to investigate its causes and possibilities of timely and effective prevention. The findings of earlier research in this area are controversial. The only unquestioned predictors of postoperative atrial fibrillation were recognized age, heart valve disease, history of atrial fibrillation paroxysms. Risk stratification in patients without valvular pathology and previous atrial fibrillation, which prevail in a cohort of patients with indications for direct myocardial revascularization, is still unclear.

**Objective:** To study the risk factors of postoperative atrial fibrillation (POAF) following coronary artery bypass grafting (CABG) on-pump in patients without valve pathology and history of atrial fibrillation.

**Methods:** 160 patients hospitalized for CABG were enrolled into a prospective comparative study. Odds ratio with 95% CI was calculated to predict POAF from various parameters.

**Results:** POAF lasting >30 seconds occurred in 32 (20%) patients. The identification of such risk factors as age >60 years (3,03 (1,09-8,4),  $p<0,01$ ), history of Q-positive myocardial infarction (5,22 (2,29-11,87),  $p<0,001$ ), II B stage of chronic heart failure (6,88 (2,02-23,46),  $p<0,001$ ), left ventricle ejection fraction <40% (3,42 (1,4-8,33),  $p<0,01$ ), dilation of left atrium (4,2 (1,87-9,44),  $p<0,01$ ) and left ventricle (2,39 (1,01-5,64),  $p<0,01$ ), NT-proBNP level >80 pg/ml (3,92 (1,63-9,44),  $p<0,01$ ), multi-vessel coronary disease (2,3 (1,03-5,17),  $p<0,05$ ), inotropic support (2,34 (1,03-5,29),  $p<0,05$ ), off-pump surgery time >80 min (2,59 (1,17-5,7),  $p<0,05$ ) was found helpful to alert the clinician about higher probability of new-onset atrial fibrillation after CABG and to guide prophylactic therapy.

## Using the index of cystatin C in the diagnosis of early stages of chronic kidney disease in patients with chronic heart failure

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**Objective:** The aim of our study is to investigate the index cystatin C as a marker for early diagnosis of chronic kidney disease (CKD) in patients with chronic heart failure (CHF).

**Methods:** The study included 110 patients (61 women and 49 men) with CHF I-IV NYHA functional class (FC). The average age of patients was  $64,5\pm 8,1$  years. The control group consisted of 20 healthy volunteers. All patients measured levels of creatinine and cystatin C in blood serum. GFR was calculated using formulas MDRD (2009), CKD-EPI (2011), as well as the level of cystatin C blood formula Hoek (2003):  $GFR [ml/min/1,73m^2] = (80,35/cystatin\ C [mg/ml]) - 4,32$ . Signs and stages of CKD

were evaluated according to the classification K/DOQI (2010). The results were processed with the programme "Statistica 6.0" (StatSoft Inc., USA).

**Results:** The causes of heart failure patients was hypertension – 40 patients and coronary heart disease in 36 patients, the combination of hypertension and coronary heart disease was observed in 34 patients. The test parameters in the control group were creatinine and cystatin C blood, respectively –  $65,2\pm 20,2$   $\mu mol/l$  and  $0,61\pm 0,2$   $mg/l$ ; GFR by MDRD and CKD-EPI, respectively –  $102,3\pm 13,1$  and  $90,2\pm 13,2$   $ml/min/1,73m^2$ . In a study of indicators of blood creatinine in the whole group remained in the normal range ( $92,2\pm 16,7$   $\mu mol/l$ ). Cystatin C levels appeared elevated in 60 patients with CHF compared to healthy individuals ( $1,4\pm 0,3$   $mg/l$ ,  $p<0,01$ ). We noticed that the GFR calculated by the formula Hoek using cystatin C ( $57,7\pm 15,2$   $ml/min/1,73m^2$ ,  $p<0,001$ ) was lower as compared to the measures determined by the concentration of blood creatinine (MDRD –  $77,6\pm 15,9$  and CKD-EPI –  $79,3\pm 17,1$   $ml/min/1,73m^2$ ). It pointed to the signs of CKD among patients. With the worsening of heart failure rate of cystatin C had a tendency to increase. In patients with I FC it was  $0,9\pm 0,08$   $mg/l$ , II class –  $1,3\pm 0,07$   $mg/l$ , III FC –  $1,4\pm 0,08$   $mg/l$  and IV FC –  $1,6\pm 0,04$   $mg/l$ . GFR calculated by the cystatin C level decreased with worsening CHF (GFR I FC –  $73,8\pm 15,1$ ; II –  $60,3\pm 11,2$ ; III –  $55,3\pm 10,1$ ; IV –  $53,3\pm 11,1$   $ml/min/1,73m^2$ ). It pointed to the signs of CKD among patients, even with normal creatinine levels. In all cases, the stage of CKD in patients with CHF should not exceed C3a.

**Conclusion:** The results of the study suggest that cystatin C may be regarded as a sensitive indicator in the diagnosis of early stages of CKD in patients with CHF.

## Functional state of kidneys in case of chronic heart failure in patients with manifestations of atrial fibrillation

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**Objective:** To study the functional state of kidneys in patients with chronic heart failure (CHF) and manifestations of atrial fibrillation (AF).

**Material and methods:** 31 patients with CHF were examined in the cardiac care unit of the Nizhny Novgorod Region State Clinical Hospital №5. 19 patients (the main group) had persistent atrial fibrillation; the remaining 12 patients (control group) had a sinus rhythm. Patients were of approximately the same age and sex. The average age of the patients from the main group was  $65\pm 4,3$ , from the control group –  $65,9\pm 3,8$  years. Both groups were mainly composed of women (11 and 8 respectively). Functional state of kidneys was evaluated by serum creatinine level, albuminuria and glomerular filtration rate (GFR), calculated by CKD-EPI formula (2011). Results were processed by software Statistica 6.0 (StatSoft Inc., USA).

**Results:** Average serum creatinine levels in patients with AF were significantly higher than in the control group (respectively 106,4±8,7 and 86,3±5,7 µmol/l; p<0,027). But they did not manifest any symptoms of renal failure. Whereas, GFR in patients with AF was significantly lower than in the control group (respectively 57,2±6,1 and 73,9±5,7 ml/min/1,73 m<sup>2</sup>; p<0,019). Moreover, patients with AF manifested unreliable, but more prominent albuminuria (respectively 268,4±214 and 164,2±190,6 mg/l; p<0,161).

**Conclusions:** Patients with CHF and manifestations of AF do not have symptoms of renal failure, but have significantly higher levels of serum creatinine, significantly lower GFR, and unreliable, but more prominent albuminuria as compared to the patients without AF. Absence of reliable difference in albuminuria levels can testify to decreased kidney function in patients with CHF. Thus, it can be stated that patients with CHF and manifestations of AF have a more pronounced decrease in renal function than patients without AF.

## Diagnosics of acute kidney injury in patients with acute coronary syndrome in real clinical practice

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**Objective:** The aim of our study is estimation of the frequency of the development of acute renal injury (ARI) in patients with acute coronary syndrome (ACS) following serum creatinine index in "real-world" clinical practice.

**Methods:** 190 patients (112 men [59%], 78 women [41%]) emergently admitted to the Vascular Center of Nizhny Novgorod Regional General Hospital named after N.A. Semashko with ACS were examined for ARI. The average age was 67,0±12,3 years old [43; 86]. ACS was the main problem in all cases. All the patients have passed clinical examination, the troponin I (TN I) and creatinine levels were revealed, ECG control being performed. As there was no information on the serum creatinine level before hospitalization, the initial rate was considered to be the rate corresponding to the computed glomerular filtration rate (GFR) 75 ml/min/1,73m<sup>2</sup> (ADQI, 2002). GFR was estimated using CKD-EPI calculation (2011). The results were processed with the programme "Statistica 6.0" (StatSoft Inc., USA).

**Results:** The performed study has revealed the following particularities. The average serum creatinine indexes in a whole were 104,1±51,9 µmol/L [28,2; 608,9], GFR – 68,3±21,5 ml/min/1,73m<sup>2</sup>. Considering "basal" indexes of serum creatinine level (according to the conception ADQI, 2002) increasing of this index is noticed in 38 (20%) patients out of 190 patients. It was considered as a sign of ARI. In the following analysis it was revealed that the persons having the signs of ARI following the blood serum index, had mostly arterial hypertension (AH) – 96%, 29% of them suffered from diabetes mellitus (DM), type 2, 22% of them

had atrial fibrillation and 8% had chronic tubulointerstitial nephritis. The other patients having no ARI the concomitant pathology was less presented. So, they had AH – 61% and DM – 21%. Statistically the number of hypertensive patients ( $\chi^2=30,2$ ; p<0,01) and patients with DM ( $\chi^2=19,3$ ; p<0,01) was greater in the group with ARI.

**Conclusions:** The performed study witnesses of the signs of ARI in the patients with ACS following the blood serum creatinine index up to 20% of cases. The predisposing factors to its development were AH, DM, irregular heartbeat and also presence of kidney diseases in anamnesis.

## Digitalis intoxication

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**Introduction:** We present a case of ventricular tachycardia attributable to digitalis intoxication.

**Case report:** A 90 years old man with a history for permanent atrial fibrillation, ischemic heart disease, hypertension and chronic kidney disease, presented with a 3-week history of impairment of the general status and cognitive decline. His usual medication included aspirin, isoptin, bisoprolol, digoxin and coumadin. Heart rate on admission was 40 beats per minute (bpm), blood pressure and temperature were normal, with no respiratory distress. Negative chronotropic medication was discontinued. The heart ultrasound showed a preserved left ventricular function, no left ventricular hypertrophy. Biochemistry showed a potassium level at 3.5 mmol/L (3.6-4.6 mmol/L), a calcium level at 2.22 mmol/L (2.2-2.52 mmol/L), creatinine 367 µmol/L (62-106 µmol/L) and urea 17 mmol/L (3.2-7.5 mmol/L). Hematology showed a white cell count of 11.4x10<sup>9</sup>/L. Serum digoxin level was significantly elevated at 4.01 nmol/L (1-2.6 nmol/L) on admission, and then spontaneously fell to 2.28 nmol/L on the second day. On the second day, a 12-lead ECG showed a ventricular tachycardia with an alternating frontal plane axis. Emergency treatment of ventricular tachycardia consisted of intravenous amiodarone, resulting in cardioversion in sinus rhythm. We then initiated an immune therapy with 80 mg of digoxin-specific antibodies. No congestive heart failure was observed and hypokalemia was prevented. No recurrence of ventricular arrhythmia was observed. However, we observed an increase in serum digoxin levels the following 3 days (6.4 and 8.9 nmol/L).

**Discussion:** This case illustrates a digitalis intoxication complicated with bidirectional ventricular tachycardia in a patient with atrial fibrillation. Treatment consisted of amiodarone followed by immune therapy, resulting in cardioversion with no recurrence of toxicity despite increasing levels of total serum digoxin during 72 hours. This observation can be explained by the fact that serum digoxin is bound to the Fab fragment, thus unable to react with receptors in the heart. This case shows that standard digoxin monitoring after administration of specific antibodies should be handled with caution. It may also be useful to monitor free digoxin concentrations during several days after the administration of immune therapy, especially in patients with renal failure.

## Masked hypertension in organized cohort: prevalence, markers, and heart remodeling

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**Objectives:** The masked hypertension (MH) is the actual problem of medicine due to association with high risk of cardiovascular complications. The aim of study was assess MH prevalence and markers in organized cohort (employees with antihypertensive treatment [masked non-effective therapy; MNT] or without it [MH]). Especially important aim was to reveal the associating MH cardiac remodeling during systematic preventive medical examination.

**Methods:** Cross-sectional cohort study of employees (n=477) of large industrial enterprise with office blood pressure (OBP) <140/90 mmHg. The ambulatory BP monitoring (ABPM), ECG, echocardiography, anthropometry, blood chemistry were performed. The selection criterion for ABPM records was the quality adequate for sophisticated analyses: duration  $\geq$ 24 hours, absence of data gaps >1 hour. The criterion for MH and MNT were OBP <140/90 mmHg and mean BP in working hours (08:00-17:00, [WBP]) >134 and/or 84 mmHg. We defined MH and MNT markers as patient characteristics significantly associated with the ratio of OBP and WBP. The ECG, echocardiography, and Doppler-Echo were applied for asses the diastolic dysfunction. Results: The total number of employees with normal OBP was 185, mean age 53.2 $\pm$ 5.5, males – 38.4%. The MH prevalence was 10.8%, MNT – 34.6% (45.4% of employees with normal OBP). The main differences included: between MH group and normotensive persons – higher left ventricular (LV) mass index (129 $\pm$ 21.2 vs. 109.5 $\pm$ 28.8 g/m<sup>2</sup> in males, 105.2 $\pm$ 43.2 vs. 82.4 $\pm$ 25.3 g/m<sup>2</sup> in females, p<0.05) and weight (85.4 $\pm$ 13.3 vs. 81.3 $\pm$ 10.1 kg, p=0.05); between MNT group and employees with effective antihypertensive treatment (normal OBP and WBP) – weight (89.4 $\pm$ 16.1 vs. 85.4 $\pm$ 15.8 kg, p<0.05), triglycerides (1.56 $\pm$ 0.95 vs. 1.23 $\pm$ 0.55 mmol/l, p<0.01) and uric acid (388.5 $\pm$ 89.5 vs. 357.2 $\pm$ 84.5 mmol/l, p<0.05), LV hypertrophy signs (interventricular septum thickness 1.34 $\pm$ 0.19 vs. 1.26 $\pm$ 0.19 mm, LV posterior wall thickness 1.27 $\pm$ 0.13 vs. 1.21 $\pm$ 0.16, p<0.05), incidence of coronary heart disease (n=3 vs. n=15, p<0.05) and the higher number of patients with angiotensin converting enzyme inhibitors intake (64.1% vs. 46.9%, p<0.05). The concentric LV hypertrophy and concentric LV remodeling were in 60% of MH patients and 78,1% of MNT patients. These data were comparable with those of patients with sustained hypertension. The eccentric LV hypertrophy was in 5% and 1,6%, normal LV geometry was in 20% and 4,7% of untreated and treated employees, respectively. In this study the professional factors were not associated with MH and MNT.

**Conclusions:** MH and MNT in organized cohort were diagnosed in approximately 50% employees. The MH and MNT markers of this group include traditional risk factors. The MH heart remodeling is comparable with sustained hypertension lesions of myocardium. High MH and MNT prevalence makes it necessary to detect these hypertension phenotypes carefully.

## Clinical and immunological features of left ventricular diastolic dysfunction formation in workers at high risk of dust pathology

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**Objective:** To explore conditions of formation of left ventricular diastolic dysfunction (LVDD) among workers at high risk of dust pathology.

**Material and methods:** We examined 58 workers of mining, processing, and metallurgical industries of the Sverdlovsk region, who contacted with aerosols fibrogenic action (AFA), at high risk of dust pathology. Clinical examination, ECG, study of respiratory function (ERF) with bronchodilator, blood oxygenation (SpO<sub>2</sub>), evaluation of glucose, lipid profile, immunological examination, and echocardiography were performed in all patients (pts).

**Results:** We detected LVDD in 42 pts (72.4%). The average age of pts with LVDD was 47,9 $\pm$ 1,4 years, without LVDD (16 pts) – 45,9 $\pm$ 2 years (p=0.45). The average experience with AFA for pts with LVDD was 23,4 $\pm$ 1,7 years, without LVDD – 18,6 $\pm$ 1,9 years (p=0.061). Patients with and without LVDD also did not differ significantly by the presence of left ventricular hypertrophy (p=0.075), hypertension (p=0.252), ischemic heart disease (p=0.156), carbohydrate and lipid metabolism. Patients with LVDD had significantly increased absolute level of leukocytes (t=2.900; p=0.007), lymphocytes (t=2.354; p=0.023) and monocytes (t=2.086, p=0.044), and decreased neutrophils (t=2.623; p=0.012). Patients with LVDD compared with pts without LVDD had significantly increased CD4 (t=3.023; p=0.005), CD8 (t=2.407; p=0.019), CD19 (t=2.148; p=0.037), reduced CD25 cells (t=4.050; p=0.004) and nitro-blue tetrazolium recovery test (t=2.685; p=0.010). Thus, in pts with LVDD revealed opposite changes of the immune status. In the study of ERF in pts with LVDD compared with pts without LVDD the following parameters were changed: vital lungs' capacity (t=1.975; p=0.057), bronchial conductivity (t=2.368; p=0.023), SpO<sub>2</sub> (t=3.416; p=0.002), but ERF and SpO<sub>2</sub> were normal for all patients.

**Conclusions:** It was established that AFA influenced at the LVDD formation, regardless of the presence / absence of cardiovascular diseases (left ventricular hypertrophy, hypertension, and coronary heart disease). Patients with LVDD revealed opposite changes of the immune status and a decrease in ERF and SpO<sub>2</sub> compared with pts without LVDD. Conditions of LVDD formation against the backdrop of changes and bronchopulmonary immune systems of workers at high risk of a dust disease require further study.

## Gene fibrinogen B polymorphism in patients with non-valvular atrial fibrillation at low risk of thromboembolism

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**Objective:** The aim was to investigate the association of 455G-A polymorphism of fibrinogen B gene (FGB), fibrinogen plasma



level and clinical outcomes in patients with non-valvular atrial fibrillation at low risk of thromboembolism by CHA<sub>2</sub>DS<sub>2</sub>-VASc. Material and methods: 98 patients (mean age 53.8±10.8 years, 82.7% males) with non-valvular atrial fibrillation at low risk of thromboembolic complications by CHA<sub>2</sub>DS<sub>2</sub>-VASc not undergoing anticoagulation therapy were examined. The main endpoints (ischemic stroke or transient ischemic attack, myocardial infarction, systemic thromboembolism) have been registered during 24 months observation period. Fibrinogen concentration was detected by Sysmex CA-500. Patients underwent genotyping by polymerase chain reaction with electrophoretic detection of the data (leukocyte DNA employed as the substrate). The predictive role of the variables was calculated via the odds ratios (OR) and their confidence intervals (95% CI). The significance of the differences was assessed through  $\chi^2$  criterion.

**Results:** G/G genotype of FGB was detected in 69.4% of patients, genotypes A/A and G/A – in 30.6% of cases. The average fibrinogen plasma concentration was 2.61±0.45 g/l and appeared to be significantly lower in G/G genotype than in A/A and G/A (2.51±0.31 g/l vs 2.82±0.63 g/l,  $p<0.05$ ). The observed frequency of the endpoints was significantly higher in G/G patients compared to the owners of A/A and G/A genotypes (30.0% vs 11.8%,  $p=0.01$ , OR 3.21, 95% CI 1.1-9.41).

**Conclusions:** Therefore, 455G-A and 455A-A polymorphisms of FGB gene can predict the development of cardiovascular complications in patients with non-valvular atrial fibrillation at low/middle risk of thromboembolism by CHA<sub>2</sub>DS<sub>2</sub>-VASc. Genotyping of the above genetic marker can be useful in identification of patients at higher risk of thromboembolic complications.

## Dilated cardiomyopathy in cardiovascular diseases morbidity patterns

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**Objective:** Evaluation of dilated cardiomyopathy (DCM) morbidity patterns according to the cardiovascular care unit data.

**Methods:** There were analyzed 7048 patient's records of the cardiovascular care unit of The Nizhny Novgorod Regional Clinical Hospital named after NA Semashko covering the period 2012–2014. The studied histories revealed 37 DCM cases, including 34 males and 3 females at the age from 24 to 75. Average age of the patients compiled 50,1±16,3 years. There were studied age-sex structure of DCM patients, the presence of leading or secondary pathology, and severity of chronic cardiac insufficiency (CHF). CHF was evaluated according to the stages (Strazhesko-Vasilenko classification) and functional classes (FC) according NYHA. The data analysis was fulfilled with the help of the program Statistika 6.0 and in percentage correlation.

**Results:** Of all the cardiovascular profile cases in the hospital, DCM was diagnosed in 0,6%, with male (92%) and middle-age patients (26 cases – 70,2% at the age 41–60) prevailing. The majority of cases (23–62,1%) showed secondary DCM. The leading

disease in secondary DCM cases was essential hypertension (HTN) (11–47,8%). Combination of HTN with ischemic heart disease (IHD) was registered in 5 cases (21,7%), isolated IHD in 6 cases (26%). Recentness of DCM verification on the whole compiled from 0 to 5 years (average 1 year). Of all DCM cases 26 patients (70,2%) had heart rhythm disorder and impaired heart conductivity, 17 (65,4%) – atrial fibrillation, 9 (34,6%) – His bundle blockade (HBB). The majority of DCM patients (30 – 81%) had associated diseases: 15 (40,5%) chronic obstructive pulmonary disease and 10 (26%) gastrointestinal diseases. On the whole in the group CHF was registered up to IIA stage (16 – 43,2%) and IIB stage (19 – 51,3%). 1 case had symptoms of III stage (2,7%), and 1 – I stage (2,7%). Prevalence of fairly advanced CHF among the DCM patients was confirmed by the presence of III FC of inadequate blood supply in 33 cases (89,2%).

**Conclusions:** DCM is encountered in patients of special cardiovascular profile up to 0,6% cases. Its morbidity pattern shows secondary DCM prevalence. The majority of DCM cases are males. The leading pathology in the secondary DCM development is HTN. Most DCM patients suffer from heart rhythm disorder and impaired conductivity as well as severe cardiac insufficiency.

## A comparison among some electrocardiographic and echocardiographic variables with ventricular mass index to detect left ventricular hypertrophy

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**Objective:** To determine accuracy of electrocardiographic and echocardiographic variables, comparing them against ventricular mass index (LVDi) measured by the echocardiogram mode M to find out left ventricular hypertrophy (LVH).

**Methods:** From a sample of 88 ECG and echocardiograms of patients seen in hypertension consultation during 2014, were compare the following variables: Sokolow-Lyon ( $S1+R5 >35$  mm), modified Sokolow (longest S + longest R  $>35$  mm), RaVL  $>1.1$ mV and Cornell ( $RaVL+SV3 >20$  in women and 28 in men), back wall diameter ( $>12$  mm) and septum diameter ( $>13$  mm in men and 12.5 mm in women) were compared against LVDi. Pearson's correlation matrix was calculated in all couples of variables and statistic significance was determined finding P values.

**Results:** We found statistically that Cornell index had the biggest electrocardiographic correlation with LVDi, 0.27 ( $p=0,031$ ) followed by modified Sokolow 0.25 ( $p=0.041$ ). Values of RaVL 0.23 ( $p=0.065$ ) and Sokolow-Lyon index 0.18 ( $p=0.14$ ) did not have statistical significance. Between echocardiographic variables, septum diameter has a stronger relationship with LVDi 0.67 ( $p>0.0001$ ) than back wall diameter 0.62 ( $p<0.0001$ ). Both were more valuable than electrocardiographic indexes. Regarding gender differences, Cornell was more sensitive to find LVH in women (17,6%) than in men (2,6%). Conversely, modified Sokolow was more sensitive in men (26,3%) than in women (13,7%) . There was a high prevalence of LVH according to LVDi outcomes in hypertension consultation during 2014 (38 patients, 43.1%).

**Conclusions:** It is important to detect LVH on an early stage to prevent and to treat cardiovascular diseases. There are some electrocardiographic and echocardiographic measurements described by European Society of Cardiology (ESC) and American College of Cardiology (ACC) as parameters of LVH, which we compared against LVDi, assessed by the echocardiogram mode M. There is a feeble relationship among some electrographic indexes and echocardiogram that is not accurate enough to establish a diagnosis precisely. It would be valuable to research more about electrocardiographic parameters to diagnose and to follow LVH as silent organ damage of hypertension, improving the approach to people with cardiovascular high risk.

### **Descriptive trial of the activity of hypertension in a district hospital**

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**Objective:** To characterize, analyze and compare the different variables of the information collected from 168 patients seen in consultation hypertension during 2014.

**Methods:** We gathered and analyzed medical records and ambulatory blood pressure monitoring (ABPM) data, including gender, age, type of hypertension, high blood pressure controlling, keeping as cut-offs diurnal and nocturnal blood pressure values below 140/90 and 125/75, respectively.

**Results:** We assessed 168 medical reports and ABPM of 98 women (58.3%) and 68 men (41.6%). A global mean age was 60.4 years, 62.5 per women and 57.2 per men. The pattern of blood pressure curve was, 76 patients had a dipper pattern, 60.5% women and 28.5% men. Non-dipper pattern was observed in 69 patients, 42 women (60.8%) and 27 men (39.1%). Night-peaker was found in 5 patients, 2 women (40%) and 3 men (60%), over-dipper in 8 women (41.1%) and 10 men (58.8%). 73 patients were controlled (43.1%), 45 women (61.6%) and 28 men (44.2%). Among 95 (53.8%) uncontrolled patients were 53 women (53.8%) and 42 men (44.2%). Diurnal and nocturnal systolic and diastolic hypertension was the most common type found, being seen in 34 patients (15 women and 19 men). Daily blood pressure average was 132.8/78.5 and during the night it was 119.1/67.1, being mean BP 131.8/75.4 in females and 133.9/82.5 in males throughout the day and 119.7/70.2 in nocturnal time.

**Conclusions:** Hypertension is a major cardiovascular risk factor of morbidity and mortality. Patients who were assessed had resistant high blood pressure that required three or more sorts of medications to control the disease. Age average was lower in men than in women, which could be correlated with an earlier emerging of high blood pressure in the first gender. Some periods of high blood pressure matched more with a specific gender, such as diurnal isolated diastolic hypertension in men and diurnal and nocturnal systolic blood pressure in women. It was also found that more than half of patients were not controlled, which shows how hard it is to control and follow long term therapy. These data must be understood regarding therapeutic adherence in any particular case. Physicians must be encouraged to lead an approach of this disease on early stages to avoid silent organ damage.

### **Comparison between left ventricular hypertrophy and left axis deviation in hypertension consultation**

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**Objective:** To corroborate ECG left axis deviation influence as diagnostic factor of left ventricular hypertrophy (LVH).

**Methods:** From a sample of 88 ECG and echocardiograms of patients followed in hypertension consultation during 2014, were measured variables such as ECG axis value and deviation, comparing them against left ventricular mass index assessed in an echocardiogram mode M (LVDi) according to gender and age. Pearson's correlation matrix was calculated in all couples of values and statistic significance was determined finding P values.

**Results:** There were 34 out of 88 (38,6%) ECGs that had left axis deviation, 18 (52,9%) men with an axis mean of -33,8 degrees, and 16 women (47,1%) and an axis mean of -18,4 degrees. 54 (61,6%) patients have a normal axis, of whom 37 (68,5%) were women and 17(31,4%) men. Average age in left axis deviation group was in women 63,2 years and 60,8 years in men. Mean age in people without deviation was 60.3 years in women and 43.5 in men. There was a faint correlation between axis deviation and ventricular mass but it was not significant, corresponding to 31% of exams ( $p=0,086$ ). Respect to the association distributed by gender, it did not show an important association either ( $p=0,227$  in women and  $p=0,364$  in men). Ventricular mass index had some correlation with axis value, being on average in people with deviation 104.7  $g/m^2$  in women and 112,4  $g/m^2$  in men and the same variable was 102,4  $g/m^2$  in women and  $g/m^2$  in men without ECG alterations.

**Conclusions:** LVH is one sign of organ damage of cardiovascular diseases described many times as asymptomatic and it might be interrelated with left axis deviation. We highlight that this association would not be strong enough to be statistically significant, but it might indicate changes in heart's shape. Nevertheless, our trial has several limitations, mainly due to lack of accuracy of electrocardiogram techniques or individual factors such as obesity or pulmonary diseases that might have change the results. It is important to continue searching more accurate variables in ECG suitable to detect and to assess LVH early on time.

### **Impact of iron deficiency correction in heart failure patients**

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**Background:** Iron deficiency (ID) is the most common cause of anemia in heart failure (HF). Its presence, even without anemia, is associated with a reduction of functional capacity and exercise tolerance. The latest guidelines profess a systematic evaluation of ID and studies showed advantages in its correction with IV iron, in chronic HF.

**Objectives:** To evaluate the prevalence of ID, with and without anemia in acute HF (AHF) and the impact of ID correction in hemoglobin levels, and in the in-hospital, long-term mortality and readmission (3, 6 and 12 months) in HF-Preserved Ejection Fraction (HF-PEF) and HF-Reduced ejection Fraction (HF-REF). Methods: Prospective study of patients (pts) consecutively admitted in the AHF unit of an University Hospital over a year. Anemia diagnosed according to WHO; absolute ID if ferritin <100 ng/ml and relative ID if ferritin 100–300 ng/ml and transferrin saturation <20%. IV iron sucrose was administered and dosage calculated by to Ganzoni.

**Results:** From the 162 hospitalized patients with HF, with 74.8±12.5 years, 71.8% women; 107 had anemia (66,1%), 75 (46.3%) had ID anemia (76,4% absolute and 23.6% functional ID) and 38 patients had ID without anemia (65.8% absolute ID and 34,2% functional ID). 62,5% pts with ID anemia and 44,7% patients with ID without anemia were treated with IV iron sucrose. The increase in hemoglobin levels compared with the untreated patients at 3 months was: for ID anemia patients' 1.3±1.7 vs 0.6±1.2 g/dL (p=0.1) and for ID without anemia 0.7±1.5 vs -0.5±1.1 g/dL (p=0.026). Early readmission rate at 3 months for HF-PEF pts with treated vs untreated ID anemia was 36.0% vs 68.8% (p=0.074). In other subgroups of HF pts there was no significant difference in in-hospital and long term mortality and readmission for treated vs untreated pts with ID anemia or ID without anemia pts.

**Conclusions:** The prevalence of ID with and without anemia was very high in this AHF population. The administration of IV iron leads to a significant increase in hemoglobin, especially in ID group without anemia. HF-PEF IV iron treated pts tend to have a lower early re admission rate at 3 months. Larger studies are needed to adequately evaluate the impact of ID treatment on long term mortality, and readmission in HF acute setting.

## Impact of polymorphisms of the CYP2C9 gene on maintenance Warfarin dose in the ethno-geographically distinct populations of Russians and Sakha (Yakuts)

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**Objective:** In this study, we evaluated the effects of CYP2C9 polymorphisms on the warfarin dose required to maintain a therapeutic INR (2.0–3.0) in the two ethno-geographically distinct populations of the Sakha (S) and Russian (R) patients. Methods: 77 patients (53-Sakha, 24-Russians) with atrial fibrillation (68%), congestive heart failure (60%), hypertension (49%) and cardiac valve replacement (26%) were recruited. International normalized ratio and plasma warfarin concentrations were determined. Genotyping was carried out by RT-PCR (real-time PCR). The three genetic polymorphisms of the gene CYP2C9 were studied: CYP2C9\*1, CYP2C9\*2, CYP2C9\*3. Fisher exact

probability test and chi-square test (with Yates correction) were applied to compare data among the S and R groups; also Mann-Whitney test was used.

**Results:** Among 46 S carriers of the CYP2C9\*1/\*1 polymorphism 10 (19%) patients developed bleeding, among "non-CYP2C9\*1/\*1" carriers only 1 (1.9%) patient developed bleeding. Differences are not statistically significant (p=0.6). Among 19 R carriers of the CYP2C9\*1/\*1 polymorphism 3 (13%) patients developed bleeding, while among "non-CYP2C9\*1/\*1" carriers no bleeding symptoms were registered. Differences are not statistically significant (p=0.5). No statistically significant difference was found in bleeding frequency among S and R CYP2C9\*3 carriers. Overanticoagulation (INR>3.0) developed in 13 (25%) S CYP2C9\*1/\*1 carriers, compared with 1 (2%) "Non-CYP2C9\*1/\*1" carrier. However, differences are not statistically significant (p=0.4). Overanticoagulation (INR>3.0) developed in 1 (5%) S CYP2C9\*1/\*1 carriers, compared with 2 (9%) "Non-CYP2C9\*1/\*1" 1 carrier. The results are of borderline significance (p=0.07). The mean daily dose requirement at R carriers of CYP2C9\*1/\*1 and "non-CYP2C9\*1/\*1" differed significantly (p=0.03), at S carriers the results were of borderline difference (p=0.05).

**Conclusions:** No significant association between CYP2C9 polymorphisms and the frequency of bleeding and excess anticoagulation (INR>3.0) was found. This may be explained by the number of cases included. CYP2C9\*1/\*1 polymorphisms compared to other polymorphisms shows statistically significant differences in the warfarin dose in Russian patients. The trend is similar among Sakha patients. The results can be used for the development of a pharmacogenetic-guided warfarin dosing algorithm for ethno-geographically distinct populations of Russia.

## Association of cardiovascular risk factors, renin-angiotensin-aldosterone system gene polymorphisms with pregnancy outcomes in women with hypertension

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**Objective:** The purpose of our study was to assess the association of cardiovascular risk factors, renin-angiotensin-aldosterone system gene polymorphisms with pregnancy outcomes in women with hypertension.

**Methods:** Prospective cohort study. The study included 300 patients (200 – with hypertension, 100 – without hypertension). Women with hypertension were divided into 4 groups: 106 patients with chronic hypertension (CH), 63 – with gestational hypertension, 10 – with preeclampsia (PE), 21 – with PE superimposed on CH. Control group included 100 women without hypertension. Isolation of genomic DNA was carried out from 125 patients and amplified using biotinylated primers according to the manufacturer's instructions («Lytech», Russia). Three polymorphic variants were screened: angiotensin-converting enzyme (ACE) (I/D (Del/Ins) genotype), angiotensinogen (AGT 174 T/M genotype) and angiotensin II

type 1 receptor (ATR1 1166 A/C genotype). Statistical analysis was performed using the statistical software package version 11.5.0 MedCalc. Gene-gene interactions were studied using entropy-based multifactor dimensionality reduction (MDR) method (software version 3.0.2).

**Results:** Pregnant women with CH and with PE superimposed on CH were more frequently of age over 35 years, overweight, obese and smoking and a high incidence of hypertension in the family history compared with pregnant women without hypertension. In pregnant women with CH a higher frequency of D allele and DD-genotype of ACE (I/D) and C allele of ATR1 (A1166C) were observed and compared with a control group. In pregnant women with PE a higher frequency of M allele and MM-genotype AGT (T174M) was noted. To assess independent associations of clinical and genetic factors with combined adverse outcome (fetal growth restriction or/and premature delivery or/and small gestational weight) we have used MDR. The best interaction model included: age >35 years (0.54%), hypertension in the family history (4.18%), failure to achieve target blood pressure to 27–28 weeks (13.22%) and C allele of ATR1 A1166C (0.24%). The established model precisely predicted combined adverse outcome in 79.5% cases (sensitivity – 79%, specificity – 80%, OR 15.0; 95% CI [5.1–44.0],  $p < 0.05$ ).

**Conclusion:** Analysis of cardiovascular risk factors, renin-angiotensin-aldosterone system gene polymorphisms may be helpful for evaluation adverse outcomes in pregnant women with hypertension.

## Insulin resistance and endothelial dysfunction in young patients with arterial hypertension and abdominal obesity

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**Objective:** The purpose of our study was to estimate serum levels of insulin resistance and endothelial activation markers in patients aged 18–44 years with arterial hypertension (AH) and abdominal obesity (AO).

**Material and methods:** The study included 154 patients (79 men and 75 women) who were divided into 4 groups: group 1 – with AH and AO (n=35), group 2 – with isolated AH (n=25), group 3 – with isolated AO (n=22), group 4 – control group (n=72). All patients were clinical examined. The serum levels of insulin with calculation Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), leptin, adiponectin, plasminogen activator inhibitor type 1 (PAI-1), angiotensin II and endothelin were measured by an enzyme-linked immunosorbent assay. Statistical analysis was performed using the statistical software package STATISTICA 10.0 (StatSoft Inc., 2011, USA). Quantitative data are expressed as mean  $\pm$  SD or median interquartile (25–75%), according to type of distribution. Continuous variables were compared using independent t-test or Mann-Whitney U-test, and categorical variables were compared using the  $\chi^2$  test or Fisher's exact test, as appropriate. All statistical tests were 2-tailed, and  $p < 0.05$  was considered significant.

**Results:** The glucose level ( $6.17 \pm 1.77$ ,  $5.16 \pm 0.47$ ,  $5 \pm 0.5$  and  $5.03 \pm 0.44$  mmol/l,  $p_{1-2,3,4} < 0.05$ ), basal insulinemia ( $16.1$ ;  $10-25.3$ ;  $10.2$ ;  $8.2-17.9$ ;  $8.4$ ; and  $10.3$   $7.0-11.5$ ;  $7.1-20.3$  mU/ml,  $p_{1-2,3,4} < 0.05$ ) and HOMA-IR index ( $5.76 \pm 1.45$ ;  $4.75 \pm 1.75$ ;  $4.5 \pm 1.24$ ;  $2.11 \pm 0.49$  respectively  $p_{1-2,3,4} < 0.05$ ) were higher in group 1 compared to other groups. Leptin was also higher in group 1 ( $35.9 \pm 25.5$  ng/ml) compared to group 2 ( $16.3 \pm 10.6$  ng/ml,  $p_{1-2} < 0.05$ ), group 3 ( $18.1 \pm 12.8$  ng/ml,  $p_{1-2} < 0.05$ ) and control group ( $11.8 \pm 9.4$  ng/ml,  $p_{1-2} < 0.05$ ). Adiponectin level was lower in group 1 compared to the other groups ( $7.8 \pm 4.8$ ,  $12.2 \pm 7.4$ ,  $13.5 \pm 4.3$  and  $11.8 \pm 4.9$  ng/ml,  $p_{1-2,3,4} < 0.05$ ). The highest levels of PAI-1 were found in group 1 ( $456 \pm 186.9$  ng/ml) and group 2 ( $418.4 \pm 189.1$  ng/ml) compared with group 3 ( $374.1 \pm 157.1$  ng/ml) and control group ( $316.2 \pm 145.5$  ng/ml,  $p_{1,2,3-4} < 0.05$ ). Increased levels of angiotensin II identified in patients group 2 ( $86.4$ ;  $44.6-89.6$  pg/ml) compared to group 1 ( $25.7$ ;  $7.4-46.5$  pg/ml,  $p_{2-1} < 0.05$ ), group 3 ( $5.9$ ;  $4.2-9.6$  pg/ml,  $p_{2-3} < 0.05$ ) and control group ( $7.7$ ;  $5.7-9.7$  pg/ml,  $p_{2-4} < 0.05$ ). In the same group we found increased endothelin concentrations ( $3.2$ ;  $0.39-11.1$  fmol/ml) compared with group 1 ( $0.55$   $0.34-2.3$  fmol/L,  $p_{2-1} < 0.05$ ), group 3 ( $0.50$ ;  $0.41-1.90$  fmol/ml,  $p_{2-3} < 0.05$ ) and the control group ( $0.47$ ;  $0.29-1.68$  fmol/ml,  $p_{2-4} < 0.05$ ).

**Conclusions:** In young patients with arterial hypertension and abdominal obesity we found insulin resistance, increased levels of leptin and plasminogen activator inhibitor type 1 and decreased level of adiponectin compared to isolated hypertension and isolated abdominal obesity. In patients with isolated hypertension revealed increased concentration of endothelin and angiotensin II compared to the other groups. There wasn't significant difference in concentrations of adipokines and levels of insulin resistance and endothelial activation markers in patients with isolated abdominal obesity compared to a control group.

## Intravascular hemolysis secondary to aortic stenosis – a case report

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**Introduction:** The authors present a clinical case of intravascular hemolysis related to a native valve stenosis.

**Case report:** A 59 years old male patient with a previous percutaneous valvuloplasty for mitral stenosis, 10 years from present time; presented to the emergency room with one month long fatigue and shortness of breath with exertion and leg edema. He had pale mucosa, systolic heart murmur grade III/VI and fine lung crackles, venous jugular ingurgitation until the mandible angle, leg edema and a palpable liver 5cm below the costal margin (at right mid-clavicular line). Blood tests showed Hb 9,0 g/L, MCV 92,1 fL, MCH 30,5 pg, normal renal function, total bilirubin 6 mg/dL with direct fraction 1.28 mg/dL, LDH 337 U/L, normal liver enzymes. He was admitted in ward with the diagnosis of heart failure. Heart evaluation by echocardiogram revealed mitral stenosis with mitral valve area of 1.6 cm<sup>2</sup> without significant insufficiency, aortic stenosis with peak gradient 98 mmHg and mean gradient 71 mmHg, pulmonary artery systolic pressure 41 mmHg and good systolic function. The anemia study showed a

hemolytic anemia based on normal iron and normal vitamin B<sub>12</sub> and folic acid, no thyroid pathology, high indirect bilirubin levels, reticulocytes 7%, low haptoglobin and normal peripheral blood morphology. The endoscopic study had no findings. The aortic stenosis was admitted as the cause for the hemolytic anemia as the hemoglobin electrophoresis was normal as well as the glucose-6-phosphate determination, negative Coombs test and no history of oxidants or pathogens. The patient was proposed for double aortic/mitral replacement but he refused.

**Discussion:** The most common cardiovascular cause for intravascular hemolysis is prosthetic valves, but there are few described cases that relate the with native valve insufficiency/stenosis particularly with severe aortic stenosis (with mean gradient >50 mmHg).

### Levosimendan, a clinical case

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**Introduction:** During the acute exacerbation of heart failure, accelerated cellular loss occurs due to deterioration of ischemia, mechanical strain, neurohormones production, inflammation and oxidative stress, and progressive myocardial failure. It is suggested that on these patients, levosimendan exerts a cardio protective effect that could improve patients' survival.

**Case report:** Women, 67 years old. She appealed to the Emergency Department (ED) for worsening of fatigue on exertion, edema in lower limbs with, orthopnea and paroxysmal nocturnal dyspnea with 15 days of evolution. History of heart failure with depressed ejection fraction (EF), hypertension, permanent atrial fibrillation (AF), mitral insufficiency. At examination she presented arrhythmic pulse, subcrepitant rales in both hemithoraces, hard edema up to mid-thigh, Godet +++ in both limbs. Analytically: hemoglobin 9 g/dL, leukocytosis, NT-proBNP 26800 pg/ml. Electrocardiogram: AF with rapid ventricular response (+/- 140 bpm). Transthoracic echocardiography: dilated left ventricle, moderate depression of systolic function (ejection fraction 35%). Aortic and tricuspid valves open with preserved mitral valve regurgitation. It was assume worsened chronic heart failure, class IV NYHA, acute tracheobronchitis and AF with rapid ventricular response. She began empirical antibacterial therapy with levofloxacin. Despite therapy optimization with furosemide 200 mg/50cc continuous infusion to 2 c/h, amiodarone 600 mg/50cc continuous infusion 6 cc/h, ramipril 5 mg and spironolactone 25 mg per day, there was a worsening of the patient's clinical condition characterized by polypnea, tachycardia, evidence of fluid overload, oliguria and jaundice, being assumed ischemic hepatitis/state of low debit. Transferred to heart failure unit where she started levosimendan protocol infused over 24 hours. There was great response to the drug with clinical improvement, urine output in 24: 6280cc. Improvement in hepatic and renal function. She was discharged in NYHA Class II with NTproBNP 434 pg/ml.

**Discussion:** The authors discuss the importance of levosimendan in treatment of acute decompensation of severe chronic heart failure in situations where conventional therapy is not sufficient.

### Heart and blood, two bonded failures? Prevalence and prognosis of anemia and hematinic factors deficiency in heart failure

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**Background:** Anemia is common in chronic heart failure (HF) and is associated with more symptoms, worse functional status, greater risk of hospitalization and reduced survival. Iron deficiency (ID) is the most common cause of anemia in HF. Studies suggest that prognosis of ID in HF patients (pts) with or without anemia is improved by treatment. Most data comes from HF with reduced ejection fraction (HF-REF) studies, but small studies suggest similar results for HF with preserved ejection fraction (HF-PEF) pts. Little is known in acute HF (AHF). The role of folic acid and vitamin B<sub>12</sub> deficiency in AHF is not set already. Objective: To evaluate prevalence and prognosis of anemia and haematinic factors deficiency in AHF unit regarding HF type.

**Methods:** Pts with HF admitted consecutively in an AHF unit of a university hospital were enrolled over a year. HF-REF was considered when left ventricle ejection fraction <45%; anemia when hemoglobin <12 g/dL for women and <13g/dL for men; ID when ferritin <100 µg/l or from 100 to 299 µg/l if transferrin saturation <20%; vitamin B<sub>12</sub> deficiency when <200 pmol/l; folate deficiency when <6.25 nmol/l. Follow-up at 3, 6 and 12 months. Results: For 162 pts (64 HF-REF, 98 HF-PEF), anemia was diagnosed in 107 (66.1%), ID anemia in 75 (46.3%) and ID without anemia in 38 (23.5%). From ID anemia pts, 30 had HF-REF (46.8% of HF-REF pts) and 45 had HF-PEF (46.2% of HF-PEF pts). From ID without anemia pts, 9 had HF-REF and 29 HF-PEF. For 158 pts, 17 (10.4%) had vitamin B<sub>12</sub> deficiency and 5 (3.2%) folate deficiency. For ID anemia pts in-hospital and 3, 6 and 12 months mortality were for HF-REF vs HF-PEF respectively 6.9 vs 0%, 11.1 vs 9.5%, 11.5 vs 12.2%, 28.6 vs 30.4% (all p>0.05). Readmissions HF-REF vs. HF-PEF at 3, 6 and 12 months were 25 vs 50% (p=0.047), 41.7 vs 60% (p=0.155), 64.7 vs 91.7% (p=0.032). For ID without anemia pts in-hospital and 3, 6 and 12 months mortality were for HF-REF vs HF-PEF 11.1 vs 3.4%, 0 vs 14.3%, 0 vs 16.3%, 0 vs 41.7% (all p>0.05). Readmission HF-REF vs HF-PEF at 3, 6 and 12 months were 62.5 vs 21.4% (p=0.026), 75 vs 31.8% (p=0.075), 85.7 vs 61.5% (p=0.26).

**Conclusions:** Prevalence of anemia and ID was very high in both HF-REF and HF-PEF pts in acute setting. Results show that prognosis of ID HF-PEF pts is at least as bad as in HF-REF suggesting they also might benefit from treatment. Although not as prevalent, vitamin B<sub>12</sub> and folate levels should also be evaluated.

### Prevalence of behavioral risk factors cardiovascular disease among students receiving higher education

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**Objective:** To study the prevalence of behavioral risk factors of cardiovascular diseases among students in higher education.

**Material and methods:** In 2014 and 2015 a survey based on standard questionnaire, developed by the adapted standard techniques was conducted in the Altai State Pedagogical University (PU) and the Altai State Medical University (MU). There were 623 students, aged 18-24 years (19,3±0,07). Evaluate information about the respondent: gender, age, school, eating habits, smoking, alcohol consumption, physical activity. All students were divided by gender and type of profile of the institution. 210 of them were young men (33,6%, 19,5±0,1), 416 were women (66,4%, 19,3±0,1). Total number of students PU was 325 (52% 20,3±0,1), MU was 300 (48%, 18,4±0,1).

**Results:** Eat excess salt 44,8% of respondents. MU Students is in 1,2 times more common salt consumed in excess, than students of PU (50 and 40%, respectively, p=0,015). More than half the students 53,3% do not eat vegetables and fruits. Do not eat fish 2 times a week, 59,5% of students. Amount of girls who eat fish at least 2 times a week more than boys (63,7 and 51%, p=0,003). MU Students who consume fish at least 2 times a week are 65%, PU students are 54% (p=0,006). Low physical activity among students of PU was in 10%, among MU in 12% (p>0,05). Never smoked is 78,2% of respondents, 21,8% trying smoking students. Active smoking are 9,6%, exposed to passive smoking are 13% of students. Smoking prevalence among young men is 16,2%, among women is 6,2% (p=0,000). Smoking history was 3±0,5 years of PU girls and 0,8±0,1 years (p=0,000) of MU girls. Female of PU in 12 times more exposed to tobacco smoke in comparison with girls of MU (23,8 and 2%, p=0,000). Drink alcohol is 73,4% of students and 3,3% of them consumed it excessively. Boys in 5 times longer excessively consume alcohol compared to girls (10,1 and 2,0%, p=0,002).

**Conclusions:** Youths in 2.6 times more smoke and in 5 times more drink alcohol compared with girls (p=0,002). Girls rarely eat fish. Students of MU in 1,2 times more consume excess salt and eat fish at least 2 times per week than students of PU (p<0,05). Girls of PU have more experience of smoking and more exposed to passive smoking in comparison with girls of MU (p<0,05).

## Psychosocial risk factors for heart disease among students in a metropolis

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**Objective:** To study psychosocial risk factors of cardiovascular diseases among the students of Barnaul city.

**Material and methods:** In 2014 and 2015 a survey about the perception of stress on a scale of Cohen and as the presence of anxiety and depression using the Hospital Anxiety and Depression Scale was conducted at the Altai State Pedagogical University (PU) and the Altai State Medical University (MU).

There were 623 students, aged 18–24 years (19,3±0,07). All students were divided by gender and type of university. At study was 210 young men (33,6%, 19,5±0,1) and 416 women (66,4%, 19,3±0,1). Total number of students PU was 325 (52% 20,3±0,1), MU students was 300 (48%, 18,4±0,1).

**Results:** The level of stress perception below the average among all students was 22%, average level was 22%, medium-high was 25% and a high was 31%. Subclinical expressed anxiety and depression had 20,4 and 9,3% of students, respectively, clinically significant anxiety and depression had 14,6 and 2,4%. The high level of stress perception among women was 35.8%, and was in 1,8 times higher in comparison with the young men 19.1% (p=0,000). The incidence of subclinical and clinically significant anxiety among girls was higher in 1,5 times (23 vs 15,3%, and 17 vs 9,5%, respectively, p=0,017). Depending in type of school: PU students had significantly more frequent medium-to-high level of stress perception (29%), students MU had it in 21% (p=0,029). MU students had a high level of stress perception above 1,7 times more compared to the PU students (38% vs 22,4%, p=0,000). Clinically significant anxiety and depression among students MU was in 2 and 7 times more likely than students in PU (p=0,006).

**Conclusions:** The high level of stress perception among students was 31%, every fifth student had subclinical anxiety. The girls had high level of stress perception in 1,8 times more compared with boys (p=0,000) and in 1.5 times more had subclinical and clinically significant anxiety (p=0,017). MU students were more prone to stress and had clinically significant anxiety and depression in 2 and 7 times more, respectively, compared with students of PU (p=0,006).

## Neutrophil to lymphocyte ratio – a novel severity biomarker for patients with heart failure with reduced ejection fraction

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**Objectives:** The neutrophil/lymphocyte ratio (NLR) is a recently uprising biomarker in Cardiology, after being used as a poor prognostic predictor in Infectious Diseases and Oncology. Illustrating the imbalance between neutrophils – an active inflammatory component and lymphocytes – a regulatory and protective component of the inflammatory cascade, it was associated with increased morbidity and mortality in patients with acute coronary syndromes and acute decompensated heart failure (ADHF). Our aim was to analyze the role of NLR as a predictor of severity in patients with heart failure, since this correlation has not been assessed yet.

**Methods:** We retrospectively analyzed data from heart failure patients admitted consecutively to our clinic. NLR was evaluated in relation to ADHF, NYHA class, NT-proBNP levels, ejection fraction (EF) and length of hospital stay (LOS), as markers of heart failure severity.

**Results:** 1012 patients with a mean age of 70.7±11.4 years were included in the study. 53.2% were female and 49.7% had

an EF<50%. NLR was correlated with NT-proBNP ( $r=0.504$ ,  $p<0.001$ ), NYHA class ( $r=0.457$ ,  $p<0.001$ ), LOS ( $r=0.397$ ,  $p<0.001$ ) and EF ( $r=-0.351$ ,  $p<0.001$ ). ROC curve analysis identified NLR as a predictor for ADHF with an AUC of 0.762 (95% CI 0.731-0.795,  $p<0.001$ ), NYHA IV class with an AUC of 0.791 (95% CI 0.759-0.821,  $p<0.001$ ) and EF<35% with an AUC of 0.695 (95% CI 0.663-0.734,  $p<0.001$ ) with a cut-off value calculated by the Youden index of  $NLR>2.95$ ,  $>3.23$  and  $>2.84$ , respectively. In multivariate logistic regression  $NLR>3$  was an independent predictor of NYHA IV class ( $p<0.001$ ) and ADHF ( $p<0.001$ ). In subgroup analysis,  $NLR>3$  remained an independent predictor of NYHA IV class and ADHF only in patients with heart failure with reduced ejection fraction (HFrEF). In this subpopulation, the prediction model using both NLR as well as NT-proBNP compared to NT-proBNP alone had an increased AUC for NYHA IV class [0.834 (95% CI 0.789-0.892) vs. 0.809 (95% CI 0.743-0.862)] and for ADHF [0.847 (95% CI 0.802-0.898) vs. 0.836 (95% CI 0.789-0.884)].

**Conclusion:** NLR is an easily-accessible and cost-effective auxiliary biomarker of heart failure severity.  $NLR>3$  is independently associated with ADHF and NYHA IV class in patients with HFrEF and it adds predictive value for these endpoints when used alongside the NT-proBNP.

### Minimally invasive versus standard full sternotomy for cardiac surgery: which is the best choice?

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**Objectives:** Minimally invasive cardiac surgery is becoming a routine approach in many hospitals. The aim of this approach is to reduce surgical trauma and avoid postoperative respiratory dysfunction, chest instability, chronic pain and the incidence of deep sternal wound infection associated with median sternotomy. In this article, we have compared outcomes between traditional sternotomy and minimally invasive approach in several surgical fields.

**Methods:** We retrospectively reviewed 4116 patients who underwent cardiac surgery at our Institution between January 2010 and June 2015. The choice of the surgical approach was based on the surgeon's preference. We included patients with valve pathologies, aortic root disease and coronary artery stenosis.

**Results:** Minimally invasive aortic valve surgery is now most commonly performed surgical approach; 1396 patients received isolated aortic valve replacement; 445 of them underwent standard full sternotomy (F-AVR, 31.8%, 46.7 male; mean age of  $74.6\pm 8.6$ ), the remaining 951 patients were treated with a minimally invasive approach by an upper J hemisternotomy (J-AVR) ( $n=636$ , 53.4% male; mean age of  $71.9\pm 10.9$ ) or right anterior mini-thoracotomy (RAT) ( $n=315$ , 54.6% male; mean age of  $72.2\pm 11.5$ ). 798 patients underwent mitral valve replacement ( $n=229$ ) or repair ( $n=569$ ) using a right minithoracotomy (R-MVR,  $n=333$ ) or standard full sternotomy (F-MVR,  $n=465$ ).

Regarding aortic root surgery, 82 patients (32%) were treated with upper J hemisternotomy (J-AAR) (82.9% male; mean age of  $57.0\pm 14.5$ ). Hybrid myocardial revascularization that consists in an off-pump bypass (left internal thoracic artery to the anterior descending coronary artery) through a left anterior small thoracotomy (LAST) and eventually percutaneous coronary angioplasty was adopted in 98 patients with a survival rate of 100%. In the remaining 3 groups, mortality rate was higher in the standard approach, but not statistically significant. The incidence of all postoperative complications, the post-procedural intensive care unit and hospitalization stay were analyzed for each group.

**Conclusions:** This study demonstrates the safety and feasibility of minimally invasive surgery. The data shown here illustrate a relative efficacy of minimally invasive over traditional sternotomy approach. Minimally invasive surgery seems to lead to better psychological acceptance of the surgery and better results also in high risk patients.

### CHA2DS2-VASC and HAS-BLED scales in elderly patients with atrial fibrillation

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**Objectives:** Nowadays, the CHA2DS2-VASc scale (and formerly the CHADS2 scale) is used to calculate the risk of new embolic events in patients with atrial fibrillation. Furthermore, the HAS-BLED scale is used to assess the risk of bleeding in these patients. Despite being widespread in clinical practice, there is scarce information about its applicability in Spanish populations. The study aim is to determine whether the CHADS2, CHA2DS2-VASc and HAS-BLED scales predict the incidence of major cardiovascular and major hemorrhagic events in patients with high morbidity and mortality, and diagnosis of atrial fibrillation during a 3–4 year follow up period.

**Methods:** Observational and prospective study. Consecutive patients with diagnosis of permanent non-valvular atrial fibrillation (NVAf) were recruited after discharge of internal medicine at the Hospital General Universitario Gregorio Marañón (HGUGM) in the years 2010 and 2011. Medical records of these patients were reviewed until the end of 2014. Several epidemiologic, clinic, laboratory and treatment parameters were studied.

**Results:** 116 patients were recruited with a mean age of  $80.9\pm 8.7$  years. During the follow up period, 52.6% of cardiovascular events, 17.2% of total bleedings were recorded and 69.8% of the patients died. The CHADS2, CHA2DS2-VASc and HAS-BLED scales average in the study patients were  $3.2\pm 1.1$ ,  $5.2\pm 1.6$  and  $4\pm 1$  respectively. 99.1% of patients had CHA2DS2-VASc equal or more than 2. 93.1% were under antithrombotic treatment, 6.9% did not receive antithrombotic therapy and 26.7% were only with antiplatelet. 33.3% were not properly anticoagulated despite the sample had more cardiovascular events (12.9%) than mayor bleedings (2.5%).

**Conclusions:** In patients with permanent atrial fibrillation treated in Internal Medicine in our center, the embolic and bleeding risk, according to CHA2DS2-VASc and HAS-BLED scales is extremely high with a very high mortality in the following period of 3–4 years. In obedience to the CHA2DS2-VASc scale, almost all patients had indication for anticoagulation therapy, however up to 1 in 3 patients received only antiplatelet therapy or none antithrombotic treatment. The elevation by 1 unit in CHA2DS2-VASc or HAS-BLED scale in these patients was not associated with a statistically significant increased risk of cardiovascular events or increased bleeding respectively.

### **Role of arterial blood gas analysis and of electrocardiogram in the diagnosis of pulmonary embolism in patients with chronic obstructive pulmonary disease**

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**Background:** Acute exacerbation of chronic obstructive pulmonary disease (COPD) is a frequent reason for hospitalization in emergency and medical wards. Pulmonary embolism (PE) may be a trigger of acute dyspnea in patients with COPD and it is extremely frequent in COPD patients with acute exacerbation. Since PE can lead to similar presentation to acute exacerbation of COPD, it is often difficult to distinguish between these two entities and delay in PE treatment may be associated with worse outcome. In general, blood gas analysis and electrocardiogram may be of help in patients with PE suspect. However, their role in COPD is still not clear.

**Objective:** To evaluate the role of arterial blood gas analysis and of electrocardiogram in COPD patients presenting with a suspect of PE.

**Methods:** 1043 COPD patients with suspected exacerbation were evaluated in 31 Italian centers. In each center all the included patients underwent angio-computed tomography to confirm or rule out PE. PE was diagnosed in 132 patients (12.7%). The presence of respiratory alkalosis at blood gas analysis and the presence of right branch block (RBB), of rightward shift of the QRS axis, and of S1Q3T3 pattern at electrocardiogram were evaluated. Sensibility and specificity of these parameters were assessed.

**Results:** An arterial blood gas analysis was available in 936 patients (89.7%). A total of 121 patients had a respiratory alkalosis (12.9%). Respiratory alkalosis had a sensitivity of 17.6 (95% CI 13.5, 22.6%) and a specificity of 89.2% (95% CI 86.4, 91.4%) for the diagnosis of PE. An electrocardiogram was available in 1035 patients (99.1%). RBB, of rightward shift of the QRS axis, and of S1Q3T3 pattern were present in 14.6, 6.6, and 3% of the patients, respectively. RBB had a sensitivity of 18.2% (95% CI 12.2, 26%) and a specificity of 85.8 % (95% CI 83.4, 88%), rightward shift of the QRS axis had a sensitivity of 10.6% (95% CI 6.1, 17.5%) and a specificity of 94% (95% CI 92.2, 95.4%), and S1Q3T3 pattern had a sensitivity of 9.8% (95% CI 5.6, 16.6%) and a specificity of 98.0 % (95% CI 96.8, 98.8%) in the diagnosis of PE respectively.

**Conclusions:** Findings our large multicenter study suggested that nor arterial blood gas analysis neither electrocardiogram parameters had a sufficient sensitivity in the diagnosis of PE in patients with suspected exacerbation of COPD. Conversely, S1Q3T3 pattern appeared to have a good specificity in this field.

### **Hypertension secondary to antiangiogenetics: an emerging topic in medical departments**

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**Objectives:** Hypertension (HTN) is a well-recognized side effect induced by antiangiogenetics (AAG) employed for cancer treatment. It represents a “class-effect” common to all AAG with prevalence ranging between 30 and 60%. Since AAG have significantly improved patients (pts) survival, and some evidence of a possible association between HTN development and better prognosis does exist, HTN related to AAG (AAG-HTN) and its management are becoming a matter of interest in internal medicine departments.

**Methods:** All cancer pts receiving an AAG have been addressed to the Internal Medicine Department of Treviglio-Caravaggio Hospital (Italy). Before starting AAG all pts underwent clinical and instrumental evaluation aimed to define cardiovascular (CV) risk. Office, ambulatory and home blood pressure (BP) were measured according to the ESH/ESC guidelines for all the duration of AAG treatment until 30 day after its withdrawal. An adjustment of antihypertensive therapy was applied to all hypertensive pts with uncontrolled HTN before AAG starting. AAG-HTN was defined as SBP >140 mmHg and/or DBP >90 mmHg (either as newly diagnosed HTN or worsening of pre-existing one).

**Results:** Between March 2012 and May 2015, 51 consecutive AAG-treated pts were evaluated (median age 67 years, range 49–84; and male/female 33/18). The AAG employed were: bevacizumab (n=19), sorafenib (n=13), sunitinib (n=12), axitinib (n=3), pazopanib (n=2), and regorafenib (n=2); 5 of them, with disease progression after one AAG, received a second AAG. Before starting AAG 39 pts (76%) had a history of HTN (in 2 diagnosed ex novo at basal evaluation; in 8 others requiring an adjustment of anti-hypertensive therapy before starting AAG). CV risk factors were evaluated, the most reported being: diabetes and obesity (n=11), dyslipidemia (n=9), active smoking (n=6), coronary heart disease (n=4), TIA (n=3). Development of AAG-HTN was observed in 28 out of 41 evaluable pts (68%) and was treated according to the current guidelines. BP control was achieved in 74% of them and, importantly, a trend of association between disease progression and absence of AAG-HTN development was documented (p=0.048).

**Conclusions:** Our data confirms the high prevalence of AAG-HTN in AAG-treated cancer patients. Moreover, as it displays peculiar features compared to HTN in general population, the evaluation and management of these pts requires a multidisciplinary approach for which internal medicine departments may have a crucial role.



## Thirteen years prognostic significance of electrocardiographic left ventricular hypertrophy in patients with arterial hypertension

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**Objective:** The aim of the study was to examine 13-years prognosis in patients (pts) with positive Lyon-Sokolow score and Cornell voltage QRS duration product and presence of echocardiographic left ventricular hypertrophy (LVH).

**Methods:** We examined 104 pts (61 male and 43 female; mean age 55.3±8.4 years) with echocardiographic LVH. The LVH cut-points were 125 g/m<sup>2</sup> for male and 110 g/m<sup>2</sup> for female. Electrocardiographic LVH was defined as the presence of Lyon-Sokolow score (LS) >38 mm and Cornell voltage QRS duration product (CP) >2.440 mm\*sec. The clinical and laboratory examination, electrocardiography, echocardiography, exercise testing, and 24-hours ambulatory blood pressure monitoring were done.

**Results:** Average left ventricular mass index (LVMI) was 170.8±32.1 g/m<sup>2</sup> and duration of hypertension was 12.5±7.7 years. During 12 years of follow-up in 33 (31.7%) pts occurred cardiovascular and cerebrovascular adverse events (ACE = myocardial infarction, cardiac or sudden death, angina pectoris, cerebrovascular insult). At the beginning of the study pts with ACE had greater: LVMI (188.9±37.9 g/m<sup>2</sup> vs. 162.4±25.1 g/m<sup>2</sup>; p<0.001). Patients with ACE had greater QTc interval dispersion than patients without ACE (72.5±20.5 ms vs. 53.8±19.2; p<0.001). There were positive correlations between LVMI and LS (r=0.367; p<0.01) and CP (r=0.357; p<0.01). ACE occurred in 9 (60%) pts of 15 pts with positive LS, and in 22 (24.7%) pts of 89 pts with negative score (odds ratio 4.06; 95% CI 1.31 to 12.63; p<0.05). ACE occurred in 11 (61.1%) pts of 18 pts with positive CP and in 20 (23.2%) pts of 86 pts with negative product (odds ratio 4.57; 95% CI 1.56 to 12.25; p<0.01).

**Conclusion:** Patients with echocardiographic LVH and positive LS and/or CP have additional risk for new cardiovascular adverse events than patients without electrocardiographic LVH during 13-years of follow-up and treatment.

## Red yeast Chinese rice – effect on lipid parameters in primary prevention and statin intolerant patients

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**Objective:** Statins represent the therapy of choice in secondary prevention as well as in primary prevention with LDL-cholesterol levels >190 mg/dl.

**Methods:** In a series of 34 consecutive dyslipidemic subjects (11 males; 35-85 yrs; 24 in primary prevention, 13 statin intolerant

pts) we studied the effect and safety of the red yeast Chinese rice product Arterin (Omega Pharma; 10 mg monacolin K and 13 different monacolins once daily) over a period of 6 months. Results: The individual life style did not change significantly with the 6 months. Total cholesterol decreased by 27,3% after 8 weeks and 27,1% after 6 months, LDL-values by 28,8 and 27,5%, triglycerides by 129,2 and 23,3%, whereas HDL-levels increased by 6,7 and 11%. 12 subjects reached a LDL-cholesterol value below 100 mg/dl. HbA1C, blood sugar, CK, uric acid, fibrinogen showed no significant different levels over the study period. We observed no severe side effects; there was no drop-out in the whole study group.

**Conclusion:** The red yeast rice product Arterin has a well balanced statin-like influence on lipid parameters with only minor side effects; Arterin may be a good alternative treatment in these patients.

## Comorbidity and adherence to treatment in patients with chronic heart failure

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**Objective:** Low adherence to medical treatment is a widely extended problem among patients with chronic heart failure (CHF). There are a lot of social and pharmacoeconomic factors of nonadherence. However, influence of psychological characteristics on adherence to treatment in patients with CHF has not been studied yet. The aim of this study was to investigate adherence to treatment in patients with CHF.

**Methods:** 203 patients with CHF (130 males and 73 females, mean age was 62±10 years) were studied. CHF was defined according to ESC Clinical Practice Guidelines of Acute and Chronic Heart Failure, 2012. The main causes of CHF were coronary artery disease and arterial hypertension. Charlson comorbidity index was calculated. Psychological state was estimated using the Personality Questionnaire of Behterevsky Institute (LOBI), MMPI, characterologic questionnaire by K. Leongard. Level of adherence to medication and non-medication therapy of the patients with CHF was studied.

**Results:** Only 61 (30%) patients were full adherence to medication treatment, and 37 (18.2%) – to non-medication therapy (recommendations for self-care and lifestyle changes). The sensitive (38.4%), paranoiac (36.9%), neurotic (27.8%) types of relation to disease were dominated in the internal structure of the disease. Age adjusted Charlson comorbidity index was 5.0±2.1 scores. Patients with high comorbidity (Charlson comorbidity index > 4 scores) had higher T-score which characterized by hypochondriac syndrome (78.3±15.3 and 62.7±10.6, resp. p=0.01), dysthymic character accentuation (13.6±3.7 and 11.0±4.5 scores resp. p=0.006), which indicated weakness of energy resources, reducing emotional background.

**Conclusions:** Nonadherence to treatment in patients with CHF is associated with desadaptive type of relation to disease. Patients with desadaptive type of relation to disease are included into group of risk for nonadherence to treatment and need more intensive observation.

## The association between blood pressure components and cognitive functions and cognitive reserve

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**Objective:** Hypertension (HTN) is a chronic medical condition. The prevalence of this vascular disease is rising all over the world. This study aimed at evaluating the association between blood pressure components and cognitive functions and cognitive reserve.

**Methods:** In this cross sectional study, 500 subjects from general population were evaluated. Subjects underwent the neuropsychological tests and blood pressure measurement and were considered for the analysis of data.

**Results:** The hypertensive patients (HT) were less efficient than the normotensive (NT) in the test of memory with interference at 10 sec (MI-10) ( $-32\%$ ,  $p=0.043$ ), clock drawing test (CLOX) ( $-26\%$ ,  $p<0.001$ ), and mini-mental state examination (MMSE) ( $-7.4\%$ ,  $p=0.02$ ). Lower MMSE, MI-10, and CLOX were predicted by higher systolic (OR, 0.94,  $p=0.032$ ; OR 0.96,  $p<0.001$ ; OR 0.94,  $p<0.001$ ) and higher pulse blood pressure (PP) (OR 0.95,  $p=0.04$ ; OR 0.97,  $p<0.001$ ; and 0.92,  $p<0.001$ ).

**Conclusion:** This study contributes to the belief that a link exists between BP and cognition, higher values of systolic BP being associated to impaired cognitive function.

## Treatment of acute decompensated heart failure with levosimendan

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**Objective:** to study efficacy of levosimendan (LS) in patients with acute decompensation of chronic heart failure (CHF).

**Material and methods:** Clinical records of 55 patients ( $52.6\pm 9.5$  years) with the left ventricle (LV) ejection fraction (EF)  $<40\%$ , who were urgently admitted to Cardiological Hospital of Nizhny Novgorod due to acute decompensated CHF were analyzed. They had coronary heart disease with average duration of  $18.2\pm 10.6$  years. 49 patients had previous myocardial infarction (MI) with average time before admission of  $6.7\pm 4.9$  years. CHF was confirmed by presence of 3 symptoms from the listed dyspnea with orthopnea, lung crepitations, peripheral edema, increase in a pulsation of jugular veins, congestion signs in a small circle of blood circulation on chest X-ray. Initial standard treatment of CHF was not successful of CHF therefore introduction of LS by intravenous infusion within 24 hours in a dose of  $0.1$  mcg/kg/min was carried out. Before and after (24 hours) introductions of LS LV condition was estimated by means of an echocardiography on the device "ALOCA SSD-4000" (Japan). All patients underwent clinical examination. The results were processed with the programme "Statistica 6.0" (StatSoft Inc., USA).

**Results:** By initial investigation LV hemodynamic parameters were as follows. The end diastolic size (EDS) was  $68.7\pm 10.8$  mm; end systolic size (ESS)  $-58.5\pm 11.8$  mm; the end diastolic volume (EDV)  $-224.9\pm 86$  ml; end systolic volume (ESV)  $-161.9\pm 69.3$  ml; EF  $-26.7\pm 7\%$ ; the cardiac output (CO)  $-59.1\pm 26.6$  ml. As a result of introduction of LS in 24 hours significant improvement of the LV hemodynamic parameters was registered. EDS decreased to  $62.8\pm 9.6$  mm ( $p<0.036$ ), and ESV to  $128.5\pm 53.0$  ml ( $p<0.0003$ ). EF significantly increased to  $35.9\pm 6.4\%$  ( $p<0.00001$ ). Also reduction of ESS to  $51.9\pm 10.0$  mm and increase of CO to  $66.9\pm 19.8$  ml was noticed, but these changes were not statistically significant ( $p<0.113$  and  $p<0.168$  respectively). In 24 hours at all patients dyspnea at rest was stopped, crepitations in lungs disappeared, edema, decreased, the pulsation of jugular veins disappeared, and the stagnation phenomena on a small circle of blood circulation according to chest X-ray decreased.

**Conclusion:** Administration of LS significantly improves the LV systolic function of heart and causes regress of clinical signs of acute decompensated of CHF.

## Galectin-3 and coronary atherosclerosis in patients with myocardial infarction

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**Objectives:** The problem of myocardial infarction (MI) does not lose its relevance worldwide. This condition is characterized by high morbidity and mortality of adult population. In recent years various biomarkers which are involved in the pathogenesis of MI are actively studied. Galectin-3 is one of such markers which is used in heart failure and neoplastic aberration. The role of this biomarker in MI is not studied completely yet. The purpose of the study – to estimate the differences in galectin-3 concentration in blood serum depending on the severity of coronary atherosclerosis in patients with ST-elevated MI.

**Material and methods:** 87 patients (65 – males, 22 – females; mean age  $58.9\pm 9.6$ ) admitted with ST-elevated MI were examined. Clinical and anamnesis data were collected, standard laboratory and instrumental methods were performed, including angiography. In all patients galectin-3 level was measured by enzyme-linked immunosorbent assay (ELISA) on the first day after disease onset. The studied biomarker level was measured in 81 patients on the 10–14th days after MI onset. The baseline serum values of galectin-3 were  $0.0-2.28$  ng/ml.

**Results:** Galectin-3 levels, measured in MI patients on the first day after disease onset, were elevated as compared to the baseline values ( $9.5$  [ $3.3, 11.9$ ] ng/ml). On the 10–14th days after MI, elevated galectin-3 levels ( $15.6$  [ $9.9; 37.4$ ] ng/ml) were observed ( $p<0.01$ ). Patients were divided into 3 groups, according to the results of angiography: patients with single-vessel lesion – 46 (53.5%); with two-vessel lesion – 20 (23.3%) patients; and three-vessel lesion – 20 (23.3%) patients. When determining the relationship between galectin-3 level and the severity of coronary atherosclerosis it was found out that the concentration of the biomarker in patients with three-vessel coronary artery disease is higher than in single vessel disease

patients (35.8 [13.2; 43.0] ng/ml vs 11.1 [9.5, 31.5] ng/ml,  $p=0.02$ ). Correlation analysis confirms this relationship ( $r=0.29$ ,  $p=0.01$ ). In the groups with two or three-vessel lesions galectin-3 level increases dynamically by the 10–14th days of MI ( $p<0.01$ ). A direct correlation between biomarker levels on days 10–14 and door-to-balloon time (min) ( $r=0.27$ ,  $p=0.02$ ) has been defined. Conclusion: The possibility of using galectin-3 in estimating the severity of coronary atherosclerosis in patients with ST-elevated MI is shown.

## A broken-heart syndrome mimicking multiple diagnoses of troponin elevation

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**Introduction:** Takotsubo cardiomyopathy is an entity characterized by reversible left ventricular apical ballooning in the absence of coronary artery stenosis. In 85% of cases, it is triggered by an emotionally or physically stressful event. Our aim is to highlight the potential wide variety of clinical manifestations and complications that make so challenging the differential diagnosis of this disease.

**Case report:** We report a case of an 81 years old white widow, with a history of heart failure with preserved systolic function. She was admitted to the emergency room with an acute chest pain after a disagreement with her son and tiring housekeeping. Analysis showed mildly increased troponin levels. Electrocardiography (ECG) showed ST-segment elevation in leads V2 through V6. Chest radiography ruled out pleuroparenchymal condensation. The patient was admitted with the diagnosis of acute ST-segment-elevation myocardial infarction, initially with no clear indication for revascularization. The patient showed clinical signs and symptoms of congestive heart failure, including hypotension, bradycardia, refractory chest pain and dyspnea, which required further workup for alternative diagnosis. Analysis presented significant troponin elevation, high NT-proBNP and rising inflammatory markers and D-dimer. ECG revealed ST-segment elevation in leads V3 through V4. Hypocapnia and hypoxemia was substantiated in arterial blood gases. Holter study ruled out dysrhythmias. Computed chest tomography excluded pulmonary embolism, aortic dissection and bronchopneumonic infiltrates. Pheochromocytoma was also excluded. Transthoracic echocardiogram exhibited a decreased systolic function and apical akinesia. The patient underwent cardiac catheterization, which disclosed no coronary artery stenosis. Left ventriculography concluded systolic ballooning of the apex and basal hypercontraction. After optimization of heart failure therapy, troponin negativity and ST-segment normalization was obtained. Repeated transthoracic echocardiograms attested complete resolution of the wall motion abnormality and normalization of the ejection fraction by the 7th week.

**Discussion:** Patients who survive the acute episode typically recover normal systolic function within 1 to 4 weeks. The pertinence of this case is to demonstrate that takotsubo cardiomyopathy can show longer recover periods with an increased incidence of complications, requiring prompt recognition and adequate treatment.

## Pulmonary embolism and inferior vena cava thrombosis in a patient with right atrial thrombosis, a case report

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**Introduction:** A case of thrombus in the right atrium (RA) extending to inferior vena cava (IVC) and acute pulmonary thromboembolism (PTE) in a patient with respiratory infectious clinic; and test performed to reach the diagnosis and treatment. Case report: We present a 61 years old male. He was admitted with fever of 38°C, cough, dyspnea, interstitial infiltrate in the right lower lobe in chest X-ray, and atrial flutter 3:1, heart rate of 151 beats per minute in electrocardiogram (ECG). Empirical antibiotic therapy, heart rate control with digoxin and diltiazem starts, and urgent transthoracic echocardiography (TTE) is requested, where mild ventricular hypertrophy can be seen with an ejection fraction of the left ventricle of 30–35%, thrombus in the right atrium (RA) 1.5x1.5 cm. The following CT scan with contrast showing a filling defect consistent with thrombus RA extending to IVC, hepatic and intrahepatic, PTE bilateral acute, signs of pulmonary hypertension without signs of right cardiac overload and consolidation with air bronchogram in basal segment the right lower lung lobe. It contacts the service interventional radiology and vascular surgery, declining his speech by extending the thrombotic process, opting for conservative treatment by anticoagulation with acenocumarol. During admission, the patient presented increased heart rate with heart failure and bilateral pleural effusion that required admission to intensive care unit with subsequent compensation, remaining stable and anticoagulated. Study of autoimmunity, tumor markers and thrombophilia were negative. Controls for 37 days with ETT and CT were performed and favorable development was assessed with clot disappeared in RA and IVC. The patient is given high anticoagulation indefinitely.

**Discussion:** In cases of extensive venous thrombosis, it is not always indicated cardiovascular surgery. If there thrombus in RA are not suitable for interventional radiology procedures. In these cases the treatment of choice is anticoagulation with low molecular weight heparin, warfarin or acenocumarol and supportive treatment.

## The age adjusted cutoff plasma level of D-dimer for ruling out acute pulmonary embolism

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**Objectives:** Accurate pulmonary embolism diagnosis is challenging. D-dimer test has very high negative predictive value. The aim of this study is to validate the advantage of age-adjusted D-dimer cutoff level, defined as age multiplied

by 10, compared to fixed level of 500 µg/L, in adult patients evaluated for acute pulmonary embolism (PE).

**Methods:** This is a retrospective, single center study that includes all the patients that were admitted between 2011 and 2014 to the emergency room at our center for suspected diagnosis of PE. We reviewed for these patients the demographic data, risk factors for PE, D-dimer plasma level, imaging studies, clinical diagnosis and 3 months follow up. Primary outcome was defined as the diagnosis of PE in patients with D-dimer levels >500 µg/L but below the age adjusted cutoff level, representing a negative age-adjusted D-dimer result.

**Results:** Data of 1241 patients was reviewed. 654 patients with D-dimer level above 500 µg/L and low or intermediate risk for PE were included in the study. 208 patients had a D-dimer level above 500 µg/L but below the age adjusted cutoff level, of them 1 was diagnosed with PE (0.48% [95% CI, 0-2.6%]). 446 patients had a D-dimer level above the age adjusted cutoff level, of them 28 were diagnosed with PE (6.28% [CI, 4.2-8.9%]) during the follow up period. The negative predictive value was 99.5% for the age adjusted cutoff level. This data was similar to the negative predictive value of the well established cutoff level of 500 µg/L in previous trials ranging from 97 to 100%.

**Conclusions:** Our study show that age adjusted D-dimer cutoff level can be safely used to exclude PE in patients with a low or intermediate clinical probability for acute PE, alleviating the need to continue with unnecessary imaging tests. This validation study results are in line with previous studies.

## Potentially inappropriate use of medicines in advanced age patients with heart failure in Spain

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**Objectives:** To analyze the inappropriate prescribing (IP) in elderly patients with chronic heart failure (CHF), IP instruments used in the prescription of potentially inappropriate medicines (PIMs) STOPP and Beers criteria, and in potential prescribing omissions (PPOs) START and ACOVE criteria.

**Methods:** Observational, prospective study on patients aged >74 hospitalized at 7 internal medicine services, was financed by Spain's Ministry of Health. 295 participants with CHF (from a cohort of 672). The variables were obtained from medical histories and interviews.

**Results:** 51.2% were aged 75 to 84 and >85 – 48.8%. The mean age was 83.9. Reasons for hospitalization: first-time 33.9%, chronic disease 66.1%. Charlson index: low comorbidity 32.5%, mean 37.3%, high 30.2%. Dependency relation was found between gender and risk, women tending more to low and mean comorbidity. Pluripathological patients – 82%. Mean baseline of Barthel index

65.6, Barthel at hospitalization 38.6, at discharge 44.6. A longer mean stay (MS) is related to a lower Barthel score at discharge ( $p<0.01$ ). Non-pluripathological patients have a higher Barthel baseline score ( $p<0.001$ ). MS 11.2 days. Non-pluripathological patients 11.7, pluripathological 11.1 ( $p=0.688$ ). 75 to 84 11.8 days, >85 10.5 days ( $p=0.247$ ). IP – 90.2%, at least one of the Beers, STOPP, START or ACOVE. Beers – 40.7%, STOPP – 64.4%; PIMs – 69.5%. START – 66.1% positive, ACOVE – 70.8%; PPOs – 79.3%. Mean number of medicines – 12.2, non-IP patients – 12.1, IP – 12 ( $p=0.907$ ). In men there is a greater probability of non-PI than PI. In patients taking medication 0-4 and +10, the risk of finding non-PIM/PIM is significant (OR 0.94, IC 0.895–1.007). In the group with 0–9 medicines the risk of non PPO/PPO is significant (OR 3.04, IC 0.24–6.50). The number of medicines consumed by patients with PIMs is higher; there are no differences between non-PPO and PPO. There is a greater probability of finding non-PIM than PIM; in men (OR 1.33, IC 1.01–1.74) for women (OR 0.60, IC 0.365–0.99). No dependency exists between gender and PPO.

**Conclusion:** Our study was carried out on advanced age patients with high comorbidity a level of dependency and pluripathologies. Neither pluripathology nor age are factors that significantly influence average hospital stay. There is considerable inappropriate prescribing, with a higher level of omission in prescribing. Medicine consumption is high, with no clear association between the number of medicines and IP, PIMs or PPOs.

## Which is the prevalence of hypertension in patients admitted in vascular surgery and trauma areas?

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**Objectives:** Episodes of poorly controlled hypertension are among the most frequent during hospitalization in the elderly. We aimed to analyze the prevalence of episodes of blood pressure levels above 140/90 between patients in the areas of Traumatology and Vascular Surgery.

**Material and methods:** Descriptive analysis of patients admitted to the Trauma Services and Vascular Surgery who had higher blood pressure than 140/90 mmHg during admission. Decompensation rate in two groups, patients with and without documented history of hypertension, is analyzed.

**Results:** From June 2008 to December 2014, 1659 cases were presented to Internal Medicine and Cardiology according to patients admitted to Trauma Services and Vascular Surgery. Of these patients, 1098 (66.2%) had a documented history of hypertension. The main problem was poorly controlled hypertension in 72 patients (4.3%), and control of vascular risk factors in patients with decompensated hypertension and some other vascular risk factor in 27 (1.6%). The total number of patients who were consulted by uncontrolled hypertension was 99 (6%). After the initial evaluation of all patients, blood pressure above 140/90 was detected in 201 (12.1%), of which only 187 were pre-hypertensive (11.3%). That means, patients known to suffer from high blood pressure were 1098, and the

number of decompensation during admission was 187 (17%). Of the patients who did not have hypertension among its antecedents (561) had high blood pressure was detected in 14 (2.5%). In 5 cases, poor control of blood pressure was the pathology responsible for the prolongation of hospital stay.

**Conclusions:** There is a significant rate of decompensation of blood pressure, about one in 8 patients (12.1%) in patients admitted to the units of Traumatology and Vascular Surgery. One in six presented hypertension known high blood pressure (17%), compared to only 2.5% of the previous non-hypertensive patients. Early assessment of blood pressure levels by Cardiology or Internal Medicine could be beneficial in terms of morbidity.

### **Are metabolically healthy obese individuals really healthy? Vascular health in relation to risk factors load in obesity**

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**Objectives:** Not all obese individuals demonstrate similar metabolic profiles. The present study was designed to investigate an association between various obesity phenotypes and vascular atherosclerotic changes.

**Methods:** The 246 study participants were divided into three groups according to presence of obesity and metabolic risk factors (MRF): group 1 included 91 non-obese metabolically healthy subjects; group 2 included 64 obese metabolically healthy subjects; group 3 consisted of 91 obese metabolically unhealthy subjects. Augmentation index (AI) was performed using SphygmoCor (version 7.1, AtCor Medical, Sydney, Australia). Results: AI differed significantly between groups, such that AI increased from group 1 to group 3 in a continuous fashion. The metabolically healthy obese subjects had significantly higher AI than non-obese metabolically healthy individuals ( $p=0.016$ ). In univariate GLM analysis, significant by group differences in AI persisted even after adjustment for age, sex and mean blood pressure. Combination of obesity and more than two MRF was associated with further deterioration in terms of AI ( $p<0.0001$ ). The strongest influence on AI was HTN (standardized beta=0.199,  $p=0.001$ ), DM (standardized beta= 0.134,  $p=0.047$ ) and hyperlipidemia (standardized beta=0.131,  $p=0.032$ ).

**Conclusions:** Metabolically healthy obese individuals show an increased arterial stiffness compared to non-obese subjects, despite a comparable MRFs. Obesity, per se, is associated with an adverse effect on blood vessels. Combination of obesity and more than two MRF is associated with further deterioration in terms of AI.

### **Low density lipoprotein subfractional distribution in patients with coronary atherosclerosis estimated by Gensini score**

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**Objective:** Plasma lipoproteins represent a heterogeneous population of particles varying in density, lipid-protein content, and size. According to size low density lipoproteins (LDL) are composed of large (LDL1), medium (LDL2) and small dense (sd) particles (LDL3-7). The aim of the study was to evaluate lipoproteins distribution in patients differing by CA severity estimated by Gensini score (GS) and to determine gender differences in their subfractional distribution.

**Material and methods:** Patients aged 33-80 with CA verified by coronary angiography were included into the study ( $n=310$ ; M/F 203/107;  $62.5\pm 9.3$  yrs). Plasma lipids and apolipoproteins (apo) AI and B were determined by routine methods. LDL particles distribution was analyzed using the Lipoprint LDL System (Quantimetrix, USA).

**Results:** Patients were split into 2 groups by GS median: A – no/minimal CA ( $GS=0-34$ ,  $n=149$ ), B – severe CA ( $GS\geq 35$ ,  $n=161$ ). No significant differences between groups A and B in total cholesterol (C) ( $5.1\pm 1.1$  vs  $5.1\pm 1.4$  mmol/l), LDL C ( $3.2\pm 1.0$  vs  $3.3\pm 1.3$  mmol/l), HDL C ( $1.0\pm 0.3$  vs  $1.0\pm 0.3$  mmol/l), TG ( $1.8\pm 0.8$  vs  $1.9\pm 1.1$  mmol/l), apo B ( $95.0\pm 24.9$  vs  $90.6\pm 27.2$  mg/dl) were found excepting higher apo AI level in group A ( $162.5\pm 29$  vs  $152.7\pm 25.8$  mg/dl,  $p=0.002$ ). Analysis of lipoprotein subfractional distribution in the whole cohort has shown that men had lower than women portion of intermediate density lipoproteins (IDL) B ( $p=0.000$ ), IDL A ( $p=0.000$ ) and large LDL1 ( $p=0.047$ ) as well as increased LDL2 ( $p=0.000$ ) and sdLDL: LDL3 ( $p=0.003$ ), LDL5 ( $p=0.025$ ). In group A, men had low portion of IDL C ( $19.9\pm 6.7$  vs  $23.1\pm 9.9\%$ ,  $p=0.01$ ), IDL B ( $13.9\pm 4.4$  vs  $17.6\pm 6.8\%$ ,  $p=0.004$ ), and IDL A ( $14.9\pm 5.3$  vs  $19.4\pm 9.3\%$ ,  $p=0.000$ ) and more atherogenic profile with elevated LDL3 portion ( $3.4\pm 3.4$  vs  $2.4\pm 4.7\%$ ,  $p=0.045$ ). In group B, men as compared to women had significantly lower portion of IDL A particles ( $15.1\pm 6.4$  vs  $20.6\pm 12.3\%$ ,  $p=0.000$ ) and large LDL1 ( $31.7\pm 12.0$  vs  $35.8\pm 19.5\%$ ,  $p=0.000$ ). At the same time, they exhibited an accumulation of sdLDL3 ( $3.7\pm 5.6$  vs  $2.3\pm 2.6\%$ ,  $p=0.000$ ) and LDL4 ( $0.5\pm 1.7$  vs  $0.2\pm 0.6\%$ ,  $p=0.000$ ).

**Conclusions:** Gender differences were identified in lipoprotein subfractional distribution depending on presence and severity of CA: among men low portion of intermediate density lipoproteins and large physiologically active particles LDL1 were determined and pronounced atherogenic shifts in subfractional lipoprotein profile associated with rise of sdLDL3-4 particles with increasing CA extent estimated by GS were observed.

### **Blood pressure variability as a criterion of efficiency of antihypertensive therapy**

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**Background:** The risk of development of cardiovascular complications in patients with arterial hypertension (AH) depends not only on the absolute level of blood pressure (BP), but also on blood pressure variability (BPV).

**Objective:** To study BPV in AH patients on the background of receiving the new drug form of Perindopril A (Servier, France) – tablets, dispersible in the mouth.

**Material and methods:** The study included 30 patients with AH.

All patients were administered perindopril A, a form soluble in the mouth, at a dose of 10 mg in monotherapy or in combination with indapamide-retard (Servier, France) in case of failure of the objective BP achieving. The total follow-up was 3 months (4 visits). Intra-visit BPV is calculated as a standard deviation (SD) of the average of 3 BP measurements at one visit. Inter-visit – as SD of mean BP for pairs of successive visits. BPV on different days – as SD of morning values minus evening values with calculation of the average figures for the week after each visit, and before the end of the study according to the data of BP self-monitoring (BPSM).

**Results:** The initial SBP/DBP was 159,6±1,5/96,5±0,8 mmHg in the average for the group in 3 months of follow-up, all patients had achieved objective BP. Intra-visit BPV for SBP and DBP at baseline was 8.4 and 4.6 mmHg and significantly decreased to 4.6 and 4.0 mmHg only to the 3rd month of treatment. Significant change of inter-visit BPV is registered between the 1st and 2nd visits for SBP and DBP (6,7±4,7 and 3,3±2,4 mmHg, respectively), and between the 2nd and 3rd visits (4,4±3,1 and 2,7±1,9 mmHg). According to the results of BPSM, beginning from the 2nd week of therapy, there was a significant decrease of BPV, measured in the morning and in the evening (1st visit – 2,1±0,4 for SBP and 1,6±0,2 for DBP; 2nd visit – 1,3±0,3 for SBP and 1,7±0,3 for DBP; 3rd visit - 1,6±0,3 for SBP and 1,3±0,2 for DBP mmHg), indicating a sustained reduction of blood pressure during the day.

**Conclusions:** Initial intra-visit BPV and its dynamics depend on the degree of AH and objective BP achieving. Effective therapy was accompanied by a significant reduction of SBP inter-visit variability with the achievement of SD level less than 4.8 mmHg that, according to the researchers, is associated with a reduced risk of death from any cause. To assess the daily BPV, fluctuations of BP measured in the morning and evening were the most revealing.

### **Peculiarities of clinical course and fundamental parameters of patients with acute myocardial infarction with ST segment elevation and hyperuricemia**

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**Objective:** To make comparison study, with scrutinizing the background, clinical order and functional condition of myocardium of patients with hyperuricemia and without it during the acute period of myocardial infarction with ST segment elevation (STEMI).

**Material and methods:** 178 patients have been studied that had STEMI. Patients were split into 2 groups. The first group consisted of 88 patients with STEMI and hyperuricemia (64 men and 24 women) mean age 77 (71; 82) years. Second group consisted of 90 patients with STEMI without hyperuricemia (39 men and 51 women), mean age 74 (67–81) years. Functional condition of the cardiovascular system was assessed with echocardiography. Comparison of the groups was done with Mann-Whitney criteria and accurate 2 parties Fishers criteria.

**Results:** In line with background results statistically significant increase of indicators of group 1 in comparison with the 2 group was marked on following levels: chronic heart failure (II–III NYHA) 35% vs 16% (p<0,01); atrial fibrillation 15% vs 9% (p<0,05); pneumonia 9% vs 1% (p<0,02); chronically renal disease 34% vs 4% (p<0,01); gout 23% vs 4% (p<0,01). Patients of the group 1 had more cases of complicated STEMI and fatal cases than in group 2 and equals 78% vs 64% and 35% vs 20% (p<0,05), consequently. In complications structure of STEMI acute left ventricular failure was indicated with frequency of 56% for the first group of patients and 29% for the second group (p<0,01). Nosocomial pneumonia in the acute period of STEMI was 22% in the group 1 and 8% for the group 2 (p<0,01). In line with echocardiography mean of left ventricular dimension in diastole for the group 1 was higher than for the 2 patient group and was equal to 5,2 (4,9–5,5) cm and 4,9 (4,6–5,5) cm (p<0,01). Patients with STEMI and hyperuricemia had more often increased left and right atrium inter zone: in 1,5 times dilation of the left atrium (p<0,01); in 1,4 times dilation of the left ventricle (LV); in 2,5 times dilation of the right ventricle (p<0,01). LV ejection fraction (EF) of both patient groups was decreased however statistically more significant that of patients with STEMI and hyperuricemia, that equaled 40 (34–50)% and 45 (40–50)% (p<0,02). Statistically significant differences in regional contractility dysfunction LV as dyskinetic, akinetic and hypokinetic were not detected in both patient groups. During estimation of regurgitation flows significant mitral regurgitation was indicated 63% vs 38% (p<0,01) for patients with STEMI and hyperuricemia.

**Conclusions:** 1) Patients with hyperuricemia had IM with complicated background with more often development of cardiovascular, lungs and kidney pathology than patients with MI but without hyperuricemia. 2) In line with statistics patents with MI and hyperuricemia in comparison with patients with MI but without hyperuricemia faced complicated duration of acute disease period, with the development of the acute left ventricular failure, pneumonia and fatal cases. 3) Patents with MI and hyperuricemia had more indicated decrease of systolic function of the left ventricle than patients with MI but without hyperuricemia. 4) In patients with MI and hyperuricemia significant mitral regurgitation was detected more often.

### **Cardiovascular complications in patients with non-small cell lung cancer in combined treatment using neoadjuvant cisplatin-based chemotherapy**

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**Objectives:** Combined treatments in lung cancer patients are accompanied by increased number of chemotherapy complications, including cardiovascular complications (35%). Cardiovascular complications are considered as leading causes of death in patients with non-small cell lung cancer (NSCLC) in combination therapies. The aim of the study – to estimate the frequency and character of cardiovascular complications in patients with NSCLC on phases combined treatment depending of type antitumor therapy.

**Material and methods:** 120 patients with NCCLC aged 50,1±8,3 years were examined. All patients underwent bronchoscopy, electrocardiography (ECG), echocardiography, ECG monitoring, radiography and computed tomography of the chest cavity. Patients with NCCLC were divided into 3 groups. The first group (n=50) before the operation was carried out 3 cycles of neoadjuvant chemotherapy (NCT) in the EP mode (80 mg/m<sup>2</sup> on the first day and etoposide 120 mg/m<sup>2</sup> on 1, 3 and 5 days). Early cardiotoxicity (24–48 hours after administration of chemotherapy) and late cardiotoxicity (after year) were evaluated. The second group (n=50) was performed by surgery treatment. In third group (n=20) of the postoperative course remote gamma-therapy at dose of 62–70 gray was held. Statistical analysis “SPSS-16.0” was used.

**Results:** There were such cardiovascular diseases as arterial hypertension (AH) (40,8%), ischemic heart disease (25%), paroxysmal atrial fibrillation (7,5%) in patients with NSCLC. The patients in the early postoperative period had acute myocardial infarction (AMI) – 8% and AMI with death (2%). Results suggested that cardiovascular complications were significantly higher after a pneumonectomy in comparison with lobectomy/bilobectomy (45% vs 16,7%; p<0.05). ST-segment depression was recorded in 16% of patients after the NHT, and in – 45% patients after radiotherapy (RT) (p <0.05). Arrhythmias (ventricular premature beats, sinus tachycardia, atrial fibrillation) were revealed in 26% of patients of the first group, in 34% of patients of the second group (in the early postoperative period), and in 55% of patients of third group. A significant decrease in ejection fraction left ventricle (LVEF) was observed only in patients of the third group after the application of radiotherapy (RT). There was not significantly evidence of NCT on LVEF.

**Conclusion:** Arrhythmias, asymptomatic disorder of repolarization on the ECG might be mediated by cisplatin-containing therapy. Reduced ejection fraction of LV, and are related to RT subendocardial ischemia.

## Acute heart failure – a descriptive study in Coltea hospital, Bucharest

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**Objectives:** Acute heart failure is a constant challenge for internists and cardiologists. Hospitalizations for exacerbations of chronic diseases are a burden on both the health care systems and the patients' quality of life, so there is great interest in understanding the underlying factors.

**Methods:** We report the clinical experience with acute heart failure cases of the Cardiology Clinic in Coltea Hospital, Bucharest. From the total number of admissions in our clinic in 2014, almost 15% were for decompensated heart failure.

**Results:** There were 189 patients, 20% of whom had multiple readmissions in the same year. There was an almost even distribution on sexes, while the median age was 76. Less than 4% of admissions were for acute pulmonary edema, the rest being decompensation of chronic heart failure (NYHA class IV). 40% of the patients had systolic dysfunction, with the main underlying etiology being ischemia. Half of the patients had valvular disease,

either mitral or aortic; worth noting is that for 20% of the subjects, the main etiology was hypertensive cardiopathy. More than half of the group had pulmonary hypertension, with only a small minority of cases being of embolic etiology or having an associated pulmonary disease. More than two thirds of the subjects had atrial fibrillation, while the prevalence of type II diabetes in the study group was 36%, most of the cases with a poor glycemic control. Half of the patients had chronic kidney disease, with 20% of them being stage 4 and associating important electrolyte disturbances. Another subgroup of patients with a poor prognosis because of the need to adjust treatment was the 10% with persistent hypotension. The average length of hospital stay was 8 days. There was only a weak correlation between the NT-proBNP value at admission and the duration of hospitalization. It is worth mentioning that by the end of the year, 10 patients of the 189, meaning 5% of the total, had died in our clinic.

## Long term clinical outcome of patients admitted to a chest pain unit in an internal medicine department: significant reduction of mortality and acute coronary events

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**Background:** Patients with chest pain still represent a great challenge for health care providers in medical institutions, mainly in internal medicine wards. Chest pain units are being incorporated in medical centers to utilize the diagnostic approach for such patients. Long term follow up of patients discharged after hospitalization with chest pain is missing.

**Objectives:** To report our 2 years experience with a chest pain unit located in our internal medicine department in a tertiary medical center, and to compare findings with those of patients who were hospitalized in the same department during the year before the chest pain unit was established.

**Methods:** We have retrospectively collected data for patients admitted to our department during the year before the establishment of the chest pain unit, and prospectively for all the patients who were admitted to the chest pain unit for consecutive 2 years. Long term follow up will be performed for all the subjects, at an average of 50 months following discharge.

**Results:** Before the establishment of the CPU, 258 patients were admitted with the main complaint of chest pain, compared to 789 patients during the first 2 years of the CPU. In hospital stay was 67±45 hours during the preCPU year compared to 27±20 hours in the CPU first 2 years (p<0.001). CCTA was performed in 7% of the subjects during the preCPU year, compared to 77.5% in the subsequent 2 years (p<0.001). Primary end points occurred in 15.9% during the preCPU year compared to 10.4% in the CPU first 2 years (p=0.017).

**Conclusions:** The application of the CPU to our internal medicine department enabled a rapid investigation for patients with chest pain, shortened the in hospital stay for patients with chest pain and significantly reduced the occurrence of primary end points.

## Mortality from acute myocardial infarction in the Aktobe region of Kazakhstan

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**Objective:** Studying of mortality following acute myocardial infarction (AMI) in the Aktobe region of Kazakhstan.

**Methods:** Sources of information for the article were the following: data of the Statistics Committee of the Ministry of National Economy of the Republic of Kazakhstan relatively persons died of AMI (ICD-I21), as well as data on the population of the region from the national Census. A retrospective study of the period between 2004–2013. Crude (CR) and ASR (age-standardized rate, world standard) mortality rates per 100,000 of the corresponding population were calculated. Average value (P), the average error (m), 95% confidence interval (95% CI), the average annual increase/decrease (T, %) has been determined. Results: 986 deaths from AMI has been reported for 2004–2013, of which 596 (60.4%) men and 390 (39.6%) women. The average age of died was 63.6±0.5 years (95% CI=62.6–64.6), and the trend has tended to increase (T=+0.4%). The average age of the death in men was 59.8±0.5 years (95% CI=58.8–60.8, T=–0.2%) and women – 69.3±0.9 years (95% CI=67.5–71.1, T=+0.9%), (p<0.05). The average CR in the general population in the region was 13.8±1.00/0000 (95% CI=11.8–15.8) and decreased in dynamics from 19.5±1.7 (2004) to 8.8±1.10/0000 in 2013 (p<0.05), (T=–8.6%). CR for men were 17.3±1.40/0000 (95% CI=14.5–20.1) and for women – 10.5±0.80/0000 (95% CI=9.0–12.0), (p<0.05). The rate of diminution amounted to T=–9.9% and T=–6.6% respectively in men and women. It was found that the average ASR for the entire population of the region was 15.0±1.10/0000 (95% CI=12.8–17.1), men – 22.9±1.90/0000 (95% CI=19.1–26.7) and women – 9.4±0.70/0000 (95% CI=8.0–10.8), and gender differences were significant (p<0.05). Trends of ASR repeated the same changes that were typical for CR. The rate of diminution in the total population amounted to – T=–8.7%, men – T=–10.2% and women – T=–6.5% respectively.

**Conclusions:** Analysis of mortality from AMI showed that rates have in dynamics a marked tendency to decrease in all studied groups. Mortality rates in the male and female population had a statistically significant difference (p<0.05). Descriptive epidemiological features of mortality from AMI serve as a basis for further analytical stage, to evaluate the risks and lost life potential.

## Cardiac carcinoid syndrome

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**Introduction:** Carcinoid tumors are a heterogeneous group of neoplasms arising from Kulchitsky cells, which are characterized by the production of biogenic amines generally located in the

gastrointestinal tract. Cardiac localization of this tumor is a rarity that is why the aim of this analysis is to describe a case report of a patient with a cardiac carcinoid syndrome.

**Case report:** 66 years old male was studied because pleural effusion, abdominal pain, weight loss and steatorrhea. The subject during his stay developed right heart failure so we requested urgent thoracic CT angiography dismissing pulmonary embolism, the echocardiography showed severe tricuspid regurgitation that made us suspected a cardiac carcinoid syndrome which was confirmed in the biopsy of bone marrow and liver metastases as a neuroendocrine tumor. Urine analysis: 5-HIA >55 mg/24h, blood analysis: gastrin 18 High (H), VIP 10.2 (H), A cromogranin >2100 (H), CA-125: 206.9 U/ml (H).

**Discussion:** Cardiac involvement occurs in 40% and metastatic liver disease due to production of vasoactive substances that most often affect the tricuspid and pulmonary valves. Cardiac involvement is associated with a worse prognosis. The echocardiography helps in the diagnosis of this disease because tricuspid affection suggests cardiac carcinoid tumor. Because of the atypical clinical presentation of this disease, it could be useful, in certain cases, to support the diagnosis with other complementary tests such as echocardiography added to laboratory analysis and anatomical pathology study.

## Evaluating the effectiveness of long-term treatment with beta-blockers in the quality of life of patients with chronic heart failure

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**Objectives:** To examine quality of life at patients with chronic heart failure (CHF).

**Methods:** 172 male patients at the age of 40 to 55 years old with CHF have been examined. All patients were divided into 3 groups by functional class (FC) CHF: 35 patients with CHF I FC, 70 patients with CHF II FC and 75 patients with CHF III FC. We examined the quality of life (QL) in patients with chronic heart failure by the Minnesota Living with Heart Failure questionnaire (MLHFQ). To assess the dynamics of the studied parameters during long-term therapy with beta-blockers, patients were divided into 2 groups: in 1st group – 83 patients who received beta-blocker – bisoprolol in the complex treatment, in 2nd group – 89 patients who received having  $\alpha$ 1blocked property beta-blocker – carvedilol.

**Results:** Baseline values QL showed that the total index in patients with CHF FC I amounted – 26.5±2.2 points, in patients with class II CHF – 39.1±3.2 and III CHF FC – 45.6±2.8 points. Baseline values of the total QL index increases with CHF FC. The results of parameter estimation for the Minnesota QL questionnaire in the surveyed patients showed that in patients treated with bisoprolol showed statistically significant reduction in the total index of QL in patients with CHF FC I 31% (p<0.01) and CHF FC II – 34.9% (p<0.001) after 6 months of treatment, respectively, compared with baseline. Long-term therapy with bisoprolol in patients with FC III CHF accompanied by a decrease



QL index by 29.7% ( $p < 0.05$ ) at 6 months compared with baseline. The results of parameter estimation for the QL in the surveyed patients showed that in patients treated with carvedilol showed statistically significant reduction in the total index of QL in patients with CHF FC I 33% ( $p < 0.01$ ) and CHF FC II – 36.8% ( $p < 0.001$ ) after 6 months of treatment, respectively, compared with baseline. Long-term therapy with carvedilol in patients with FC III CHF accompanied by a decrease QL index by 40,1% ( $p < 0.001$ ) at 6 months compared with baseline.

**Conclusion:** Long-term treatment with beta-blockers has a positive effect on the parameters of the quality of life in patients with CHF.

## Serum adiponectin and leptin levels and the main components of the metabolic syndrome

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**Objectives:** To reveal the correlations between the adipocytokine/hormones adiponectin and leptin levels and the most important metabolic syndrome (MS) components (insulin resistance (IR), arterial hypertension and dyslipidemia) parameters.

**Methods:** 115 persons included in the study were divided into two groups: the main group – 90 patients (36 men and 54 women) with MS, mean age  $50,6 \pm 7,3$  years old and the control group - 25 healthy people (11 men and 14 women), mean age –  $37,1 \pm 7,2$  years old. The anthropometrical measurements, biochemical blood tests, heart and liver ultrasonography and fasting serum insulin, adiponectin and leptin levels estimations (by the enzyme-linked immunosorbent assay) were carried out in both groups. IR index was evaluated by Homeostasis Model Assessment 2 (HOMA2) calculator (version 2.2).

**Results:** The mean adiponectin level in patients with MS was  $15,8 \pm 3,2$  that was significantly lower than in control group ( $p < 0,001$ ). The leptin level was significantly higher than in control group:  $56,9 \pm 27,5$  ng/ml ( $p < 0,001$ ). Reliable correlations between the body mass index (BMI), the waist circumference (WC), waist-to-hip ratio (WHR) and adiponectin and leptin levels were revealed in the study:  $r$  (Pearson's correlation coefficient) =  $-0,56$ ,  $p < 0,001$ ;  $r = -0,49$ ,  $p < 0,001$  (for BMI, WC, respectively) for adiponectin and  $R$  (Spearman's rank correlation coefficient) =  $0,36$ ,  $p < 0,001$ ;  $r = 0,29$ ,  $p = 0,006$  and  $r = -0,6$ ,  $p < 0,001$  (for BMI, WC and WHR, respectively) for leptin. Reliable correlations between hormones levels and systolic and diastolic blood pressure (SBP and DBP) were also founded: negative with adiponectin:  $r = -0,40$ ,  $p < 0,001$  and  $r = -0,46$ ,  $p < 0,001$  (for SBP and DBP, respectively) and positive with leptin:  $r = 0,5$ ,  $p < 0,001$  and  $r = 0,34$ ,  $p = 0,001$  (for SBP and DBP, respectively). Moreover, adipocytokine/hormone's level showed strong reliable correlation with fasting serum insulin and cholesterol level, IR-NOMA2. Adiponectin:  $r = -0,48$ ,  $p < 0,001$   $r = -0,36$ ,  $p < 0,001$   $r = -0,43$ ,  $p < 0,001$  (for insulin, IR-NOMA2 and cholesterol, respectively) and leptin:  $r = 0,59$ ,  $p < 0,001$ ;  $r = 0,65$ ,  $p < 0,001$ ;  $r = 0,23$ ,  $p = 0,04$  (for insulin, IR-NOMA2 and cholesterol, respectively).

**Conclusions:** There were revealed decreased serum adipocytokine/hormone adiponectin and increased leptin levels

in patients with MS compared to healthy people. Adiponectin and leptin levels significantly correlated with the parameters that characterize the most important components of MS.

## Correlation between C-reactive protein levels and progression of non-coronary atherosclerosis 1 year after myocardial infarction

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**Objectives:** Clinical practice requires the dynamic assessment of signs and symptoms of polyvascular disease (PVD) after acute coronary events. The further progression of PVD may indicate ineffective secondary prevention after myocardial infarction. Subclinical inflammation, assessed by biomarker levels, is considered to be an underlying pathophysiological mechanism, contributing to its progression. The aim of the study is to assess the correlation between the rate of non-coronary atherosclerosis progression and C-reactive protein (CRP) levels in patients 1 year after myocardial infarction (MI).

**Material and methods:** 168 patients with ST-segment elevation myocardial infarction (STEMI) were examined. All patients underwent coronary angiography and percutaneous coronary intervention (PCI) of the infarct-related artery. Doppler ultrasound screening of non-coronary arteries (brachiocephalic artery (BCA), the main arteries of the lower limbs) was performed at 10 days of the MI course and 1 year after MI. Levels of C-reactive protein were measured by ELISA at days 10 and 1 year after MI. All MI patients were enrolled into 4 groups according to the presence and severity of initial non-coronary stenoses: Group 1 without stenosis, Group 2 -  $< 30\%$  stenosis, Group 3 -  $30-49\%$  stenosis, Group 4 -  $\geq 50\%$  stenosis.

**Results:** Any signs of PVD were found in 95% of patients with STEMI. Non-coronary atherosclerosis progressed in the majority of patients with MI over a 1-year follow-up period. The incidence rates of the progression of BCA stenosis and lower extremity arterial stenosis increased over a 1-year follow-up period in Group 2 from 21.4 to 44%; in Group 3 from 8.3 to 22.6% and in Group 2 from 35.7 to 54.8% and in Group 3 from 13.1 to 22.6%, respectively. Significant progression of stenosis occurred in 32 (19%) patients with BCA stenosis and 42 (25%) patients with lower extremity arterial stenosis. There were no significant differences in CRP levels, measured at 10-14 days of STEMI in patients with progression of non-coronary atherosclerosis and without it. But patients with progression demonstrated significantly higher levels of CRP compared to patients without progression 1 year after MI. CRP levels in the group with progression were 8.04 (4.48; 11.60) mg/L ( $p = 0.01$ ), whereas in the group without progression - 2.40 (1.06; 3.83) mg/L. Serum CRP levels decreased by 38% ( $p = 0.04$ ) in patients with progression in comparison with initial levels, whereas a 2.5-fold reduction of CRP levels was found in patients without its progression, compared to baseline values ( $p = 0,005$ ).

**Conclusions:** The progression of BCA stenosis is associated with persistent elevated levels of CRP in the acute phase of MI. Reduction in CRP levels within 1 year and the levels of this biomarker 1 year after myocardial infarction suggest a correlation between inflammation and the progression of atherosclerosis.

## Daily rhythm of blood pressure and metabolic axes in patients with the 5th stage chronic kidney disease

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**Objective:** To establish the relation between the indicators of daily rhythm of arterial blood pressure (BP) and biochemical axes with patients undergoing the routine hemodialysis.

**Methods:** 24 hypertensive patients who undergo the routine hemodialysis in the City Hospital №6 in Izhevsk were included. The amount of men and women was equal. The average age of the patients was  $51,5 \pm 10,4$ . The procedures were implemented using the device 4008S (Fresenius, Germany) 3 times a week, 4 hours each. Estimation of electrophoretic activity of erythrocytes (EAE) was held using the set "CytoExpert" (OJSC Axion Holding, Izhevsk, 2010).

**Results:** According to the data received the daily rhythm (Dipper) was 8% with systolic blood pressure (SBP) patients and 24% of those with diastolic blood pressure (DBP). Most patients' daily rhythm type was night-peacker. Thus the night increase of SBP was marked in 68% of cases whereas DBP increased in 44% of cases. There were patients with improper decrease of night BP (non-dipper): 24% with SBP patients and 32% of those with DBP. There were no patients with excessive decrease of BP detected in our research. Most respondents in the research tend to have tachycardia (mean HR was  $78,6 \pm 9,1$  bpm). The vegetative index Credo complied with dominant parasympathetic tone with 98% of patients and dominant sympathetic tone with 12% of patients. The average value of pulse pressure is  $50,6 \pm 9,0$  mmHg. This indicator correlated with the level of parathormone ( $r=0,78$ ;  $p<0,001$ ) and phosphorus ( $r=0,63$ ;  $p<0,01$ ). A strong correlation between morning rise of SBP and DBP with the level of carbamide ( $r=-0,77$ ;  $p<0,001$  and  $r=-0,87$ ;  $p<0,001$  respectively), potassium ( $r=-0,8$ ;  $p<0,001$  and  $r=-0,8$ ;  $p<0,001$  respectively) and phosphorus ( $r=-0,7$ ;  $p<0,001$  и  $r=-0,78$ ;  $p<0,001$  respectively) was established. A strong correlation between the level of natrium in blood and the level of morning rise of SBP ( $r=0,74$ ;  $p<0,001$ ) was established. As the research results show the degree of BP night decrease clearly correlates with the indicator erythrocytes fluctuation (AREF) (SBP  $r=0,73$ ,  $p<0,001$ ; DBP  $r=0,63$ ,  $p<0,01$ ). The indicator AREF is also related to HR ( $r=-0,64$ ,  $p<0,01$ ).

**Conclusions:** Thus daily rhythm types night-peakers and non-dippers dominate with AH patients undergoing the routine hemodialysis. The pharmacotherapy for AH patients must combine metabolic values correction with reducing BP and HR. The degree of BP decrease at night is related with the indicator ERE.

## Acute coronary syndrome without obstructive coronary atherosclerosis in clinical practice

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**Objectives:** Acute coronary syndrome (ACS) may develop not only due to atherothrombosis. There are cases with the typical clinical picture of heart attacks and with normal or near-normal coronary arteries (CA) (stenosis  $<50\%$ ) shown by the coronary angiography (CAG). According to various studies, frequency of myocardial infarction in these cases ranges from 5 to 25%.

**Material and methods:** 821 patients (aged 29 to 82 years, average age  $60,6 \pm 21,4$ ) with ACS (myocardial infarction – AMI or unstable angina - UA) admitted to City Clinical Hospital EK Eramishantseva in the period from February to December 2014 were assessed. All the patients underwent CAG within 24 hours after admission.

**Results:** 78 (9,5%) patients had normal CA. Muscle bridges were found in 3 patients with UA, 1 patient was with dissection of coronary artery with thrombosis leading to AMI with ST-segment elevation. 2 patients have experienced local spasm of the coronary arteries during CAG. 72 patients had either unchanged CA or insignificant stenosis of the CA (up to 30%). 59 patients had a clinical picture of UA, 19 (10 men aged 29-75 years, 9 women aged 35-82 years) – AMI (12 - AMI with ST-segment elevation, 6 - AMI without ST-segment elevation).

**Conclusions:** ACS may develop in individuals with normal or near-normal coronary arteries. The reasons for this phenomenon may be different. Coronary angiography in these patients can help to identify the exact cause of ACS and to determine the optimal treatment.

## Brain natriuretic peptide as a prognostic factor in patients with sepsis in the absence of heart failure

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**Objectives:** Sepsis is a clinical syndrome characterized by systemic inflammation due to infection. Fever or hypothermia, leukocytosis or leukopenia, tachypnea, and tachycardia are the cardinal signs of the systemic response, and define the systemic inflammatory response syndrome (SIRS), which may have an infectious or a noninfectious etiology. Current theories about the onset and progression of sepsis and SIRS focus on dysregulation of the inflammatory response, including the hypothesis that a massive and uncontrolled release of proinflammatory mediators initiates a chain of events that lead to widespread tissue injury. This response can lead to multiple organ dysfunction syndrome (MODS), which is the cause of the high mortality associated with these conditions. B-type natriuretic peptide (BNP) is a neurohormone that has been

isolated first in the porcine brain and later in human ventricular cardiomyocytes. BNP and N-terminal pro-BNP are used for the early diagnosis of heart failure (HF) in patients presenting to the emergency room with dyspnea. Recently, elevated BNP levels have been measured in patients with septic shock and have been attributed to myocardial dysfunction due to sepsis. Because BNP synthesis is also induced by endotoxin and inflammatory mediators, the mechanisms leading to elevated BNP levels in patients with sepsis remain unclear. Little information is available concerning N-terminal pro-BNP levels in patients with critical illness, especially with sepsis.

**Methods:** We prospectively studied 259 patients with sepsis in the absence of heart failure. BNP levels were obtained for all patients. The relationship between BNP and clinical outcomes was tested using multivariable analysis models.

**Results:** 82 patients died during the 90-day follow-up (31.7%), 53 died in the current hospitalization (20.5%) and 80 patients were readmitted (30.9%). Bivariable logistic regression analysis of demographic data, risk factors and laboratory tests; a statistically significant correlation was found between BNP mortality and morbidity. On multivariate analysis models, elevated values of BNP remained a strong predictor of mortality and morbidity for 90 days in patients with sepsis.

**Conclusion:** We have shown in a population of hospitalized patients with sepsis that BNP is a strong independent predictor of greater morbidity and mortality.

## Reduced bone mineral density as additional marker of cardiovascular remodeling in postmenopausal women

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**Objective:** To assess the correlation between structure-geometrical cardiac remodeling, pulse wave velocity (PWV), results of 24-hours monitoring of blood pressure (BMP) and bone mineral density (BMD) in patients with essential arterial hypertension (EH).

**Methods:** We examined 156 women with confirmed diagnosis of EH stages I-II. The control group included 52 age-matched healthy volunteers-women. All participants underwent echocardiography, BMP. Arterial stiffness was measured by brachial-ankle PWV using an automated device. BMD was estimated by dual-energy X-ray absorptiometry using T-criterion. Statistical analysis was done with Statistica 6.0 (StatSoft, USA).

**Results:** In postmenopausal hypertension women reduced BMD was associated with adverse concentric remodeling variant - increased myocardial mass index and relative left ventricular wall thickness ( $r=-0.49$ ,  $p=0.001$  and  $r=-0.58$ ,  $p=0.0001$ , respectively). Women with low BMD had circadian rhythm of diastolic BMP non-dipper. Women with osteoporosis had more severe arteriosclerotic changes detected by significantly higher PWV measurement than those with normal BMD ( $p<0.01$ ). In regression analysis the decrease BMD was associated with PWV elevation ( $r=-0.33$ ,  $p<0.01$ ). It reflects that arterial stiffness assessed by PWV measurement it closely connected with BMD. Positive correlation between PWV

and age, systolic blood pressure, diastolic blood pressure ( $r=0.42$ ,  $0.36$ ,  $0.29$ ,  $p<0.05$ , respectively) confirms that arterial stiffness is dependent on age and blood pressure.

**Conclusions:** Decrease of BMD is a marker of unfavorable variants of myocardial remodeling associated with increase arterial stiffness as a prognostic marker of an adverse current in postmenopausal women with EH. Including BMD measurement into EH diagnostic algorithm provides additional benefits for assessment of individual total cardiovascular risk in postmenopausal women. Comprehensive studies of patients with normal blood pressure and osteopenic syndrome provide early diagnostics of cardiovascular remodeling and secondary prevention of osteoporosis. Investigation of BMD gives a chance to clear up cardiovascular risks and individualize diagnostic and curative approaches to patients with EH and osteoporosis.

## Comorbidity as a risk factor in coronary artery bypass grafting

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**Objective:** To study occurrence frequency of comorbid pathology and EuroSCORE II at patients during coronary artery bypass grafting, to reveal an association.

**Materials and methods:** The study included 119 patients, operated in a planned way due to CHD in the Altai State Hospital. Coronary artery bypass grafting was performed according to indications under extracorporeal circulation. All the patients underwent a complete clinical and instrumental examination in view of the Guidelines on myocardial revascularization (2011). The average age of the patients was 61 years (from 37 to 79), 66.1% were male, 33.9% – female. In the anamnesis 72 (61%) patients underwent myocardial infarction. LV ejection fraction  $<50\%$  was recorded in 45 (38.1%) patients. Comorbidity index was assessed by M.E. Charlson et al. (1987) in the modification of R.A. Deyo et al. (1992). The risk of operative mortality was assessed using European System for Cardiac Operative Risk Evaluation II (2011).

**Results:** 319 diseases diagnosed at 119 patients, 2.7 per patient (1.5–3.8) diseases, in addition to the main (IHD). The absence of concomitant diseases was observed only in 5.9% of patients. More than third of patients (34.7% of cases) have more than 3 diseases. The most common comorbidities were arterial hypertension, discirculatory encephalopathy – at 81.3% of patients, CKD (CKD-EPI) – at 77.1%, diseases of the digestive system – at 66.1%, respiratory diseases – at 57.6% of patients. At the same time, patients admitted to cardiac surgery treatment Charlson comorbidity index was on average  $4.6\pm 0.8$  points. A positive correlation between EuroSCORE index and duration of in-hospital postoperative period (the duration of mechanical ventilation, stay in the ICU and the number of hospital-days after surgery) ( $r=0.68-0.76$ ) revealed. The correlation between the Charlson index and index EuroSCORE is strong ( $r=0.76$ ).

**Conclusions:** Comorbidity at CABG is characterized by a high risk of unfavorable prognosis (survival  $<21\%$  in the next 10 years). The presence of a significant frequency of comorbid diseases determines the high associated operational risk which should be considered at the stage of preoperative preparation and requires further examination and compulsory drug correction.

## Comorbidity at patients with chronic heart failure: correlation between etiologic factors, structural and functional features

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**Objective:** Studying etiological factors and structural and functional features of the cardiovascular system at chronic heart failure (CHF) patients in conjunction with the comorbidity.

**Material and methods:** Conducted in-depth clinical observations at 97 patients with CHF. There were 54 men (55.7%) and 43 women (44.3%). The average age of men was 63.9±11.8; women – 67.5±12.7 years ( $p<0.05$ ). Comorbidity index was assessed by M.E. Charlson et al. (1987) in the modification R.A. Deyo et al. (1992).

**Results:** Among the main etiological factors of CHF at analyzed patients were registered arterial hypertension – at 73.2% (of them women was 65.1%,  $p<0.05$ ), ischemic heart disease (IHD) – at 51.5% (including men – 72.2%  $p<0.05$ ). Every second (48%) patients were diagnosed combination of hypertension and IHD. At 14.4% of patients etiological cause was COPD, at 8.2% – diabetes, other causes were <5%. CHF FC: I FC – at 16.0%, II FC – 52.1%, III FC – 26.2, IV FC – at 5.7%  $p$ -ts. The average score by SHOKS was 5.7±1.2 among men; women – 4.3±1.1 ( $p<0.05$ ). Among CHF women prevailed diastolic dysfunction (DD), mostly I type (slow relaxation),  $E/A=0.89$  [0.79–0.92],  $E/e'=16.8$  [11.8–18.4], LV ejection fraction – 62.7±5.4%. Among men - systolic dysfunction, with an average LVEF – 53.2±4.2%. Diastolic dysfunction was characterized by increasing the number of patients with the second and third type of transmitral flow  $E/A=1.69$  [1.32–2.01],  $E/e'=18.6$  [13.8–19.4], which required determination of NT-proBNP 339.6±32.5 pg/ml. The average number of comorbidities was 7.3±2.3. Low comorbidity index (1–2) was at 2.9%, medium (3–4) – at 21.3%, the highest (≥5) – at 75.8%. 78.3% of the patients had at least one concomitant disease. The most frequently was diagnosed CKD (by CKD-EPI) (44% vs 37%,  $p<0.05$ ), anemia (34% vs 28%;  $p<0.05$ ), hypothyroidism (13% vs 8%,  $p>0.05$ ).

**Conclusion:** The etiological causes of CHF have a gender component and are characterized by a significant detection AH at women in the presence of preserved ejection fraction, diastolic dysfunction of I type and increasing the number of comorbidities (7.9) and men was prevailed IHD as etiologic cause of CHF with presence of systolic dysfunction and smaller number of comorbidities (6.8), which should be considered in the conduct of CHF patients.

## Suppression of intimal hyperplasia by mesenchymal stem cells in carotid balloon angioplasty

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**Objectives:** One of the major causes of the intimal hyperplasia following arterial bypass and balloon angioplasty is restenosis. The

aim of this study is to analyze the inhibitory effect of mesenchymal stem cells in animal model of carotid balloon angioplasty.

**Material and methods:** Under the general anesthesia, the rabbit carotid artery was dissected and balloon angioplasty was performed using 2F Fogarty embolectomy catheter. The balloon angioplasty carotid artery was coated with a mixture of 7x10<sup>6</sup> human cord blood mesenchymal stem cells and fibrin matrix. 2, 4 and 8 weeks after surgery, the carotid artery was harvested and immunofluorescent staining and quantitative real time-PCR were performed.

**Results:** The intimal/media ratio was reduced in the stem cell treated group compare to the non-treated group ( $p<0.05$ ). The area of re-endothelialization was significantly higher ( $p<0.05$ ) in the stem treated group than in the non-treated group. Expression of angiogenic genes such as VEGF, PDGF, KDR, Ang-1, and AAMP was increased ( $p<0.05$ ) in the stem cell treated group relative to the non-treated group.

**Conclusions:** Our study showed that human cord blood mesenchymal stem cells reduce the formation of intimal hyperplasia through the rapid re-endothelialization. This result might be applied to develop stem cell-coated stents, as well as to develop stem cell-contained sheet coat for inhibition of intimal hyperplasia after angioplasty or surgery.

## Application of the unified questionnaire for cerebrovascular disease detection in patients with arterial hypertension in outpatient clinic environment

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**Introduction:** Cerebrovascular disease (CVD) presents a significant burden in Russia. Epidemiologic prospective studies have shown high prevalence of chronic CVD and its association with an increased risk of transient ischemic attack and stroke. Objectives: To estimate the efficiency of the new unified questionnaire for CVD detection in patients with arterial hypertension in outpatient clinic environment.

**Methods:** The study included 257 patients with arterial hypertension (stages I-III) who visited internist in the Moscow outpatient clinic by any reason. Patients were interviewed using the unified questionnaire for detection of clinical forms of CVD: chronic brain blood supply insufficiency syndrome, hypertensive encephalopathy, hypertensive crises, transient ischemic attack, stroke, and other vascular diseases. Preliminary results were verified by neurologist and cardiologist. ECG-exercise test, 24-hour Holter monitoring, duplex ultrasound scan of carotid arteries, computer tomography, magnetic resonance brain imaging were performed if necessary.

**Results:** According to validated results of screening 57,6% of patients with hypertension had CVD. Newly diagnosed CVD was revealed in 52 (20,2%) patients: 48 (92,3%) of them had chronic forms of CVD – chronic brain blood supply insufficiency syndrome and hypertensive encephalopathy, 4 (7,7%) had hypertensive crises, transient ischemic attack and stroke. 29,6% of patients with hypertension had history of hypertensive crises.

**Conclusions:** The new unified questionnaire enables diagnostics of CVD in patients with arterial hypertension in outpatient clinic environment with high efficiency. It was shown that internists do not pay sufficient attention to chronic insufficiency of brain blood supply, hypertensive encephalopathy and hypertensive crisis symptoms. The questionnaire allows to reveal CVD forms at the early stages of disease and to start active preventive measures in due time.

## Prodromal symptoms and ECG criteria of sudden coronary death development among cardiological patients

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**Objectives:** 1) To evaluate prodromes and ECG criteria of the sudden coronary death (SCD) development among cardiological patients at a pre-hospital stage within a 5-year period. 2) To increase prognosis alert of initial stage doctors while discovering persons with a possible risk of SCD development and to realize the possibilities of its prevention.

**Methods:** While analyzing the reasons of sudden death EMT physicians used anamnesis, ailment clinical data, and ECG data. 266 patients with IHD were studied at a pre-hospital stage: 123 cases of SCD (basic group) and 143 cases (comparison group) with other reasons of a sudden death, of not acute – coronary genesis. The development of SCD was connected with myocardium electrical non-stability instantly happening at acute manifestation of IHD (23.3%) or within 6-12 hours from the beginning of the fatal angina pectoris (76.7%).

**Results:** In the basic group there were 81 men and 42 women. The age of 45-69 years was the factor of cardiogenetic threat with men, and 60-79 years with women. A maximum death-rate was observed at age groups of 75-79 years. Often, 2-3 days before SCD development, 55 of 123 persons had prodromal symptoms – predictors which made them to turn to polyclinic physicians. To these factors we related psycho-emotional stresses (18 cases – 32.8%), physical strain (14 cases – 25.5%), thorax pain (10 cases – 18.2%), tachycardia (8 cases – 14.5%), headache (3 cases – 5.4%), use of alcohol and sleep disturbance (1 and 1 case respectively – 3.6%). Men prevailed among victims of sudden death (twice as many as women). With men, the ventricular fibrillation (73%) was observed more often than asystole (27%), with women the relation was reversing (40% and 60%). The most threatening markers of SCD risks were the ventricular arrhythmia (54%) and scintillating arrhythmia (10%); as far as asystole is concerned – intracardiac (12%) and atrioventricular blockades (9%). The ventricular fibrillation was more often observed during the first 6 hours from the beginning of the acute myocardial infarction especially on the background of its markers. The development of the asystole was observed at a protracted heart attack (more than 6 hours), often together with the occurrences of the acute coronary deficiency, more often on the background of the cardiac asthma and pulmonary edema.

**Conclusions:** While rendering first-aid to IHD patients with the symptoms of angina destabilization (increase of the frequency of attacks, negative ECG dynamics, development of arrhythmia, worsening of heart failure) at the pre-hospital stage it is recommended urgently to provide anaesthetization, use of antiarrhythmic drugs and emergency hospitalization in the intensive care unit.

## Chronic thromboembolic pulmonary hypertension associated with thrombophilia: more than meets the eye

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**Objective:** To study the frequency of thrombophilia in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

**Methods:** We examined 36 patients with different degree of pulmonary hypertension (PH) by echocardiography: 20 people (55.6%) with the first degree (SPAP 30–50 mmHg), 9 people (25%) with the second degree (SPAP 51–80 mmHg), 7 people (19.4%) with the third degree (SPAP over 80 mmHg). Blood was testing for the presence of a lupus anticoagulant (LA), antibodies (Ab) to cardiolipin classes IgM and IgG, Ab to  $\beta$ 2 glycoprotein-1 (Ab to  $\beta$ 2GP1).

**Results:** In 16 of the 36 patients revealed a high titer of anticardiolipin Ab/LA/Ab to  $\beta$ 2GP1. In 7 patients of the main group (4 men and 3 women) was diagnosed antiphospholipid syndrome (APS). The feature of APS in patients with CTEPH was the primary character APS (71.4%), whereas secondary APS detected only in 28.6%. Patients with identified high titer of Ab to phospholipids in most cases, there had been multiple lesions in both lungs, recurrent PE.

**Conclusions:** Increase in titer anticardiolipin Ab/LA/Ab to  $\beta$ 2GP1 detected in 44.4% of patients and the comparison of clinical markers APS and increase resistance of specified Ab allowed to diagnose APS in 19.4% of cases. In 33.3% of cases there were associated forms of thrombophilia in patients with CTEPH, which helped to explain the recurrent nature of venous thrombosis/thromboembolism in this subgroup of patients. The obtained data can be the basis of the strategy of patients with CTEPH, forming groups of risk of recurrent venous thrombosis and CTEPH.

## Hemorrhagic complications in patients with acute coronary syndrome of different age groups

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**Objectives:** The risk of hemorrhagic complications in elderly patients present with acute coronary syndrome has always

been considered a subjective risk factor to perform primary percutaneous coronary intervention (PCI) by clinical cardiologists. The aim of the study – to assess and compare the incidence of bleedings in patients of different age groups undergoing primary percutaneous coronary intervention.

**Material and methods:** 110 medical records of patients with acute myocardial infarction (mean age 61,8±10,5 years), who were admitted in the hospital for the period 1, January 2012 to 31, December, 2012 and have undergone primary infarct-related artery PCI, were retrospectively reviewed. All the patients were assigned to two groups according to their age: Group 1 <70 years and Group 2 ≥70 years.

**Results:** ACS patients, who have undergone PCI, demonstrated a 5% incidence of bleedings. Thus, there were no evidence to confirm a tendency of elderly ACS patients after PCI towards higher incidence of bleedings and transfusions. Importantly, elderly ACS patients had higher initial disease severity. The treatment therapy did not differ significantly in both groups.

**Conclusions:** The incidence of hemorrhagic complications was insignificantly higher in elderly patients with acute coronary syndrome undergoing primary percutaneous coronary intervention, compared to younger patients. However, incidence of hemorrhagic complications should not cause unjustified refusal of percutaneous coronary intervention in these patients.

## STEMI issues in the elderly

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**Objective:** To evaluate clinical features, in-hospital outcomes and hemorrhagic complications in elderly patients with STEMI.

**Material and methods:** 356 patients (mean age 61.8±10.5 years) admitted with acute myocardial infarction in 2012 were retrospectively reviewed. All the MI patients underwent successfully primary percutaneous coronary intervention (PCI) of the infarct-related artery (IRA) within 12 hours. All the patients were assigned to two groups according to age: Group 1 – <70 years and Group 2 – ≥70 years. Clinical features, in-hospital outcomes and hemorrhagic complications were the point of our interest.

**Results:** The elderly group present renal dysfunction more often (53.8% vs 19.8%, p=0.0000) such as myocardial dysfunction (23.1% vs 6.8%, p=0.0000), hypertension (97.4% vs 83.8%, p=0.0018) and postinfarction atherosclerosis (19.2% vs 10.4%, p=0.0376). There was less number of current tobacco smokers (10.3% vs 34.5%, p=0.0000), more often presented acute heart failure (32% vs 14%, p=0.0003), were more likely to in-hospital mortality (9% vs 1.4%, p=0.0007). The elderly also had hemorrhages more often (5.1% vs 0.7%, p=0.0077). Patients over 70 years had higher Syntax score. Elderly patients were more commonly scheduled to coronary artery bypass grafting as the second stage of revascularization compared to patients in Group 1 (38.7% vs. 16.7%, p=0.148). However, the second stage of routine revascularization was significantly rarely performed in elderly patients (39%) than in patients <70 years (81%) (p=0.0002). The primary reason for failure to perform the second

stage of revascularization, regardless of its type, was unjustified refusal of the patient.

**Conclusions:** The elderly patients present more severe condition in STEMI, more likely to hemorrhages and in-hospital mortality. The primary reason for failure to perform the staged revascularization after myocardial infarction in elderly patients was unjustified refusal of the patient.

## Clinical and laboratory predictors of poor outcomes in patients with pulmonary embolism of high and intermediate risk

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**Objectives:** Despite on advances in diagnosis and treatment, pulmonary embolism (PE) remains a major cause of mortality and morbidity in Europe. Assessment of prognostic value of different clinical and laboratory characteristics is in progress.

**Methods:** 70 patients (28 men, 42 women, mean age 66,2±1,8 y.o.) with confirmed by CT PE of high and intermediate risk were divided into 2 groups with complicated (need for resuscitation, obstructive shock, recurrent PE or death) or uncomplicated course of PE during 6 months follow-up period. On admission anamnesis, signs of obstructive shock, PESI scale, troponin T, heart type fatty acid binding protein (hFABP), brain natriuretic peptide (BNP), ECHO-signs of right ventricle (RV) dysfunction were evaluated.

**Results:** 44 patients (62,8%) had uncomplicated course of PE, while 26 patients (37,2%) had different complications. Signs of shock/hypotension on admission were presented in 15 patients (21.4%), in 23 (32.8%) thrombolysis (TL) were performed. Age, gender, body mass index, pre-existed chronic heart failure, previous stroke, episodes of venous thromboembolism (VTE), arterial hypertension, angina pectoris, chronic lung diseases, smoking, level of occlusion of pulmonary artery (PA), frequency of TL had no significant negative impact on clinical course of PE. Complications developed more often in patients with previous myocardial infarction (MI) (34,6% vs 9,1%, p=0.02, OR 5,29 CI 95% 1.43-19.57), atrial fibrillation (AF) (38,5% vs 9,1%, p=0,01, OR 6.25 CI 95% 1.71-22.85), permanent risk factors of VTE (96.2% vs 70.5%, p=0,02, OR 10.5 CI 95% 1.3-85.7). Absence of DVT signs was found more frequently in patients with complicated course (56% vs 31%, p=0.02, OR 2.84 CI 95% 1.02-7.92). In patients with poor outcome the rate of shock/hypotension were higher, than with favorable (38.5% vs 11.4%, p=0.01, OR 4.88 CI 95% 1.44-16.53). hFABP test was positive in 76,9% patients with poor outcome, compared to 45.4% in patients with favorable outcome (p=0.01, OR 4.0 CI 95% 1.35-11.88). Levels of troponin T, D-dimer and BNP, examined ECHO-parameters (RV and right atrium diameters, RV/LV index, systolic blood pressure in PA, hypokinesis of RV free wall, shift of intraventricular septum and LV ejection fraction) did not differ significantly between groups. Conclusion: Risk factors of poor outcome in patients with high and intermediate risk PE are: previous MI, AF, permanent VTE risk factors, absence of DVT signs and positive hFABP test.

## Left ventricle non-compaction myocardium and thrombophilia in pregnant woman. The clinical case

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**Introduction:** Non-compaction of ventricular myocardium (NCM) is an all-age patients' genetic cardiomyopathy, most common due to mutation of gene 4.5 localized in Xq28 chromosome. This congenital disorder characterized by pronounced trabeculations and intertrabecular recesses in result of abnormal embryogenesis between fetal 5th and 8th week. Reported prevalence is between 0.014 and 1.3% in the general population. The classical triad of complications includes heart failure, ventricular arrhythmias and systemic embolic events. Some patients have asymptomatic form. LVNC is commonly diagnosed by echocardiography, but also contrast ventriculography, CT and MRI can be used. Here we present the case of left ventricle NCM, manifested after respiratory infection, in 26 years old pregnant patient with congenital thrombophilia and history of myocardial infarction.

**Case report:** Signs of heart failure (shortness of breath, edema) and episodes of unsustainable ventricular tachycardia (VT) manifested after respiratory infection in result of reduction of ejection fraction (EF) to 26% in 2009. The patient has family history of sudden death (father). Double-advancing pregnancy ended in miscarriage in the period of 6-8 weeks. Antiphospholipid syndrome wasn't revealed. In 2010 the patient had myocardial infarction localized in LV inferior wall and RV, complicated by thrombus in right cavities. Intact coronary arteries were found in angiography. Embolic genesis of myocardial infarction was suspected. According to genetic testing hereditary thrombophilia was revealed, and at the same time – an increased sensitivity to warfarin, that was administered. ECHO- and MRI were performed and non-compaction myocardium of LV was diagnosed. On the background of therapy with ACE inhibitors, beta-blockers, diuretics, digoxin and warfarin condition has stabilized - signs of heart failure and VT regressed, EF was growing up to 46%. In 2014 she got pregnant despite of high risk of poor outcome for her and fetus. During pregnancy period she was observed in the hospital because of increasing symptoms of heart failure (progressing edema, shortness of breath). From the 9th week of pregnancy fraxiparine 0.6 mg twice a day subcutaneously with a control of the X factor was administered. There were no significant deviations in laboratory findings. At gestation 30-31st weeks ejection fraction decreased to 22-25%, episodes of unstable ventricular tachycardia and severe dyspnea were presented. According to worsening condition a caesarean section was performed. The alive baby was born. After operation against the background of therapy her condition improved despite of low EF (23%). Due to high risk of life-threatening arrhythmias cardioverter-defibrillator (ICD) was implanted.

**Discussion:** This case demonstrates that we achieved stabilization and improvement of pregnant patient's condition and favorable

outcome of pregnancy in patient with two hereditary disorders. This case shows, that physicians shouldn't underestimate the long-term complications, especially constantly progressing heart failure and cardiac arrhythmias. But despite of high risk of poor outcome in population, we should avoid routinely recommending to young female patients to refuse pregnancy.

## Risk factors of long-term complications after myocardial infarction

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**Objective:** Long-term complications of myocardial infarction (MI) may develop months and years after MI occurrence. Currently applied risk scales (GRACE, TIMI) have some shortcomings and not effective enough in prediction of those complications.

**Material and methods:** 457 STEMI patients successfully discharged from the hospital were enrolled (mean age 59,7±0,5 y.o.). 37 lethal cases (8,1%) and 47 recurrent MI (10%) occurred, in 66 patients (14,4%) severe heart failure (NYHA III-IV class) developed during 28,8±0,8 months follow-up period. 72 different characteristics have been examined as possible risk factors of long-term complications.

**Results:** Risk factors of all-cause mortality was age ≥60 y.o. (RR 2,94 95% CI 1,5-5,76), BMI <25 kg/m<sup>2</sup> (RR 2,14 95% CI 1,13-4,06), history of previous MI (RR 2,75 95% CI 1,31-5,76), cerebrovascular disease (CVD) (RR 2,55 95% CI 1,31-4,93), anemia (RR 5,09 95% CI 2,59-10,01), anterior MI (RR 2,23 95% CI 1,18-4,23), admission ≥6 hours after MI onset (RR 2,18 95% CI 1,19-3,99), HR at admission ≥90 bpm (RR 2,62 95% CI 1,44-4,77), systolic BP at admission <120 or >140 mmHg (RR 1,66 95% CI 0,89-3,15), signs of acute HF during admission (RR 3,03 95% CI 1,68-5,49), GFR <45 mL/min/1,73m<sup>2</sup> (RR 3,38 95% CI 1,82-6,26), WBC count >15x10<sup>9</sup>/l (RR 2,17 95% CI 1,13-4,18), BNP at admission ≥60 pg/ml (RR 5,08 95% CI 0,67-38,76), LVEF at admission <45% (RR 2,08 95% CI 1,12-3,85), LV end diastolic volume >140 ml (RR 2,06 95% CI 1,06-4,0), presence of LV aneurysm (RR 1,95 95% CI 1,07-3,58), overage HR by Holter monitoring ≥70 bpm (RR 3,18 95% CI 1,14-8,87), ventricular extrasystoles ≥50 per day (RR 3,18 95% CI 1,14-8,87), absence of primary PCI (RR 2,04 95% CI 1,04-3,99) or reperfusion (RR 2,5 95% CI 1,34-4,69), discontinuation of beta-blockers (RR 3,66 95% CI 1,79-7,49) or statins (RR 4,11 95% CI 2,29-7,38) during or after hospitalization. Recurrent MI more often happened in case of age 60-69 y.o. (RR 1,95 95% CI 1,14-3,33), history of previous CHD (RR 2,19 95% CI 1,26-3,8), GI diseases (RR 1,78 95% CI 1,04-3,04) and anterior MI localization (RR 1,78 95% CI 1,04-3,05). Risk factors of severe HF occurrence were: age ≥60 y.o. (RR 2,29 95% CI 1,44-3,66), non-smoking (RR 1,96 (1,24-3,1), 95% CI), history of kidney diseases (RR 2,46 95% CI 1,51-4,01) and CVD (RR 1,97 95% CI 1,18-3,29), anterior MI localization (RR 1,7 95% CI 1,09-2,67), signs of acute HF at early stages of MI (RR 2,54 95% CI 1,65-3,91).

**Conclusion:** According to the results a model predicting poor long-term outcomes may be elaborated.

## Heart type fatty acids binding protein as an early marker of myocardial necrosis: results of two Russian studies

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**Objectives:** Early diagnosis improves outcomes of acute coronary syndrome (ACS). Traditional markers of myocardial necrosis are not effective enough in early period of ACS. Heart type fatty acid binding protein (hFABP) is a novel and perspective biomarker of myocardial necrosis, showed its efficacy for diagnosis of MI in a number of small studies. 2 trials were organized by RSMSIM to evaluate the efficacy of qualitative measurement of hFABP for differential diagnosis of ACS.

**Material and methods:** In multicenter non-commercial investigation of clinical efficacy of early diagnosis of myocardial infarction with cardiac protein, binding fatty acids (GIANT) were enrolled 1049 patients admitted in 24 hospitals of 17 Russian cities. In another study 759 patients were enrolled by 88 ambulance crews of Moscow city station of emergency and first medical aid named after A.S. Puchkov. All the patients had suspected ACS and duration of presentation 1-12 hours. The concentration of hFABP in whole venous blood was evaluated with qualitative immunochromatographic test «CardioFABP» (Biotest, Russia). The level of troponin I was assessed with the qualitative test Troponin I WB-Check-1 (VEDALAB, France).

**Results:** Sensitivity of hFABP compared with troponin I test in GIANT was significantly higher (73.8% vs 46.7%). The specificity of the hFABP test was 92% vs 97.2% for troponin I. Accuracy of the hFABP test corresponded to 79.3%, troponin I – 62.2%. Positive predictive value (PPV) of hFABP test was 0.95, troponin test – 0.97, negative predictive value (NPV) – 0.61 and 0.45, correspondingly. Sensitivity of hFABP test reached a peak in the time interval 3-6 hours from onset of MI. In all intervals the sensitivity of hFABP test surpassed troponin test on 18-32%. In different types of ECG changes the sensitivity hFABP test was higher than troponin I on 19-73%. In ambulance trial sensitivity of CardioFABP test was 88%, specificity – 92%, accuracy – 87%, PPV – 99%, NPV – 57%. In patients with ST-segment elevation on initial ECG (n=503) sensitivity of the test was 89%, specificity – 65%, accuracy – 89%, PPV – 99%, NPV – 18%. In patients without ST-segment elevation (n=237) sensitivity of hFABP test was 86%, specificity – 82%, accuracy – 84%, PPV – 88%, NPV – 80%.

**Conclusions:** 2 trials showed high efficacy of qualitative evaluation of hFABP in diagnosis of ACS, especially in early period. The test can be recommended for more wide usage in both hospital and out-hospital practice.

## Rigidity of blood vessels in hypertensive middle-aged women

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**Objective:** To explore the relationship between changes in the level of estradiol, follicle-stimulating hormone (FSH), the process of structural adjustment of cardiovascular system in women of a late reproductive age.

**Material and methods:** 64 women with arterial hypertension (AH), not taking antihypertensive therapy. Depending on the level of estradiol and FSH, patients with AH were divided into several groups. Group 1 - 34 women with AH, 39.1±4.3 years, with physiological menstrual cycle and estrogen deficiency. Group 2 - 30 female with AH, 39.1±2.2 years, having physiological menstrual cycle and normal levels of estradiol and FSH. A control group - 20 healthy women without AH, 38.5±4.1 years with normal levels of estradiol and FSH. Duplex scanning of common carotid arteries (CCA) was performed to assess the state of the vascular bed in all female patients included in the study.

**Results:** Comparative analysis of the diameter of the CCA in the study compared to the control group showed dilatation of the average diameter of CCA, with a greater degree in patients with AH and estrogen deficiency. Blood flow velocity in CCA in patients of groups 1 and 2 is lower in comparison to the patients of the control group, primarily among patients with AH and hypoestrogenism. Resistance index was higher in patients with AH from group 1 than in patients of the control and group 2. Elastic properties of the CCA wall were decreased: from 41.3±10.8x10<sup>-3</sup>/kPa in patients with AH and normal levels of estradiol down to 36.4±10.8x10<sup>-3</sup>/kPa, p=0.034 in patients with AH and decreased levels of estradiol. At the same stiffness index was higher in comparison with the control group in patients having AH with estrogen deficiency and without it.

**Conclusions:** The obtained data clearly shows a decrease in elasticity of the wall of CCA and increasing of its stiffness in patients with AH more pronounced in patients with AH accompanying with decreased levels of estradiol and increase of FSH. Duplex scanning of the CCA in women with AH demonstrates dilatation of CCA lumen, decreased blood flow on the background of estrogen deficiency. This indicates more significant changes to the vascular wall in hypertensive patients compared to hypertensive patients having normal levels of estradiol.

## Blood urea nitrogen as a prognosis predictor in patients hospitalized with acute decompensated heart failure

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**Objectives:** Acute decompensated heart failure (ADHF) is the leading cause of hospital admissions in elderly patients. Identifying risk factors associated with increased morbidity and mortality may improve treatment and clinical outcomes. In patients with ADHF, decreased cardiac output causes renal hypoperfusion with consequent reduction in the glomerular filtration and increased reabsorption of salt and fluid, leading to a decrease in excretion of urea, and increased blood urea nitrogen (BUN). Few studies have investigated the effects of increasing BUN levels and its correlation to the prognosis in ADHF. Therefore, we aim to investigate the impact of BUN on



mortality and readmissions in patients with ADHF, the role of changes in BUN values during hospitalization and its correlation to morbidity and mortality after discharge.

**Methods:** Between January 2008 and April 2011, patients admitted to Rambam Medical Center, Haifa, Israel with the primary diagnosis of ADHF entered a prospective registry. We tested the effect of demographic data and various laboratory parameters on morbidity and 90 days mortality using bivariable logistic regression analysis among 542 patients. Patients were divided into 4 groups corresponding to the BUN value as following: BUN <20, between 20-29, 30-39 and  $\geq 40$  mg/dL.

**Results:** 124 patients (23%) had a BUN level below 20 mg/dL on admission, of those, 6.5% died during hospitalization or during the following month after discharge, for the 2nd, 3rd and 4th groups, it was 19.6%, 24.7%, 26.7%, respectively ( $p < 0.05$ ). The 90 days mortality in patients who were admitted with BUN <20 mg/dL was 10.5%, whereas, in the 2nd, 3rd and 4th groups it reached 20.3%, 22.7%, 33.1% respectively ( $p < 0.05$ ). 90 days mortality was 9.9% ( $p < 0.05$ ) in patients that were admitted and discharged with normal BUN, whereas, it was highest among those who had high BUN levels on both admission and discharge, 15.6% ( $p = 0.002$ ). Hyponatremia (serum sodium <130 mEq/l), higher BNP and increased red cell distribution width (RDW) were also correlated with higher 90 days mortality rate. AUC ROC of BUN, BNP and creatinine were 0.644, 0.622 and 0.577 respectively.

**Conclusions:** BUN values on admission represent a stronger prognostic factor than creatinine in patients with ADHF. BNP level is an independent prognostic factor. RDW, hyponatremia and BUN represent independent prognostic factors and combining these parameters increases the 90 days mortality.

### Infective endocarditis in intravenous drug users: cardiorenal relationships

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**Objective:** To study the extent of cardiac damage and extracardiac manifestations of infective endocarditis (IE) in intravenous drug users.

**Methods:** The study included 55 patients with IE (Duke criteria, 2009) [34 (61,8%) male, mean age  $42,3 \pm 14,5$  years]. Patients were divided into 2 groups: intravenous drug users [28 (51%), Group 1] and non-users [27 (49%), Group 2]. Medical history, types of IE, laboratory (GFR (CKD-EPI), CRP, RF, NT-pro-BNP) and echocardiographic parameters, class of heart failure (HF, NYHA), acute kidney injury (AKI, Increased SCr to  $\geq 1,5$  baseline), clinical features, severity of proteinuria, microscopic hematuria, total mortality were evaluated and analyzed.

**Results:** While no gender differences were present, mean age was lower in drug users than the comparison group ( $33,7 \pm 7,3$  vs.  $54,6 \pm 15,6$  respectively,  $p < 0,05$ ). Left-sided IE was more frequent in group 2 [7 (25%) vs. 25 (92,6%),  $p < 0,05$ ]; accordingly, less patients in this group had right-sided IE [21 (75%) vs. 2 (7,4%),  $p < 0,05$ ]. Prosthetic valve-IE was more frequent in group 2 [2 (7,1%) vs. 4 (14,9%),  $p < 0,05$ ]. Left ventricular ejection fraction was comparable

in both groups ( $60,7 \pm 14,5$  vs.  $58,9 \pm 6,4\%$ ,  $p > 0,05$ ). Patients in group 2 had more severe heart failure symptoms (NYHA III-IV) [6 (21,4%) vs. 16 (60%),  $p < 0,05$ ], which was associated with higher NT-proBNP values ( $421,2 \pm 10,9$  vs.  $1672 \pm 53,2$  pg/ml,  $p < 0,05$ ). The values of C-reactive protein ( $232,9 \pm 45,5$  vs.  $105,7 \pm 63,7$  mg/l,  $p < 0,05$ ) and rheumatoid factor ( $74,4 \pm 43,7$  vs.  $43,8 \pm 45,8$  U/ml,  $p < 0,05$ ) were significantly higher in Group 1. Mean GFR (glomerular filtration rate) was  $86,4 \pm 35,5$  ml/min in group I, whereas in Group 2 it was  $58,7 \pm 30,6$  ml/min ( $p < 0,05$ ). Groups did not differ by the incidence of proteinuria (78,6% vs. 80%) and hematuria (46,4% vs. 37%). AKI (Acute kidney injury) was more frequent in non-users [10 (35,7%) vs. 16 (59,3%),  $p < 0,05$ ]. More patients in Group 1 had septic pulmonary emboli [20 (71,4%) vs. 7 (25,9%),  $p < 0,05$ ]. Mortality was higher among non-users, but the difference was not statistically significant [4 (14,3%) vs. 7 (25,9%),  $p > 0,05$ ].

**Conclusions:** Intravenous drug users present with IE at a younger age, have a higher frequency of right-sided disease, septic pulmonary embolism and more active systemic inflammation compared with non-users. They also have on average milder heart failure symptoms and better kidney function.

### Functional condition of the endothelium in patients with arterial hypertension in the conditions of high mountains

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**Objective:** The role of nitrogen oxide (NO) in the development of endothelium dysfunction in patients having AH of various degrees of severity living in the high-mountain region of Elbrus (2200-3500 m.a.s.l.) was being studied.

**Methods:** 140 people were examined, of which 60 were healthy and 80 suffered from AH of various degrees: 45 patients with 2nd degree AH and 35 – 3rd degree AH, average age  $53,4 \pm 2,3$  years. All have undergone general clinic examination, digital electrocardiography, echocardiography, patients with AH - US of kidneys, thyroid, and eye ground surveying. Metabolites NO – nitrites NO<sub>2</sub> and nitrates NO<sub>3</sub> were being detected in blood plasma and erythrocytes spectrophotometrically.

**Results:** All patients with AH have showed decrease in NO<sub>2</sub> and NO<sub>3</sub> in blood components, most evident in patients with 2nd and 3rd degree AH (in plasma by 48% and 68%, ( $p < 0,01$ ), in erythrocytes by 16% and 58%, ( $p < 0,01$ )).

**Conclusion:** Thus, all groups of patients with AH have showed endothelium dysfunction, which was most evident among patients with 3rd degree AH of long-term disease (more than 10 years).

### Cardiovascular involvement in a Behçet disease

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**Objectives:** Behçet disease (BD) is a relapsing vasculitis that can affect vessels of any type and size. Recurrent oral and genital ulceration, pustules and uveitis are the main features. Among the others BD features, cardiac involvement are rare (6%) whereas vascular ones are more common. However, the disease phenotype seems to differ according to ethnic group. Our study aims to evaluate the cardiovascular involvement frequency in BD Tunisian patients and to analyze their clinical characteristics and outcomes.

**Methods:** Retrospective single center study that included a total of 97 BD patients (1997-2014). The diagnosis was based on the international study group for BD criteria.

**Results:** Cardiovascular involvement was observed in 36 patients (37,1%). There was 36 male and 2 female. The mean age at the onset was 40±10 years old. 31 patients expressed vascular events (venous thrombosis: n=23, arterial lesion: n=7, both: n=1). It revealed the disease in 8 cases (8,2%). Lower extremities deep vein thrombosis was noted in 22 patients. It was isolated or associated to other venous lesion including: superficial venous thrombosis (n=2), inferior vena cava (n=3), superior vena cava (n=5) and pulmonary artery (n=3). The most common arterial lesion was aneurysm (n=8) mainly in pulmonary artery (n=5). An aortic aneurysm occurred in 2 cases. An arterial thrombosis was noticed in 3 cases and it was associated to aneurysms. Cardiac involvement occurred in 7 (7,2%) patients (coronary disease: n=3, intracardiac thrombus: n=2, myocarditis: n=1 and pericarditis: n=1). 4 patients died of pulmonary aneurysm rupture in 3 cases despite immunosuppressive treatment. Comparison between BD patients with and without cardiovascular involvement showed a negative association with ocular-Behçet.

**Conclusions:** In our study, the BD cardiovascular involvement frequency was as high as showed by previous Tunisian study. It affects young men without any cardiovascular risk factor. Lower extremities deep veins thrombosis is the major vascular event whereas pulmonary aneurysms have still life threatening.

## Myocarditis as the mean feature of eosinophilic granulomatosis with polyangiitis

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**Introduction:** Eosinophilic granulomatosis with polyangiitis (EGPA), formerly Churg-Strauss syndrome, is a rare systemic small vessel vasculitis related to antineutrophil cytoplasmic antibodies (ANCA). Recent insights showed different clinical patterns according to the ANCA profile: ANCA negative patients (60 to 70%) had a higher cardiac involvement frequency and lower vasculitis symptoms. Symptomatic cardiac involvement occurs in 27 to 47% of EGPA cases and account for a poor prognostic factor.

**Case reports:** We report 2 cases of congestive heart failure due to myocarditis revealing ANCA negative EGPA. Case N°1: A 52

years old woman with a one year history of asthma was admitted for right heart failure concomitant to a hemorrhagic bulla. The electrocardiogram showed anteroseptal and inferior Q waves. Transthoracic echocardiography revealed a systolic left ventricular function at 25% with apical wall hypokinesia and an intraventricular thrombus. Elevated troponin and NT-proBNP were noted. Blood count showed hyper eosinophilia (4900/mm<sup>3</sup>). Coronary angiography was normal. Cardiac MRI confirmed ventricular dysfunction and wall motion abnormalities with intraventricular thrombus. Skin biopsy showed leukocytoclastic vasculitis with eosinophilic infiltrate. ANCA were negative. EGPA was so diagnosed. Intravenous corticosteroid treatment associated with 6 pulses of cyclophosphamide was started. The cardiac function has been stabilized for 18 months. Neither the less, she died from a severe congestive heart failure. Case N°2: A 44 years old woman with a long history of asthma complained about polyarthralgia, fever, paresthesia and rash. On physical examination, right heart failure associated with purpura was noted. Electrocardiogram showed sinus tachycardia and diffuse negative T waves. Laboratory examinations revealed leukocytosis with eosinophilia (15900/mm<sup>3</sup>), elevated troponin and negative ANCA. Transthoracic echocardiography indicated a left ventricular systolic dysfunction without wall motion abnormalities. Electromyography revealed multiple mononeuropathy. CT scan showed interstitial lung disease. EGPA was diagnosed. The patient received intravenous corticosteroids and 4 pulses of cyclophosphamide. She is still symptoms free.

**Discussion:** Negative ANCA-EGPA diagnosis may be challenging and mimic others eosinophilic disorders, in particular if cardiac involvement are the main feature. Myocarditis occurrence in an asthmatic patient who develops eosinophilia should suggest EGPA diagnosis and start specific treatment. In fact, as highlighted by the five factor score, cardiac symptoms are an independent predictor of death in EGPA patients.

## Gender features of chronic heart failure

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**Objective:** To evaluate gender-specific etiology, clinical presentation and treatment of chronic heart failure (CHF).

**Methods:** 200 hospitalized patients with CHF (100 men and 100 women) were included in a retrospective cross-sectional study conducted in Chita Regional Clinical Hospital. Statistical criteria such as Mann-Whitney, chi-square and Fisher's exact tests were used.

**Results:** Women with CHF were older than men (61,9±9,8 vs 58,1±12,8 years, p=0.019), had higher heart rate at admission (83±16,9 vs 77,1±15,3 beats per minute, p=0.005) and lower glomerular filtration rate calculated by Cockcroft-Gault (77,2±29,9 vs 91,5±30,9 ml/min, p<0.001). Coronary heart disease was the main reason of CHF, in men it was more common than in women (77% vs 63%, p=0.045). The frequency of hypertension (20% vs 30%), chronic rheumatic heart disease (2% vs 5%) was the same. Clinical manifestations of heart failure according to the sex have not been identified. Women more often demonstrated class 3

NYHA (46% vs 29% of men,  $p=0.019$ ). The prevalence of heart failure class 2 NYHA was high regardless of gender (56% men and 48% women,  $p=0.322$ ). The prevalence of left ventricular diastolic dysfunction was independent of sex (57% of men and 62% of women). Ejection fraction (EF) of the left ventricle in women was somewhat higher than in men ( $65,2\pm 10,4\%$  vs  $61,5\pm 9,8\%$ ,  $p=0.010$ ), while the number of patients with a reduced EF was similar in men (12%) and female (8%). Pulmonary hypertension was found in 60% of men and 43% of women,  $p=0.024$ . In men and women equally often were used  $\beta$ -blockers (82% and 83%), antiplatelet agents (78% and 80%), ACE inhibitors (23% and 22%), ARBs (35% and 41%), aldosterone antagonists (19% and 28%), cardiac glycosides (5% and 7%); while in women diuretics more often were prescribed (51% vs 32% of men,  $p=0.010$ ).

**Conclusions:** Clinical features of chronic heart failure is higher age of female patients, more frequent in women formation of functional class 3 disease, more prevalent in women cohort of diabetes mellitus and lower – pulmonary hypertension. Differences in treatment depending on gender practically not observed, and the attention is drawn to the incomplete line therapy to current clinical guidelines for chronic heart failure, necessitating ongoing optimization of therapeutic measures.

## Anemic syndrome among chronic heart failure patients

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**Objective:** To evaluate the prevalence and impact of anemia on chronic heart failure course in primary care setting.

**Methods:** 282 (86F/196M) consecutive outpatients (age 67 (62-73) years, range 39-85 years) with clinically stable chronic heart failure (CHF) NYHA class II-IV due to ischemic heart disease and arterial hypertension, mean left ventricular ejection fraction 45% (34-55) represented the study group. All patients had clinical, laboratorial evaluation, ECG, EchoCG. Patients were categorized according to the presence of anemia, as defined by the World Health Organization criteria (hemoglobin level  $<13\text{g/dL}$  in male and  $<12\text{g/dL}$  in women). Mediana of follow-up was 1 (0,5-4) year. Results: Anemia is commonly seen in patients with heart failure (18,8%) and in the elderly patients (20,2%). The prevalence of anemia was the same among female (9,2%) and male (11%); and among patients with systolic dysfunction (19,3%) and preserved function of left ventricular (18,5%). 36,9% patients had iron deficiency anemia, 6,5% – vitamin B<sub>12</sub> deficiency anemia, 10,9% – folic acid deficiency anemia, 45,6% - had no cause identified and was regarded to have «anemia of chronic disease». In all patients anemia was mild (Hb  $>9\text{g/dL}$ , range 10,5-12,9 g/dL) and associated with increasing age, heart failure duration ( $r=-0,18$ ,  $p=0,007$ ), diabetes mellitus ( $r=0,14$ ,  $p=0,036$ ), and higher hospitalizations rate ( $r=-0,18$ ,  $p=0,006$ ) due to heart failure worsening. Anemia was becoming more frequent with increasing severity of concomitant renal dysfunction ( $r=0,23$ ,  $p=0,024$ ).

**Conclusions:** For adequate management of heart failure outpatients and decreasing hospitalization rate requires regular

medical supervision and performance of blood tests for early recognition of anemia. This is especially true for elderly patients and for those who have long term duration of CHF complicated diabetes mellitus and renal impairment.

## Osteopenic syndrome in chronic heart failure

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**Objective:** To assess the prevalence of osteopenic syndrome among chronic heart failure (CHF) patients.

**Material and methods:** We examined 70 out-patients (30 M, 40 F, aged 56-88 years) with CHF and 40 out-patients without CHF (10 M, 30 F, aged 57-88 years). Examination included laboratory assessment, echocardiography, bone mineral density (BMD) in the lumbar spine and femoral neck assessment using dual-energy X-ray absorptiometry.

**Results:** Osteoporosis was recorded in 61,4%, osteopenia – in 20%, normal BMD – in 18,6% CHF patients. Osteoporosis was recorded in 32,4%, osteopenia – in 42,5%, normal BMD – in 25% non CHF patients. A total of 24,3% patients with CHF and 7,5% patients without CHF experienced hip fractures during follow up of  $26,5\pm 11,3$  months. The significant correlation was established between osteoporosis and patient's age ( $r=0,36$ ,  $p=0,002$ ), CHF duration ( $r=0,26$ ,  $p=0,039$ ), falls ( $r=0,29$ ,  $p=0,015$ ), fractures ( $r=0,42$ ,  $p<0,001$ ), chronic kidney disease, CKD ( $r=0,24$ ,  $p=0,048$ ), NT-proBNP ( $r=0,52$ ,  $p=0,007$ ), GFR ( $r=-0,37$ ,  $p=0,010$ ). Osteoporosis was associated with CKD ( $p=0,032$ , OR 3,1, 95% CI 1,1-8,8), NT-proBNP ( $p=0,043$ , OR 9,8, 95% CI 1,1-8,9) and falls ( $p=0,019$ , OR 4,0, 95% CI 1,3-12,7).

**Conclusions:** The results suggest that the low BMD is a marker of the CHF severity, and patients with CHF are in a high risk of osteoporosis and fractures incidence.

## Prevalence of metabolic syndrome and its components in urban and rural population of Central Kazakhstan

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**Objective:** To estimate the prevalence of the metabolic syndrome (MS) and its components among residents of urban and rural population in the Karaganda region, Kazakhstan.

**Methods:** Cross-sectional study includes 1453 residents: urban people (Saran city,  $n=672$ ) and rural population (Osakarovsky district,  $n=781$ ) of Karaganda region (men - 25.6%, women - 74.4%). Inclusion criteria: men and women aged from 18 to 65 with informed consent. Exclusion criteria: pregnant women, persons with mental and severe neurological diseases. MS was established according to the basis criteria of the International Diabetes Federation (2009). In addition, we evaluated the prevalence

of individual components of the MS such as obesity, arterial hypertension (AH), hypercholesterolemia and hyperglycemia. Results: MS was diagnosed in 24.2% (n=401) of residents, with no significant difference in the incidence of MS, depending on the region where they live (city – 25.8%, district – 22.7%). MS equally common in women (18.4%) and men (20.1%). MS in the age group from 18-24 years was not revealed, 25-44 – 5.9%, 45-59 – 25.2%, 60-65 – in 40.4%. Obesity among urban residents was observed in 33.4% (95% CI: 27.2; 39.7), rural – at 28.7% (95% CI: 27.2; 39.7); ( $\chi^2=4.02$ ,  $df=1$ ,  $p<0.001$ ), the differences are particularly pronounced in the age group 60 to 65 years (52.2% of residents and 33.6% - rural,  $p<0.001$ ). Established prevalence of hypercholesterolemia among urban residents (46.2%, 95% CI: 40.3; 52.1) significantly ( $\chi^2=2.1$ ,  $df=1$ ,  $p<0.001$ ) higher than frequency of hypercholesterolemia in the rural population (36.9%, 95% CI: 31.2; 42.7). AH was ranged within a wide limits from 40.9% among urban women to 24% – among men in rural areas. Statistically significant prevalence of hypertension found among urban residents ( $\chi^2=7.66$ ,  $df=1$ ,  $p<0.001$ ). Hyperglycemia in urban residents detected in 14.9% (95% CI: 7.49; 22.3) of cases, rural – 12.4% (95% CI: 5.64; 19.2) with no statistically significant differences depending on the accommodation ( $\chi^2=1.9683$ ,  $df=1$ ,  $p<0.001$ ).

**Conclusion:** High incidence of MS and prevalence of MS components such as obesity, hypercholesterolemia and AH was noted among urban population in Central Kazakhstan.

## Red cell distribution width in infective endocarditis

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**Objective:** We aimed to evaluate clinical significance, mean values and possible associations of red cell distribution width (RDW) with other laboratory variables in infective endocarditis (IE).

**Methods:** Consecutive patients hospitalized with IE according to the modified Duke criteria [n=125; 77 (61.6%) male, mean age 52±20 years old] were retrospectively included. RDW readings on admission and at discharge were analyzed in comparison to other inflammation markers. Pearson product-moment correlation coefficient was used to establish correlations. ROC-curve analysis was used to identify cut-off points for RDW values. Odds ratios (OR) were calculated with the use of logistic regression, with and without adjustment for other prognostic variables (age, gender, leukocyte count, presence of anemia).

Results: On admission mean RDW values were 15±2.02%, and 56 (44.8%) patients had abnormal RDW. A large number of participants [32 (25.6%)] died in hospital. Patients in the highest quartile of C-reactive protein (CRP) values had significantly higher RDW than those in the lowest quartile (15,6±1,9 vs. 14,4±1,8%,  $p=0,012$ ) as did those in the highest erythrocyte sedimentation rate (ESR) quartile (16±2,1 vs. 14,5±2,1%,  $p=0,005$ ). Conversely, RDW values were significantly lower in patients in the highest hemoglobin quartile (14,6±1,8 vs. 15,6±2,1%,  $p=0,042$ ). Accordingly, positive correlations of RDW with CRP and ESR

( $\rho=0,238$ ,  $p=0,008$  and  $\rho=0,251$ ,  $p=0,006$ , respectively) were noted as well as a negative correlation with hemoglobin values ( $\rho=-0,215$ ,  $p=0,016$ ). During the hospitalization RDW increased by more than 1% in 43 (34%) patients and decreased by more than 1% in 12 (9,6%) patients. The change in RDW did not significantly correlate with changes in other laboratory measures. The cut-off admission RDW value of 14,6% had sensitivity of 71,9% and specificity of 51,6% for predicting in-hospital mortality: OR= 2,73; 95% confidence interval (CI) 1,14-6,51;  $p=0,024$ . After adjustment for risk factors high RDW lost its statistical significance: OR=2,35; 95% CI 0,92-6,03;  $p=0,07$ .

**Conclusions:** Higher RDW values correlated positively with measures of inflammation and disease activity in hospitalized IE patients. Patients with high RDW on admission had a significantly higher in-hospital mortality, although after adjustment for other variables this relationship was attenuated. Thus, the prognostic significance of this biomarker deserves further investigation.

## Pharmacoepidemiology of arterial hypertension in Russia (PIFAGOR IV study)

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**Objective:** A new stage of pharmacoepidemiological study of arterial hypertension (AH) in Russia (PIFAGOR IV) to assess the structure and frequency of different antihypertensive drugs (AD) classes use in clinical practice.

**Methods:** A prospective multicenter study based on hypertensive patients survey with a specially designed questionnaire (February-July 2013). 2533 valid questionnaire from 52 cities of Russia were analyzed. Mean age 59.2 years (16–92 years), 30% men, 68% women. 69% of patients had AH history more than 5 years. 90% had AH risk factors and complications.

**Results:** 80% of patients regularly take AD; 32.8% of patients received monotherapy (vs 26% in 2008), 38.6% – combination of 2 ADs, 28.4% - combination of 3 or more ADs (37% in 2008). Mean number of ADs per patient was 2.02 (vs 2,22 in 2008). Total ADs number – 80. The structure of ADs was presented by 5 main classes: ACE inhibitors (ACEI) – share 27.8% (vs 33.2% in 2008), beta-blockers – 21.7%, diuretics – 15.7%, calcium antagonists (CA) – 11.3% and angiotensin receptor antagonists (ARA) – 10.7% (vs 3.1% in 2008), fixed combinations – 10.8% (vs 7.2% in 2008). Additional classes: centrally acting drugs (2.3%), alpha-blockers (0.1%). Among ACEI major part was enalapril – 33.6% (vs 44.7% in 2008), perindopril – 16% (vs 10% in 2008), fixed combinations 19.6% (vs 12% in 2008). In b-blockers the leading part were bisoprolol – 64.4% (vs 41.3% in 2008) and metoprolol (short and long-acting forms) – 21.4%. Among diuretics the leading drug was indapamid in short and long-acting form (total share 75%). The major part of CA was amlodipine (55.8%); short-acting form of nifedipine decreased from 21.3% in 2008 to 4.3%. Among ARA the largest share was losartan (55.4%). 66% of centrally acting drugs was moxonidine. The share of original AD was 38.3%. Mean blood pressure (BP) in patients was 140.4/86.4 mmHg (vs 137.2/85.1 mmHg in 2008;

$p < 0.0001$ ), 50.2% reached target BP (vs 69% in 2008;  $p < 0.0001$ ). High adherence (Morisky-Green test) was observed in 32% of patients, poor – in 49%.

**Conclusions:** Patients mostly use AD with proven effectiveness; the part of fixed combinations increased. However, reducing in effectiveness of treatment and poor patients' adherence were shown.

## Electrophysiological treatment methods influence on some ventricle asynchronicity indices

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**Objective:** The aim of this work is to study the effect of installation of permanent single chamber right ventricular pacemakers (PM) (VVI) and carrying out of cardiac resynchronization therapy (CRT) on the ventricle asynchronicity indices in patients with chronic heart failure (CHF).

**Material and methods:** The research included 40 patients with CHF class II-IV (NYHA) that were under observation in the Rhythm Disturbance Department of the Republic Clinical Hospital №4 (Saransk city) after implanting them the VVI (Group 1, 22 patients) and getting the CRT (Group 2, 18 patients). Echocardiogram data dynamic was analyzed that covered periods of 2 weeks and 6 months before and after the permanent single chamber PM installation and CRT.

**Results:** Normal values of the ejection fraction (EF) of  $58,0 \pm 3,4\%$  (by Simpson) were registered only in Group 1 with the CHF II class (NYHA). Among the patients with CHF III FC in Group 1 and CHF III-IV FC in Group 2 progressing reduction of the EF from  $(42,47 \pm 2,1)$  to  $(32,9 \pm 2,5)$  respectively was registered. Study of the left ventricle (LV) remodeling indices (EF/Myocardial stress (MS) and MS/LV final systolic volume (FSV) showed their reliable reduction among all the patients, especially in Group 2 with CHF IV FC ( $0,139 \pm 0,016$  and  $2,65 \pm 0,2$  respectively). Implanting of the PM and the CRT affected the myocardial contractility of the LV differently. According Echocardiogram data in the 1st group no authentic change happened: in 2 weeks after the PM implantation with CHF II FC the LV EF got to  $61,7 \pm 4,1\%$ , and with the III FC it got to  $47,6 \pm 3,2\%$ . In the CRT group the EF increase was observed already within the first 2 weeks. That related to the patients with III FC where LV EF got up to  $49,1 \pm 2,1$ , and with IV FC where it went up to  $41,6 \pm 3,5\%$ . In 6 months the LV EF in Group 1 did not change reliably, whereas in Group 2 it increased by 8,7% on average. LV remodeling indices (EF/MS, MS/FSV) increased due to the CHF; the indices are strongly correlated to the FC CHF ( $p < 0,01$ ).

**Conclusions:** Therefore electrophysiological treatment methods affect the ventricle asynchronicity indices in different ways. The single chamber PM implantation did not change functional LV work indicators significantly during the first 6 months after the surgery. On the contrary the CRT among the patients with CHF III-IV FC led to the myocardial contractility and mechanical asynchronicity indicators improvement, which makes the treatment of the patients with severe CHF very perspective.

## Levels of lipids at the first visit of dyslipidemic patients in outpatient lipid clinic of the University hospital. Correlation of these values with total cardiovascular risk

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**Objectives:** Dyslipidemia is a public health problem, due to its high prevalence and its relation with high cardiovascular morbidity and mortality. The aim of the study is to screen the patients who visit for the first time the outpatient Lipid Center in AHEPA University Hospital of Thessaloniki for a period of one year and to assess their level of total serum cholesterol, HDL, LDL and triglycerides, and to correlate dyslipidemia with total cardiovascular risk of each patient.

**Methods:** Cross-sectional study that estimates the cardiovascular risk according to Framingham General Cardiovascular Disease Risk Prediction using lipids including the modifiable risk factors like hypertension, cigarette smoking, obesity, diabetes and the non-modifiable as age, sex and family history of premature coronary heart disease. It also evaluates the major causes of secondary dyslipidemia like hypothyroidism, nephrotic syndrome, chronic renal failure, obstructive liver disease and drugs induced dyslipidemia such as progestins, anabolic steroids, corticosteroids, protease inhibitors for treatment of HIV, thiazide diuretics, b-blockers, estrogens, cyclosporine.

**Results:** We studied 111 individuals, predominantly women (55,9%). Participants were aged  $\geq 18$  years with average age of 55.5 years. They were mostly overweight with average BMI  $27,7 \text{ kg/m}^2$  and smokers (31,5%). According to the patients personal history 51,4% were hypertensive, 9% had type 2 diabetes, 7,2% had coronary artery disease while 6,3% had undergone a stroke. Secondary forms of dyslipidemia were due to hypothyroidism 20,7% and chronic renal failure 1,8%. 23,4% of participants had bright liver confirmed with ultrasound examination method. The cardiovascular risk score was very high (average of 11,2%). From laboratory exams they present mean high values of total cholesterol 266 mg/dl, high LDL 174 mg/dl, high HDL 50 mg/dl and borderline high triglycerides 258,6 mg/dl. There is a statistical significant positive correlation ( $r=0.54$ ,  $p < 0.05$ ) between BMI and CVD Risk and a statistical significant positive correlation ( $r=0.50$ ,  $p < 0.05$ ) between triglycerides levels and CVD Risk. Also it was found a statistical significant negative correlation ( $r=-0.52$ ,  $p < 0.05$ ) between HDL and CVD Risk. Finally, there is no statistical significant ( $p > 0.05$ ) correlation between LDL and CVD as well as between CHOL and CVD.

**Conclusions:** Greek population is detected to present poorly cholesterol education and subsequently high cardiovascular risk despite the recommendations for the primary prevention of CVD which mainly include low carbohydrate and fat diet, physical activity and smoke cessation. So, Greek patients appear with low percentages of compliance to these guidelines. It is also remarkable the high percentage of secondary forms of dyslipidemia.

## An early assessment, does it diminish the number of episodes of cardiac decompensation in patients with hip fracture?

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**Objectives:** The proximal femoral fracture or hip fracture represents one of the major health problems of the elderly population. Lead to an increase in morbidity, mortality, functional impairment, costs and increases the degree of dependency and institutionalization of these patients a year of the fracture. The occurrence of medical complications during hospitalization is also very high. Episodes of heart failure are among the most frequent complications. We aimed to analyze the prevalence of episodes of cardiac decompensation among patients admitted for hip fracture and a history of heart failure based on whether they were monitored by Internal Medicine or Cardiology before decompensation.

**Material and methods:** A descriptive analysis of patients admitted for hip fracture in the Traumatology and Orthopedic Unit that had a history of heart failure decompensation and performed an episode during hospitalization. Those patients who had a previous monitoring by Internal Medicine and Cardiology, with those cases were Internal Medicine and Cardiology were asked for dyspnea or edema, with the final diagnosis of decompensated heart failure: two groups were compared.

**Results:** From June 2008 to December 2014 a total of 990 patients admitted for hip fracture were presented to Internal Medicine and Cardiology. Of these patients, 79 (7.9%) had a documented history of heart failure. 34.1% (27 patients) developed heart failure during admission, of which 44.4% (12 patients) were in prior to the episode monitoring and 55.6% (16 patients) developed in the acute phase.

**Conclusions:** There is a slight decrease in the prevalence of cardiac decompensation in patients admitted for hip fracture and a history of heart failure if a previous follow up is performed by Internal Medicine and Cardiology.

## The influence of metabolic syndrome on the quality of life in patients with acute myocardial infarction with ST segment elevation

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**Objective:** The aim of this study is to determine the association between metabolic syndrome (MetS) and health related quality of life (HRQoL) in patients with myocardial infarction with ST segment elevation (STEMI).

**Methods:** The study group consisted of 559 consecutive STEMI patients treated with primary percutaneous coronary intervention

(pPCI) in Clinical Center of Serbia. A 36-month follow up was conducted among all the patients. At the end of the study, after 36 months, the data were collected for 507 patients. Short form-36 was used to assess HRQoL. AHA/NHLBI (American Heart Association and National Heart, Lung and Blood Institute) criteria were used for diagnosing the patients with MetS.

**Results:** 217(42.8%) patients fulfilled the criteria for MetS; whereas 290 patients composed the group without MeS. The presence of MetS significantly influenced the appearance of new myocardial infarction ( $p=0.004$ ), new unexpected revascularization ( $p=0.002$ ), the occurrence of symptoms for congestive heart failure ( $p=0.028$ ) as well as the increased number of hospitalizations due to heart failure ( $p=0.05$ ). The increased number of cardiovascular death cases, strokes and surgical revascularizations was detected in the group of patients with MetS; however, there was no statistically significant difference in relation to the group of patients without MetS. Multivariate logistic regression analysis of MetS with controls for age, sex and smoking shows that MetS was associated with poor quality of life (physical functioning  $p=0,001$ , OR 2,68; role physical  $p=0,001$ , OR 2,12; bodily pain  $p=0,005$ ; OR 2,56; general health  $p=0,001$  OR 2,52; vitality  $p=0,002$  OR 1,99; social functioning  $p=0,005$  OR 2,00; role emotional  $p=0,014$  OR 1,77; mental health  $p=0,016$  OR 2,14). The presence of MetS significantly affected physical component score ( $p=0,001$  OR 2,52) but it did not have any influence on mental component score ( $p=0,414$  OR 1,20).

**Conclusion:** These results suggest that the presence of metabolic syndrome among patients with STEMI significantly affected quality of life.

## Clinical implications of autoimmune diseases in acute coronary syndrome

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**Objective:** The aim of the study is to assess the prevalence of autoimmune disease (AID) in patients with acute coronary syndrome (ACS), the management and prognostic implications. Methods: The study included consecutive patients admitted after ACS from January 2011 to May 2014. For AID patients, in-hospital management and ACS presentation was compared to non-AID patients. We also compared in-hospital and 1-year major adverse events (MACE): death, recurrent myocardial infarction, stroke and major bleeding, between groups. The percentage lost to follow-up was <1%.

**Results:** Of 964 patients, 53 had AID (5.5%): 11 rheumatoid arthritis, 9 inflammatory bowel disease, 7 ankylosing spondylitis, 7 psoriatic arthritis, 5 polymyalgia rheumatica, 4 systemic lupus erythematosus and 10 miscellaneous. Mean duration of the disease was  $14\pm 3$  years. No significant differences were found in clinical and demographics characteristics between groups except for a higher percentage of previous stable coronary heart disease in non-AID patients. Compared to non-AID patients, AID patients had similar clinical ACS presentation and no differences

were found with respect to revascularization strategies or medical treatment at discharge. Overall there were 207 MACE (69% during hospitalization): 108 deaths, 52 recurrent myocardial infarctions, 19 ischemic strokes and 28 major bleedings. The two groups had comparable rates of MACE both during hospitalization (9.6% vs 12.2 %,  $p=0.58$ ) and at 1 year (26.4% vs 19.1%,  $p=0.19$ ), AID vs non-AID respectively. The presence of AID was not associated with increased in-hospital mortality (OR 1.1, 95% CI 0.4 to 3.3) but it was a risk factor for higher 1-year crude mortality (OR 2.2, 95% CI 1.1 to 4.4). However after multivariable adjusting, this association was not longer significant (OR 1.7, 95% CI 0.8 to 3.9). **Conclusions:** The presence of AID did not change ACS presentation and clinical management. Moreover it is not independently associated with worse outcomes both during hospitalization and during follow-up.

## Thromboembolic events in left ventricular non-compaction

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**Introduction:** Left ventricular non-compaction is a rare congenital condition characterized by excessively prominent trabecular meshwork. It comprises depressed ventricular function, systemic embolism and ventricular arrhythmia.

**Case report:** A 45 years old woman. Alcoholism (>100 g/day) and smoking. Past history of ischemic stroke, no sequelae, 5 years before. Identified dilated cardiomyopathy with severe left ventricle dysfunction. Viral markers for HIV, HBV and HCV – negative. ECG: sinus rhythm. Cardiac catheterization: no culprit lesions. Assumed alcoholic cardiomyopathy. Decided anticoagulation. Suboptimal control of INR. Advised on alcohol cessation. Admitted for anasarca. On new echocardiogram, identified left ventricular non-compaction. She was abstinent since the previous stroke. Euvolemia achieved with diuretic therapy. In ambulatory care, she developed acute kidney failure. Right renal artery thrombosis was identified, in a patient with unknown left renal exclusion (probably, due to chronic ischemic lesion). The patient enrolled dialysis programme. Death following dialysis complications.

**Discussion:** It is crucial to identify these patients and evaluate the adequacy of anticoagulation, with fierce control of INR.

## The clinical efficacy of combination drug therapy in patients with concomitant cardiovascular pathology in the secondary prevention of cardiovascular complications

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**Objectives:** Numerous studies have shown the efficacy of pharmacotherapy in complex rehabilitation of patients after

myocardial infarction (MI). It helps to increase exercise tolerance and improve the clinical course of the disease and may even slow the progression of atherosclerosis. Pharmacotherapy is also effective in patients with chronic heart failure. We aimed to evaluate the effectiveness of the combined drug therapy in patients with concomitant cardiac pathology in outpatient practice.

**Methods:** The study included 50 patients with concomitant cardiac pathology: stable angina (I-III FC), essential hypertension (I-III degree), chronic heart failure (I-III FC NYHA) at the stage of outpatient treatment for 6 months. All patients received fosinopril in a dose of 10-40 mg/day, carvedilol 12.5-50 mg/day, amlodipine 5-10 mg/day, hydrochlorothiazide 12.5-25 mg/day, spironolactone 25 mg/day, acetylsalicylic acid (ASA) 75-100 mg/day, atorvastatin 20-40 mg/day. The doses were selected individually under the careful supervision of the clinical condition of the patient, blood pressure, heart rate, laboratory parameters. The dynamics of the following symptoms and indicators: the number of angina attacks per week, a sample with a 6-min walking distance, heart rate, blood pressure. Among the patients males were 52% (36 people) and 48% of women (24 people). The patients were in the age group of 45-65 years. The median age was  $56\pm 6,7$  years. Statistical analysis was performed using Statistics 8.0. Differences were considered statistically significant at  $p<0,05$ .

**Results:** The ongoing pharmacotherapy in the study group was well tolerated by all patients. Cancellations, failures and side effects of the drugs were not registered. During follow positive dynamics: an increase in exercise tolerance (6-min walking test - an improvement of  $9,7\pm 5,7\%$ ), reducing the number of angina attacks per week (to  $52,7\pm 22,4\%$ ), improvement of key hemodynamic parameters: heart rate slowing (to  $10,8\pm 6,8\%$ ), decrease in SBP ( $11,8\pm 5,6\%$ ) and DBP ( $11,7\pm 7,2\%$ ).

**Conclusions:** Thus, the results of the research show marked clinical efficacy of complex therapy of patients with concomitant cardiovascular pathology in the form of improved key hemodynamic parameters, reduce angina attacks, increased exercise tolerance, which allows not only improve the clinical condition of the patient, but also affect the prognosis of the disease and is an integral component of secondary prevention of cardiovascular complications.

## Circulating endothelial cells as marker of endothelial damage in midlife women with masked arterial hypertension

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**Objectives:** Detection of endothelial damage is crucial for timely detection of target lesions and cardiovascular prevention in patients with masked arterial hypertension (MHT). The aim of the study was assessment of endothelial damage by level of circulating endothelial cells (CEC) in midlife women with MHT and manifest arterial hypertension as compared with CEC level in healthy volunteers.

**Methods:** Endothelial damage was assessed by counting CEC levels in midlife women with MHT and manifest hypertension. Patients, 28 to 49 years old, were evaluated (35 with MHT, 37 with manifest hypertension). Controls were 19 age-matched healthy volunteers. MHT was diagnosed by 30-s breath-holding test (BH test) and 24-hour blood pressure (BP) monitoring. Sitting BP was measured initially and remeasured after 30 seconds of breath holding. BH test was considered to be positive when systolic/diastolic BP (s/d BP) increased >140/90 mmHg. Manifest hypertension was diagnosed by 24-hour BP monitoring and manual sphygmomanometry. CEC level was counted in plasma (phase contrast microscopy).

**Results:** Control sBP 115 (105; 120) mmHg; dBP 77.5 (70; 81) mmHg; CEC level  $2.42 \pm 0.42 \times 10000$  cells/L. In patients with manifest hypertension, sBP 142.5 (140; 153) mmHg ( $p < 0.05$  vs control); dBP 95.6 (90; 100) mmHg ( $p < 0.05$  vs control); CEC level  $3.81 \pm 0.32 \times 10000$  cells/L ( $p < 0.05$  vs control). In patients with MHT, sBP 130 (120; 136) mmHg ( $p < 0.05$  vs control); dBP 82 (80; 89) mmHg ( $p < 0.05$  vs control); CEC level  $3.58 \pm 0.28 \times 10000$  cells/L ( $p < 0.05$  vs control;  $p > 0.05$  vs manifest hypertension).

**Conclusions:** Both masked and manifest hypertensions were associated with similar degrees of endothelial damage. Therefore, MHT is as hazardous for blood vessels as is manifest arterial hypertension. Both masked and manifest arterial hypertensions in midlife women are associated with increased amount of circulating endothelial cells. Quantitation of CEC can be used for detection of early signs of vascular damage induced by masked arterial hypertension.

## Detection of masked arterial hypertension in young age female and male population in screening

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**Objective:** To determine detection frequency of masked arterial hypertension (MAH) in young age organized population in screening.

**Material and methods:** We examined 512 young subjects aged 19-30 years old with office blood pressure <140/90 mmHg. Breath-holding test (BT) was used to detect MAH. BT was performed when excluding external factors on the test results. Sitting blood pressure (BP) was measured initially and was re-measured after 30 seconds of breath hold. BT was considered to be positive in BP increase  $\geq 140/90$  mmHg. All subjects were performed ambulatory blood pressure monitoring (ABPM), clinical examination, cardiovascular diseases (CVD) risk factors assessment, EQ-5D questionnaire interviewing in 2-3 days.

**Results:** MAH was detected in 17.6% of young subjects, among them 8.0% of women (mean age 21.0 yrs), 9.6% of men (mean age 21.0 yrs). During office BP measurement at rest before the beginning of the study young women with MAH had high normal BP in 48% of cases and young men – in 67%; all other subjects had

optimal normal office BP. The majority of MAH patients had CVD risk factors of various intensity: family history in 57% of young men and 39% of young women, smoking – in 23.8% of men and 4% of women, 19% of young men and 3.5% of young women had dyslipidemia. Characteristics of psychometric and physical properties of the subjects according to EQ-5D questionnaire, body mass index, duration of sleep were comparable.

**Conclusions:** MAH was detected in 17.6% of subjects without any complaints and anamnesis of CVD in the young organized population. MAH was more often detected in young men and was accompanied by CVD risk factors of higher intensity as compared to young women.

## Ischemic preconditioning phenomenon in medical and preventive schemes in coronary artery disease patients

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**Objective:** To build a strategy of physical exercise (PE) in coronary artery disease (CAD) patients with incomplete myocardial revascularization based on the phenomenon of ischemic preconditioning (IP).

**Material and methods:** This study lasted for 14 days and was open, prospective, in parallel groups with various PE intensity. The study included 31 CAD patients with incomplete revascularization after percutaneous coronary intervention and positive results of PE stress test. Patients >65 y.o. with ejection fraction  $\leq 40\%$ , diabetes mellitus, thyroid dysfunction were excluded from the study. Group I (n=15,  $53.9 \pm 6.2$  y.o.) performed high intensity PE after IP activation. IP phenomenon was simulated during paired stress tests supported by daily treadmill PE with 70-80% threshold power intensity of diagnostic stress test. Duration of daily PE basic period was determined by time to ST depression and/or angina symptoms. Monitored safety indices: ECG, blood pressure, heart rate during PE, and myocardial injury markers during 30 minutes after PE. Group II (n=16,  $56.1 \pm 4.8$  y.o.) performed medium intensity (50 to 60%) PE. Initially, patients in the groups were matched by major clinical characteristics. Primary endpoints: efficiency (increase in exercise and metabolic equivalents (ME) duration), safety (acute coronary symptom development).

**Results:** After 10 treadmill PE sessions with interval less than 48 hours, elevation of ischemic threshold indices were detected in group I: PE duration increased on 17.5%, ME – on 9.3%; maximum ST depression decreased from 1.82 mm to 0.98 mm. PE stress test analysis in parallel groups showed increasing duration of PE in group I vs group II on  $17.5 \pm 3.6\%$  and  $4.1 \pm 1.2\%$  ( $p < 0.05$ ), respectively, ME increasing on  $9.3 \pm 2.6\%$  and  $2.4 \pm 1.1\%$  ( $p < 0.05$ ), respectively, and maximum ST depression decreasing on  $46.3 \pm 6.8\%$  and  $9.8 \pm 1.6\%$  ( $p < 0.001$ ), respectively. Safety indices were within the reference ranges in both groups.

**Conclusions:** Daily high intensity (70-80%) PE in patients with persistent myocardial ischemia was safe. Use of IP



phenomenon simulated with daily PE of high intensity (70-80%) in CAD patients with incomplete revascularization was more effective to form adaptation to ischemia than PE of moderate intensity (50-60%). Short cycles (10 sessions) of high intensity PE ensure cardioprotective effect formation in CAD patients.

## Diagnosics of hypertrophic cardiomyopathy with hypertrophy of apical segments

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**Objectives:** The diagnostic criteria of this type of an apical hypertrophy, described Sakamoto and Yamaguchi having used for detection of its characteristics an echocardiography at which authors showed increase of degree of a thickening of an apical myocardium at patients with huge negative waves of T on ECG and a configuration of a left ventricular cavity in a diastole shaped like a card. Actual is a question of differential diagnostics as extensive character of a local hypertrophy of a myocardium of a top is led to the expressed violations of coronary microcirculation in the deep layers of the myocardium, as causes a clinical picture of coronary heart disease (CHD).

**Methods:** Our research methods included 2 years of observation during which we created group of 25 patients on the base of cardiology department of the Republican Clinical Hospital of Kazan. The group was characterized by existence of a typical clinical picture of CHD in lack of stenoses of coronary arteries according to coronary angiography. The conducted researches showed conformity of group to earlier described criteria of this form of hypertrophy: existence of signs of a hypertrophy of the left ventricle, characteristic negative teeth of T amplitude more 10mm in combination with high teeth of R in the right assignments according to an electrocardiography (ECG). Ultrasonic research allowed to reveal a hypertrophy only at a part of patients with the expressed changes of the apex: myocardium thickness more than 15 mm, lack of a hypertrophy of other parts of the left ventricle. The research objective consists in differential diagnosis of pathology with CHD and other forms of cardiomyopathies with application of a Single Photon Emission Computed Tomography (SPECT) at rest and with application of cycle ergometer test.

**Results:** The results showed that the following SPECT criteria of an assessment are exist: a myocardium of the left ventricle with visually uneven accumulation of radiopharmaceutical, extensive zones of the expressed hypoperfusion on lower-septal, lower-side walls, moderated hypokinesis of mainly basal part of an interventricular septum. The amount of transitory perfusion defect was nearly 10%.

**Conclusion:** Our findings shows that thus criteria, along with ECG and ultrasonic signs, allowed to reveal a hypertrophy, to estimate degree and localization of defeat, repeated researches allowed to estimate dynamics of these changes for the purpose of an assessment of efficiency of the appointed therapy, its corrections.

## Optimal values of systolic arterial pressure in senior and elderly patients

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**Objective:** To determine the frequency of the average systolic daily blood pressure (ADBP) and its optimal values from a position of prediction of stroke and myocardial infarction (MI) occurrence in senior and elderly patients.

**Material and methods:** 223 men with essential hypertension of 2-3 degrees (61-86 y.o, mean age - 73,3 y.o.) were enrolled in the study. ADBP was estimated by a daily blood pressure monitoring. The duration of follow up period was 5 years. All the patients received the combined hypotensive therapy in accordance with ESH/ESC guidelines (2003-2007). Depending on efficiency of hypotensive therapy the patients were divided into 3 groups, which were comparable on the age, duration of hypertension, body mass index, smoking and absence of diabetes. 62 patients (group 1) reached the target level of systolic ADBP (<140 mmHg) with mean values 132 mmHg. 83 patients of the 2nd group had systolic ADBP within 140-160 mmHg despite on treatment (average 153 mmHg). 78 patients (group 3) had resistant hypertension without significant lowering of BP (systolic ADBP within 165-180 mmHg, mean 174 mmHg).

**Results:** During follow up period MI occurred in 4 patients (6,5%) of group 1, in 3 (3,6%) - of group 2 and in 8 (10,3%) of group 3. Stroke of varying severity developed in 5 (8,1%) patients of group 1, in 4 patients (4,8%) - of group 2 and in 10 (12,8%) patients of group 3. Thus, in patients with target and high values of systolic ADBP the incidence of MI and stroke was in 2 and 3 times, respectively, higher than in patients with systolic ADBP within 140-160 mmHg.

**Conclusions:** It is possible to believe that for the prevention of MI and stroke in senior and elderly patients an optimal systolic ADBP have to be within 140-160 mmHg. Taking in account small number of patients it is necessary to consider the obtained results as preliminary and demanding further confirmation.

## Waist to height ratio significant to discriminate cardiovascular risk: better than waist circumference?

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**Background:** The influence of the obesity in health and life expectancy is unquestionable. Nevertheless, the obesity degree is not enough clinically sufficient. Nowadays it is accepted that great part of the metabolic disorders associated with the obesity are really more related with the abdominal obesity. Classic anthropometrics markers like body mass index

(BMI) and waist circumference (WC) does not discriminate the type of fat distribution pattern. The WC is the anthropometrical measurement preferred at present for finding population in risk in several studies. However height is also important in some aspects, such as insulin-resistance, and is necessary to have it into account at the time of establishing risk markers.

**Objective:** The aim of this work is to value the utility of alternative anthropometrical measures, as the waist-height ratio, comparing them with the traditional ones and determining its utility to discriminate cardiovascular and metabolic risk.

**Methods:** A descriptive, transversal study, from a worker population in an east Portuguese rural area was realized. The sample included 1883 cases whose demographics, anthropometric measures (weight, height, waist circumference, BMI and waist to height ratio), blood pressure and clinical laboratory data were available. Global cardiovascular risk was calculated by Framingham's equation.

**Results:** When we analyzed the correlation between the global cardiovascular risk and classic and alternative indexes, correlations were significant in all indexes. The more accurate index for estimating global cardiovascular risk was waist to height ratio. When we analyzed correlation by sex, for both, men and women, waist to height ratio had too the best statistical correlation with the global cardiovascular risk, following of abdominal circumference for both sexes.

**Discussion:** Our study shows that the alternative index: waist to height ratio had more statistical value for estimation of global cardiovascular risk in both, men and women, that the classics index (waist circumference, and BMI).

## Pulmonary arterial hypertension – therapeutic approach of a clinical case

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**Introduction:** Pulmonary arterial hypertension (PAH) is a chronic and progressive disease leading to right heart failure and ultimately death if untreated.

**Case report:** A 58-year-old female was admitted at our hospital with the diagnosis of idiopathic PAH (precapillary pulmonary hypertension) and functional class III of the World Health Organization (WHO) since 2009. In January 2013 he initiated clinical symptoms of fatigue and dyspnea for small efforts. Ever since a progressive worsening was observed, with and increased need for long-term oxygen therapy (LTOT), 3 liters per minute at rest and 8 to 15 liters per minute during exertion. A previous right heart catheterization showed a mean pulmonary artery pressure (mPAP) of 64 mmHg and a normal pulmonary artery wedge pressure (PCWP) of 10 mmHg with a negative vasodilatation challenge test after inhaled nitric oxide. Transthoracic echocardiography (TTE) estimated a pulmonary artery systolic pressure (sPAP) of 68 mmHg with dilated right cavities. He was treated with sildenafil 50 milligrams (mg)

orally three times per day, ambrisentan 10 mg orally per day and inhaled iloprost 2.25 micrograms 6 times per day. As his condition worsened to a functional class IV (WHO) inhaled iloprost was replaced by an intravenous form with therapeutic improvement.

**Discussion:** A brief review of clinical, imaging findings, right heart catheterization, vasoreactivity testing and updated treatment of this condition is envisaged.

## Vegetative regulation of heart rhythm at men older than 70 years old

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**Objective:** To estimate variability of a cardiac rhythm at men with the coronary heart disease (CHD) depending on age under the influence of sympathetic and parasympathetic systems.

**Methods:** Variability of a cardiac rhythm was studied at 97 men (age of 70-94 years) by means of a hardware-software complex "Dinamika-M" (St. Petersburg, Russia). Defined temporary indicators of wave structure of a cardiac rhythm: RRNN-average size and TINN-variation of R-R values of a cardiointerval. Also defined spectral characteristics: TP ( $ms^2$ ) – the general power of a range; VLF (%) – very low-frequency fluctuations (neurohumoral activity); LF (%) – low-frequency waves (a sympathetic regulation); HF (%) – high-pitched fluctuations (a parasympathetic regulation) and an index of vagosympathetic equilibrium-LF/HF.

**Results:** Patients are divided into 3 groups: the first group included 39 men of 70-79 years, the second-35 of 80-89 years, the third – 23 is more senior than 90 years. In the 1 group very low-frequency area of a range (% VLF-49) against high general power of a range of a cardiac rhythm prevailed. The LF/HF-1,17±0,26 index testified to a prevailation of sympathetic influences. In the 2 group the high-pitched component (% HF-40 in comparison with the I group - % HF-23) against high general power of a range 670±163  $ms^2$  prevails. An indicator of vagosympathetic balance of vegetative nervous LF/HF system reliable lower than 0,77±0,10, than in the 1 group. In the 3 group against a stable cardiac rhythm the general power of a range 367±162  $ms^2$  was lower, than in 1 and 2 groups. In the 3 group a parasympathetic regulation of a cardiac rhythm prevails (LF/HF indicator – 0,89±0,20). Variability of a cardiac rhythm decreases owing to depression of sensitivity of sinus node to vegetative influences and an aerobic exchange in a myocardium.

**Conclusions:** In all groups with augmentation of age the prevailation of a parasympathetic regulation of a rhythm of heart is characteristic. Neurohumoral influence on cardiovascular system at patients older than 70 years was shown by depression of quantity of extrasystoles at rest. At an exercise stress there is a shift of vegetative balance towards sympathetic activity. The obtained data were registered by means of a hardware-software complex "Dinamika-M" and allow optimizing therapy at patients of senile age.

## Structural and morphological features of heart failure in chronic kidney disease

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**Objective:** The purpose of the survey was to determine the structural-morphological peculiarities of the myocardium of the patients with chronic kidney disease with no signs of heart failure and ischemic heart disease.

**Methods:** 161 patients with chronic kidney disease of the 2-5 stages took part in the survey. Echocardiographical survey was organized by the scientists on the equipment Vivid S6, General Electric, USA. The survey revealed the width of the interventricular septum and left ventricle posterior wall, the length of the left ventricle during diastole, end diastolic, transverse ventricular dimension. The survey also calculated left ventricle myocardial mass index, sphericity index, eccentricity index. The quantity of creatinine, myoglobin, CK-MB, troponin I was determined. Morphological study of the myocardium was carried out on autopsic material of 46 deceased patients with chronic kidney disease of varying degrees of severity.

**Results and conclusion:** It is the patients with the 2nd stage of the disease who have the initial characteristics of remodeling. The higher the stage of the disease the bigger the concentric hypertrophy of the left ventricle. Remodeling progresses in terms of left ventricle sphericity incidence. Hemodialysis leads to concentric left ventricle hypertrophy decrease. Microscopic heart examination revealed the correlative link between structural myocardial changes and chronic kidney disease.

## Pericarditis in adult onset Still's disease

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**Objectives:** Adult onset Still's disease (AOSD) is an uncommon inflammatory disease characterized by spiking fever, joint pain and transient cutaneous rash. Pericarditis is the main cardiac manifestation, which is generally benign but the prognosis may be seriously involved.

**Methods:** We retrospectively reviewed the records of patients with AOSD and included those who were hospitalized in our department for pericarditis. The diagnosis of AOSD was based on both Yamaguchi and Fautrel criteria.

**Results:** Three female patients were included with a mean age of 39.3 years [19-69]. They were hospitalized for a prolonged fever and polyarthralgia. Dyspnea, basithoracic chest pain, and cutaneous evanescent rash were observed in 2 cases. The first patient hadn't any pleural or chest pain. All patients had high leukocytosis with neutrophilia. Thoracic computed tomography scan showed pleuropericarditis in all cases. In one case, the patient developed clinical signs of cardiac failure and the echocardiogram showed pericardial tamponade. She had pericardotomy with

a pericardial and pulmonary biopsy. The anatomopathologic examination didn't show any specific features. Infectious, neoplastic and other autoimmune disease were ruled out. In one case, the AOSD were established 3 years before the pleuropericarditis, and the patient was diagnosed as a flare up of her condition. In the 2 other cases, the pleuropericarditis was the initial manifestation of the AOSD. All cases were treated initially with corticosteroids. In 2 cases, the patients developed cortico-dependence and the methotrexate were added. There was a clinical improvement in all cases within few weeks.

**Conclusions:** Pericarditis in AOSD has variable phenotypic expressions: from symptom free to tamponade. When it occurs as initial manifestation all the more complicated with tamponade may lead to misdiagnosis.

## Prevalence of novel risk factors among young patients with acute coronary syndrome in Eastern India

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**Objective:** To identify prevalence of the novel risk factors among young patients with acute coronary syndrome (ACS) and having no or minimal conventional risk factors.

**Methods:** Total 70 patients (48 male, 22 female) who were admitted in our hospital with ACS, without any traditional risk factors were analyzed for hsCRP [highly sensitive C reactive protein], Lp(a) [lipoprotein (a)], homocysteine and uric acid level. Results: 44.3% of the study population have high values of hsCRP [male (M) - 67.7%, female (F) 32.3%], more so in 40-45 yrs in male (41.9%) and 45-49 yrs in female (12.9%). High homocysteine level present in 42.9% of cases, more in older age (>40 yrs) (54.6%) than <40 years age (23.1%) which is statistically significant (p=0.01). High uric acid level found in 32.9% of cases without any significant age and sex difference. High Lp(a) level is found in 41.4% of cases (M - 41.7%, F - 40.9%), more among ≥40 years (50%) than <40 years (26.9%), the difference was not found to be statistically significant [Chi-square=3.587; p=0.058; OR=2.71, 95% CI=0.95-7.7].

**Conclusion:** hsCRP is most useful cost effective screening method for ACS in younger individual among all other parameters in this part of world.

## Dispensary disease after conservative or surgical treatment

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**Objective:** To evaluate the results of dispensary observation of patients with chronic coronary heart disease after conservative and surgical treatment.

**Material and methods:** Retrospective study included 186 patients: group I - 101 patients with chronic ischemic heart

disease (CIHD) after coronary artery bypass grafting (CABG) in 2011, 2012; group II - 85 patients with CIHD, without surgical treatment discharged from hospital in 2011 and 2012. Patients in both groups were registered after  $3 \pm 0,2$  month period after discharge ( $p > 0,05$ ). The experimental observation lasted over two years. A statistical analysis was performed using software Statistica 6.0.

**Results:** The average age of included patients was 60 years old ( $p = 0,2$ ). Country inhabitants (60,4% and 56,5%,  $p = 0,5$ ) and males (88% and 57%,  $p < 0,001$ ) predominated in both groups. Arterial hypertension (AH): I - 91%, II - 88% ( $p = 0,5$ ). Assessment target level of blood pressure (BP) during registration: I - 93%, II - 71% of patients ( $p < 0,001$ ). By the end of the observation period: I - 87%, II - 52% of patients ( $p < 0,001$ ). At the registration: in group I - 90% of patients were without angina, in group II - 56,5% ( $p < 0,001$ ); the second and third functional class (FC) were more frequent among patients with conservative management tactics ( $p < 0,001$ ). After 2 years of the follow-up: in group I - 68,3% of patients were without angina, in group II - 28,2% ( $p < 0,001$ ); the second and the third FC were more frequent in the group II ( $p < 0,001$ ). Patients of group I were significantly more amenable to the recommended therapy than patients in group II ( $p < 0,03$ ). During the observation, the number and the reasons for hospitalization did not differ ( $p = 0,5$ ).

**Conclusions:** Males were dominated among patients with CIHD in both groups, but significantly more males were in the group of patients subjected to CABG. The high prevalence of AH among patients with CIHD was marked in the Altai region. The achievement of target BP among the operated patients was more frequent. Patients of group I were significantly more amenable to the recommended treatment. Patients after surgical treatment of CIHD seldom had angina. The number and the reasons for hospitalization in both groups did not differ.

### Thrombinemia parameters of the patients with chronic ischemic heart disease before and after coronary artery bypass grafting

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**Objective:** To explore the parameters of thrombinemia of the patients with chronic ischemic heart disease (CIHD) before and after coronary artery bypass grafting (CABG).

**Material and methods:** For prospective study 61 patients with CIHD undergoing CABG in 2014-2015 were included in primary group (I). The comparison group (II) consisted of 27 patients with excluded CIHD. Initially, parameters of hemostasis were evaluated in both groups at the outpatient treatment stage. The dynamics of these laboratory tests was evaluated in group I in two stages: the first stage on  $13,3 \pm 0,5$  day and the second on  $97,4 \pm 1,2$  day after CABG. Statistical analysis was performed using software Statistica 6.0.

**Results:** Estimating parameters of hemostasis at the outpatient treatment stage, it was found that there is a moderate increase of fibrinogen to  $4 \pm 0,2$  g/l ( $p = 0,006$ ), soluble fibrin monomer complexes (SFMC) -  $8,9 \pm 0,6$  mg/100ml ( $p < 0,001$ ) and the level of D-dimer -  $224,6 \pm 15,7$  ng/ml ( $p < 0,001$ ) in group I compared

to group II. The anticoagulant activity of link - antithrombin III (AT III) and protein C (Pr C) - was not changed and remained high. The inner path parameters of fibrinolysis and plasminogen in compared groups at the outpatient treatment stage were not significantly different. Patients with CIHD for a median of 13 days after conducting CABG had increased fibrinogen -  $6,8 \pm 0,2$  g/l, SFMC -  $19,5 \pm 0,5$  mg/100ml and especially D-dimer -  $1978,9 \pm 106,9$  ng/ml ( $p < 0,001$ ). The activity of AT III and Pr C remained high. However, XIIIa-dependent fibrinolysis was significantly impaired  $53,9 \pm 0,9$  min. ( $p < 0,001$ ), while the level of plasminogen remained constant. Most of the changed parameters came back to the initial ones on 97th day after CABG, with the exception of D-dimer ( $305,8 \pm 19,5$ ,  $p < 0,001$ ) and SFMC ( $10,7 \pm 0,6$ ,  $p = 0,04$ ).

**Conclusions:** Patients with CIHD had already had a lapse in the hemostasis system before the surgery, in the form of a moderate increase of fibrinogen level of and its derivatives. After CABG most patients had a significant increase of thrombinemia and the oppression of the internal mechanism of fibrinolysis, managed by normal anticoagulant system. Three months later the patients after CABG had moderately elevated SFMC and D-dimer levels.

### The registry of patients with chronic ischemic heart disease in the Altai region

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**Objective:** To evaluate the performance of the Registry of patients with chronic ischemic heart disease (CIHD) put into practice in the hospitals of the Altai region (AR).

**Material and methods:** The CIHD AR registry was developed and put into practice in 2011. The register is maintained at the present time. The registry is used in 16 hospitals, two of which provide high-tech medical care (HMC) in cardiac surgery. The number of patients in the registry at the beginning of year 2015 was 10800. The comparative analysis of the data of the AR registry and the Russian Federation (RF) registry CLARIFY was done. Statistical analysis was performed using Statistica 6. Results: In the RF 27 000 per 100 000 people and in AR 54 000 per 100 000 people had cardio circulatory system diseases (CCSD) in 2013. The average age of patients in the AR registry - 65,1, in the registry CLARIFY in RF - 59,2 ( $p < 0,001$ ). There were 66,4% males in AR, 73,1% males in RF ( $p < 0,001$ ). Arterial hypertension (AH): AR - of 86,9%, RF - 79,6% ( $p < 0,001$ ). Diabetes mellitus (DM): AR - 18,4%, RF - 16,7 % ( $p = 0,05$ ). In AR 27,1% of patients with CIHD smoke, in the RF - 20,9% ( $p < 0,001$ ). The average body mass index: AR - 28,8, and in the RF - 28,6 ( $p = 0,5$ ). Percutaneous coronary interventions (PCI) in medical history were in AR - 26%, RF - 28,6% ( $p = 0,01$ ). Coronary artery bypass grafting (CABG): AR - 13,3%, RF - 22,9% ( $p < 0,001$ ). Frequency of prescribing of inhibitors of angiotensin converting enzyme, b-blockers, calcium antagonists, diuretics to patients with AR is significantly ( $p < 0,05$ ) lower than to patients with CIHD in RF. But in AR, hypolipidemic medication was prescribed to larger number of patients than in RF ( $p < 0,001$ ). Prescribing of anti-platelet and antianginal (nitrate) therapy had no differences.

**Conclusions:** The prevalence of CCSD in AR is two times higher

than in RF, patients in AR are a bit older. The high prevalence of hypertension, DM and smoking among patients with CIHD in AR. 43,5% of CIHD registry patients were provided with HMC, but the execution of CABG and PCI remains significantly lower than in RF. Medical therapy of CIHD in AR conforms with the existing guidelines and standards, but the frequency of prescribing a number of drugs groups differs from RF.

## Aortic paravalvular leak: a relatively rare cause of heart failure

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**Introduction:** The aortic paravalvular leak (PI) is rarely the heart failure (HF) origin, as only 2-3% of cases are symptomatic. We intend to draw attention to valvular dysfunction as cause of subacute HF in a previous stable patient, as well as related conditions.

**Case report:** A 71 y.o. woman with a prosthetic aortic valve implantation 10 years earlier, under anticoagulant therapy with acenocoumarol, presented to the emergency room with a moderate retrosternal pain ('tight'). The patient had a 2 months history of fatigue, orthopnea, paroxysmal nocturnal dyspnea and lower limbs edemas that caused multiple recurrences to the health services. Physical examination revealed apyrexia, blood pressure of 118/76 mmHg, a heart rate of 98 beats/min, a respiratory rate of 26 breaths/min and pallor of mucous membranes and skin. Cardiac and pulmonary auscultation denoted rhythmic cardiac sounds with metallic click best heard in aortic focus and crackles in the right lung base. There was no abnormality in abdominal evaluation but both lower limbs presented with moderate edemas. The patient was noted to have a number of laboratory abnormalities: hemoglobin 8.7 g/dL, mean corpuscular volume 81.7fL, INR 3.2, C-reactive protein 4.0 mg/dL, total bilirubin 1.8 mg/dL, direct bilirubin 0.4 mg/dL, lactate dehydrogenase 1376 U/L; elevated levels of N-terminal pro-B-type natriuretic peptides 9900 pg/mL. The electrocardiogram showed a 1st degree atrioventricular block and the chest X-ray a cardiomegaly and a small right pleural effusion. The patient was admitted for clinical stabilization but her condition evolved unfavorably with hypotension and severe hemolysis. A transthoracic echocardiogram revealed an aortic turbulent flow with paravalvular aortic leak and the transesophageal echocardiogram confirmed the presence of aortic vegetation and failure. Empiric antibiotic therapy was started for infectious endocarditis in spite of negative blood cultures, with clinical improvement.

**Discussion:** Beyond PI are uncommon causes of HF, this presence in simultaneous of hemolytic anemia and infectious endocarditis makes this clinical report more unusual. Another interesting fact is the development of leak only 10 years after valve replacement surgery. The presence of PI may be associated with acute or subacute HF, being rare the presence of this 3 conditions in the same patient. Thus, we emphasize the importance of evaluation of valvular prostheses in all patients with unexplained acute HF.

## Long-term variability of diastolic blood pressure of from visit to visit and sensitivity to salt as early markers of masked hypertension

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**Objective:** To study of salt sensitivity and the visit to visit variability in diastolic blood pressure (DBP) in men with masked hypertension.

**Material and methods:** The study included 99 drivers and their assistants (mean age 43,3±10,4 years). Identified 2 groups: 1-st group consisted of individuals with masked hypertension (n=40, age 42,8±9,8 years); 2-nd group – healthy (n=59, age 42,3±8,4 years). Sensitivity to salt was determined by the modified method R.J. Henkin. Apply a set of test strips based on 12 dilution of sodium chloride at concentrations ranging from 0.0025 to 5.12%. Variability was defined as diastolic blood pressure from visit to visit BP variability within one year.

**Results:** Average values of the level in the two groups correspond to the low level of sensitivity. The level of salt sensitivity in men with masked hypertension aged 20–39 years was 0,02±0,015%; in persons over 40 – 0,08±0,05% (4-fold increase, p<0,008). The level of salt sensitivity in healthy aged 20–39 years was 0,01±0,005%; in persons over 40 – 0,03±0,01% (increase by 3 times, p<0,01). According to the results of analysis of variance revealed significant differences depending on the level of sensitivity to salt and smoking (p=0,03), abdominal obesity (p=0,04), age (p=0,002), family history of CVD (p=0,002) and increased DBP (p=0,004). When comparing men with masked hypertension with healthy revealed that the masked hypertension mean DBP higher than in the daytime at 4 mmHg (p=0,008), at night – 5 mmHg (p=0,03), on a visit to visit variability in DBP higher than in the daytime and at night (p=0,004). From visit to visit variability in DBP was the main independent predictor of masked hypertension in men (p<0,0001). When included in the model is the level of sensitivity to salt predictive value increased 2-fold (p=0,001).

**Conclusions:** In men with masked hypertension compared to healthy an increased level of salt sensitivity, which is associated with increased from visit to visit variability in diastolic BP. It has a pathogenetic substantiation and leads to early onset of cardiovascular disease.

## Risk of cardiovascular diseases in women with high activity of rheumatoid arthritis

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**Objective:** To analyze CVD risk factors (RF) and reveal the correlation with the activity of systemic inflammatory process

and cardiovascular risk in women with rheumatoid arthritis (RA). Methods: 190 women were included into the study. The average age was 55.8±9.2 years. RA was diagnosed by the criteria ACR/EULAR 2010. The average age of the onset of RA was 49.6±8.9 years. The average time of RA was 9.5±4.6 years. The activity of early RA according to DAS 28 was high (>5.1) 100 %, the average patient pain assessment based on VAS score 65±9.8 mm. Statistical data were obtained with «Statistica» v 6.1 software. Results: 100% patients suffering from RA had CVD risk factors. The average number of RF for a patient was 7.6 (0; 13) at the age of 55±9.5 years. The number of RF increases in 1.8 times (p<0.05) every 10 years in people over 55 years. According to the frequency RF can be ranked as follows unbalanced diet – 90%, abdominal obesity – 81%, arterial hypertension – 74%, anxiety and depression – 74%, increased cholesterol level – 70%, tachycardia – 70%, family history of early CVD – 61%, menopause under 45 years – 56%, obesity – 52%, sleep disturbance – 50%, decreased physical activity – 38%, the pathology of pregnancy – 29%, uric acid – 21%, hyperglycemia – 12%, smoking – 5%, alcohol – 1%. The affected organs were left ventricle hypertrophy – 74%, lower limb arterial calcification – 35% (Ankle Brachial Index 1.4), stenosis of lower limb vessels (0.8) – 18%. The associated clinical conditions were chronic kidney disease in 20% of patients, ischemic heart disease – 13%, transient ischemic attack – 6%. The patients had increased ESR – 97% (38.4 (16;77) mm/h), C-reactive protein (CRP) – 84% (20.1 (0;86,0) mg/L), rheumatoid factor – 80% (112.3 (0; 701) mg/L); cyclic citrullinated peptide antibody (anti-CCP) – 65% (214 (100; 507) unit/ml), total blood cholesterol level – 70% (average level – 5,4 (3.1; 10.2) mmol/L). The risk of CVD complications according to the SCORE scale was very high in 35% of cases, high – 36%, mild – 14% and low risk in 15%. When studying the correlations between total blood cholesterol level and CRP (r=0.4; p<0.001), ESR (r=0.6; p<0.003), rheumatoid factor seropositivity (r=0.9; p<0.001), DAS28 (r=0.5; p<0.004), VAS score (r=0.3; p<0.005) were detected.

**Conclusions:** Thus, the patients with RA have the increased risk of CVD complications (71%) caused by the great number of RF (in average 7.6). The RF (unbalanced diet, decreased physical activity, arterial hypertension, stress and depression, smoking, obesity, tachycardia) correlate (p<0.05) with the activity of systemic inflammatory process at the average age of 55.8±9.2.

## Two diseases, one pathology

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**Introduction:** The pathogenesis of myocardial infarction (MI) and stroke in young adults involves new factors including constitutional or acquired thrombophilia.

**Case report:** We present a case of a 46 years old type 2 diabetic, non-hypertensive and non-smoker male admitted with 2 hours of intense chest pain, at rest, with Levine's sign, nausea and vomiting. No relevant family history. At admission the patient was hemodynamically stable. ECG revealed sinus rhythm with ST elevation in inferior leads. His initial troponin I concentration was

100.53 ug/L. Transthoracic echocardiogram showed preserved left ejection fraction with postero-inferior hypokinesia. STEMI (Killip class 1) was considered. Emergency cardiac catheterization revealed 50–70% proximal stenosis of left coronary artery and subocclusion of distal circumflex artery. Angioplasty of circumflex artery was performed with good angiographic and clinical result. By day 5 of admission, the patient developed global aphasia, right homonymous hemianopsia and predominantly crural hemiparesis. Brain CT scan showed acute hypodensity of the genu of left internal capsule. Echocardiogram excluded emboli. Carotid ultrasound revealed an extensive swinging "fresh" thrombus throughout the left common carotid artery which was totally occluded and showed signs of atherosclerosis. An angio-CT was ordered and patient was submitted to a successful vascular surgery. Laboratorial examination revealed hemoglobin 13.3 g/dL, platelet count 262000/L and low free protein S (57%), total cholesterol 202 mg/dL, HDL 40 mg/dL, LDL 124 mg/dL, triglycerides 194 mg/dL and HbA1c 10.3%. Anticardiolipin antibodies, anti-β<sub>2</sub>-glycoprotein-I antibodies and lupus anticoagulant were normal. Functional protein C was 155% (normal values 70–130). Antithrombin, protein C and factor V deficiency were also excluded. It is known that the risk of stroke is highest during the first 5 days after MI. The predictors of MI-related stroke are atrial fibrillation, ST elevation and a previous history of stroke.

**Conclusion:** This case highlights that protein S deficiency may play an important role not only in MI in young adults, but also in thromboembolic complications during the follow-up period.

## Correction of erectile function and depression in hypertensive patients with natural origin medication "Eromax"

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**Objective:** The aim of this study was to evaluate of efficacy of comprehensive therapeutic correction testosterone deficiency in hypertensive patients with erectile dysfunction (ED) and depression.

**Material and methods:** 75 men (mean age was 50.2±8.1 years) with arterial hypertension (I–III stage) with ED and depression were studied. Erectile function was assessed by International Index of Erectile Function – 5 (IIEF-5), questionnaire Men's Sexual Formula (MSF), Rating Scale of Sexual Function (RSSF); depression - by Hospital Anxiety and Depression Scale (HADS). Total testosterone (TT), dehydroepiandrosterone sulfate (DHEAS), prolactin were measured in morning blood samples. For combination therapy natural origin medicine "Eromax" which includes such active ingredients as drone brood, bee pollen, and L-arginine was used.

**Results:** Out of total 75 men 65.3% (49) by the 10th day of treatment noted subjective improvement in mood, increase of self esteem and confidence in their sexual abilities, reduction of tension in marital relationships, as well as increased frequency of night erections. The study of efficacy of the therapy in view

of clinical and dynamic changes in hormonal status showed reliable increase in the TT level (from  $11.8 \pm 4.4$  to  $17.1 \pm 5.7$  nM/l,  $p < 0.02$ ) against decrease the level of prolactin (from  $548 \pm 136$  to  $285 \pm 60$  IU/l,  $p < 0.02$ ). There was also a tendency to increase of DHEAS (from  $1.2 \pm 0.3$  to  $1.5 \pm 0.7$  mcg/ml,  $p < 0.05$ ). During follow-up visit (28th day of treatment) patients experienced significant improvements according to the RSSF: libido –  $4.0 \pm 1.2$  points against original  $2.8 \pm 0.9$  ( $p < 0.02$ ); erection –  $3.8 \pm 1.1$  points against original  $2.9 \pm 1.0$  ( $p < 0.05$ ). Indicators IIEF rose from  $15.8 \pm 3.4$  to  $19.8 \pm 3.7$  ( $p < 0.05$ ). When estimating the sexual function on the base of MSF the study had revealed general decrease of men's copulation cycle before treatment. Against the carried out therapy the grade point average of men's sexual function increased from  $17.7 \pm 2.5$  to  $23.8 \pm 2.9$  ( $p < 0.02$ ). According to the HADS tested patients showed significant reduction in levels of anxiety and depression ( $p < 0.02$ ).

**Conclusion:** The combined treatment with natural origin medicine "Eromax" which includes such active ingredients as drone brood, bee pollen, and L-arginine significantly improves testosterone status, symptoms ED and depression in hypertensive men.

### Cardiotoxicity of anticancer treatments: a 10-year experience of an advanced heart failure unit in Portugal

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**Objectives:** The cardiotoxicity of anticancer agents can lead to significant complications that can affect patients being treated for various malignancies. The most common clinical presentation of cardiotoxicity is cardiomyopathy (CMP) leading to chronic heart failure (HF). The purpose of this study was to characterize the patients with chemotherapy-induced CMP, including demographic and clinical characteristics, disease course and outcomes.

**Methods:** A retrospective data analysis has been done, describing the cancer patients admitted to the advanced heart failure unit (AHFU) with decompensated HF during the period of 2004–2014. Results: 32 cancer patients (29 F/3 M) with a mean age of 52.3 years (F:52.2/M:63.7) were admitted to the AHFU during a 10-year period. More than half of the patients (59.4%) were treated for breast cancer, 28.1% were diagnosed with hematological malignancy and 12.5% with other tumors (lung, ovarian, uterine and bladder). On presentation, 6 patients (18.8%) were in NYHA functional class II, 14 (43.8%) were in class III and 12 (37.5%) were in class IV. The mean left ventricular ejection fraction (LVEF) on admission was 32% (16–55). The median time between initiation of chemotherapy and HF diagnosis was 3.9 years (1 month–18 years) and the symptoms most frequently encountered on admission were exertional dyspnea, orthopnea, fatigue, arrhythmia and generalized edema. We emphasize the presence of 2 or more cardiovascular risk factors, such as hypertension, diabetes and dyslipidemia, in 17 patients (53.1%). In our sample, most frequently used chemotherapeutic agents

were anthracyclines, followed by the alkylating agents and the monoclonal antibodies. 21 patients (65.6%) were also submitted to radiation therapy. The mortality rate was 15.6% (5 patients), 3 patients (9.4%) received heart transplant, and 13 (49.6%) achieved stabilization or improvement of the LVEF with the HF treatment.

**Conclusions:** Chemotherapy-induced CMP increases morbidity, often interferes with cancer treatment regimens and can negatively affect long-term outcomes. In our sample of patients, radiation therapy, comorbidities and previous heart disease appeared to have a high predictive value to worse outcome. Improvement of the LVEF was achieved when cardiac dysfunction was detected early and a HF treatment was promptly initiated. In addition, more efforts are needed to promote strategies for screening, early detection and treatment of cardiotoxicity in cancer patients.

### Post-capillary pulmonary hypertension in the patient with severe biatrial dilation

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**Introduction:** Diagnosis of conditions with post-capillary pulmonary hypertension (PH) is usually straightforward but can be challenging.

**Case report:** We present a 73 years old woman with complaints of progressive breathlessness and easy fatigability over the last year. She had known stage 1 hypertension and atrial fibrillation under anticoagulation therapy, since 8 years ago. Physical examination revealed a systolic murmur at the left sternum border and mild peripheral edemas. The transthoracic echocardiogram showed an increased systolic pulmonary artery pressure (sPAP 49 mmHg), moderate left atrial (LA) dilation and mild right atrial (RA) dilation. Biventricular systolic function was preserved; ventricles were normal sized, with no hypertrophy; the E/E' ratio was 8.9; moderated tricuspid regurgitation (TR) was present, without another valvular abnormalities. B-natriuretic peptide was 113.6 pg/mL. High-resolution CT scanning showed no significant abnormalities in the lung parenchyma and no signs of chronic thromboembolic disease. Pulmonary function tests showed mild obstructive lung disease with no changes in DLCO. The heart catheterization confirmed PH (mean PAP 39 mmHg; sPAP 70 mmHg) with elevated pulmonary wedge pressure (23 mmHg) and a transpulmonary gradient of 16 mmHg, favoring reactive post-capillary PH diagnosis. Laboratory tests for autoimmunity and HIV were negative. Portal hypertension and significant coronary artery disease were excluded. The transesophageal echocardiogram showed moderate to severe biatrial dilation (LA 105 ml, RA 99 ml), severe TR and elevated sPAP (65 mmHg), excluding other valve diseases. The cardiac magnetic resonance (CMR) confirmed nondilated, nonhypertrophic ventricles with biatrial dilation, but no areas of delayed enhancement or pericardial thickening. During this period, the patient was treated with furosemide to relieve symptoms, needing progressive dosage increase.

**Discussion:** This patient presents with a post-capillary PH with biatrial enlargement but no signs of LV disease or

valvular abnormalities. She had no ventricles hypertrophy or dilation, and almost normal E/E', which make heart failure with preserved ejection fraction an unlikely diagnosis. On the other hand, there was no delayed enhancement on CMR nor pericardial abnormalities, which make restrictive cardiomyopathy and constrictive pericarditis less likely. Our case presents a diagnostic challenge in which the definitive diagnosis remains unclear.

## Advanced heart failure due to cancer therapy

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**Introduction:** Sunitinib malate is tyrosine kinase inhibitor with established efficacy in the treatment of metastatic renal cell carcinoma. Sunitinib associated cardiotoxicity was reported in approximately 10% of the patients. Cardiac dysfunction is reversible after discontinuation or dose modification. This case describes the development of heart failure in a metastatic renal cell carcinoma patient who received this novel agent.

**Case report:** A 68 years old patient, with hypertension, type 2 diabetes mellitus and renal cell carcinoma. Thoracoabdominal CT and bone scintigraphy showed multiple pulmonary and bone metastasis. Treatment with sunitinib (50 mg/day) was initiated. After few weeks, patient presented with dyspnea, orthopnea, pretibial edema and decreased effort capacity. Previously in outpatient consult oxygen therapy was prescribed. No improvement was noted, so he was admitted in emergency department. He was hospitalized for decompensated heart failure as complication of chemotherapy. TTE showed LVEF decrement to 30%, LVEDD increased. BNP level was increased and cardiac biomarkers negative. CXR showed bilateral pleural effusions and multiple nodules. Sunitinib treatment was interrupted. During early period of hospitalization, intravenous diuretic treatment was used. Digoxin, diuretic, beta blocker, aldosterone receptor antagonist and statin treatment was initiated. He improved after initiation of treatment for heart failure and withdrawal of sunitinib. Due to clinical findings and risk factors of the patient, cardiac scintigraphy was performed. There was inferior wall perfusion defect with normalization on rest. No invasive treatment was performed for ischemic cardiomyopathy. At discharge, he was asymptomatic of heart failure, functional capacity increased to the NYHA class II. The patient died after few months due to progression of renal cell carcinoma.

**Discussion:** For patients who develop symptomatic cardiac dysfunction, discontinuation of sunitinib, initiation of standard heart failure treatment is appropriate. It is necessary to exclude other causes of heart failure. Left ventricular dysfunction might be due, in part, to direct cardiomyocyte toxicity. Patients treated with sunitinib should be closely monitored for hypertension and LVEF reduction, especially those with a history of coronary artery disease or cardiac risk factors. Cardiotoxicity due to sunitinib malate can cause severe heart failure and requires interruption of the cancer treatment. An important issue is the reversibility of cardiac events and the effect of a cardiac event on the course of the oncologic treatment.

## Infective endocarditis due to *Proteus mirabilis* infection

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**Introduction:** Endocarditis due to *Proteus Mirabilis* is very uncommon. We report a case of a patient with prolonged fever in whom the diagnosis of *P. mirabilis* endocarditis was not established on admission but was made later.

**Case report:** A 54 years old male presented to the hospital with fever and dyspnea. Admission blood cultures grew *Proteus mirabilis* in 4 sets. Piperacillin/tazobactam was administered and fluids and dopamine were initiated due to septic shock. Transthoracic echocardiogram revealed moderate aortic valve stenosis. No vegetation was seen. On hospital day 10 the patient developed Coomb's positive hemolytic anemia with hemoglobin concentration of 6.5 g/dl and required endotracheal intubation because of respiratory failure and repeated blood transfusion. Antibiotic regimen was changed to meropenem. For the next 5 days patient's temperature decreased and repeated blood cultures returned negative. 10 days later the patient developed fever accomplished by leukocytosis, severe thrombocytopenia, and acute renal failure. Blood cultures were positive for same *Proteus mirabilis* again. Transesophageal echocardiogram revealed moderate aortic valve stenosis due to bicuspid aortic valve and moderate aortic regurgitation. There was evidence of a mobile, echogenic mass on the anterior valve leaflet consistent with vegetation. An echo lucent cavity was visible above the aortic valve represented a para-aortic abscess. Surgical treatment was discussed and denied by patient's legal guardian. The patient deceased on hospital day 34.

**Discussion:** We have reported herein a case of infective endocarditis due to *Proteus mirabilis*, which is very uncommon. One study found reports of only 8 cases of endocarditis due to *Proteus* species between the years 1950 and 2010, which fulfilled the modified Duke criteria for definite or possible infective endocarditis. In regard to treatment, the optimal antimicrobial treatment for *Proteus* endocarditis is unknown. A recent study reported a case of *Proteus* endocarditis that was successfully treated with ampicillin and gentamicin. 2 more cases were treated successfully with ceftriaxone. Persistent fever and positive blood cultures for more than 7–10 days is a class IB indication for urgent surgery.

## Relationship between ventricular arrhythmias and the QT interval in ischemic stroke

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**Objective:** To study the nature of ventricular arrhythmias and their relation with QT duration in ischemic stroke.

**Methods:** The studied group (SG) included 108 patients with arterial hypertension and ischemic stroke: 51% men and 49% women (mean age 61,6±1,1 yrs). The control group (CG) was



made up of 78 hypertension without a stroke: 50% men and 50% women (mean age  $58,2 \pm 1,2$  yrs). The groups were matched for severity of hypertension and for concomitant diseases. 24-hour Holter monitoring was performed on the 2–3 day after stroke. Ventricular extrasystoles (VEs) were evaluated according to classification of Lown and Wolf. QTc duration of over 440 ms, with an episode lasting at least 20 sec. was regarded as QTc prolongation. The summative duration of the episodes within 24 h was evaluated as well.

**Results:** The recorded high – grade VEs in SG and CG were similar in rate: 63 and 62,9% respectively. However, in the presence of a stroke polymorphic and early VEs occurred more often, by 1,8 times ( $p < 0,05$ ). Prevalence of short episodes of ventricular tachycardia tended to occur (10,2% versus 2,6%,  $p < 0,1$ ). Adverse mixed diurnal profile was predominant in 51,1% of cases and was noted more often, by 1,7 times ( $p < 0,005$ ). The average incidence of VEs in SG comprised  $435,5 \pm 180,3$ , exceeding the number in CG by 2,2 times. The maximal number of VEs per hour in SG was  $43,6 \pm 16,5$ , exceeding twice the indices in CG. The average incidence of all high-grade VEs was larger, however authentically reliable were only the indices exceeding the early VEs, by 21,8 times ( $p < 0,05$ ). A tendency was noted to increased incidence and duration of unstable ventricular tachycardia, by 8,1 ( $p < 0,1$ ) and 7,1 ( $p < 0,1$ ) times, respectively. No VEs increase occurred in a mild stroke. A proportional increase was noted in severe strokes and of moderate severity. The incidence of high-grade VEs correlated with stroke severity ( $r = 0,251$ ;  $p < 0,01$ ) and with age ( $r = 0,323$ ;  $p < 0,001$ ). The total duration of prolonged QTc interval correlated with the incidence of VEs within 24 h ( $r = 0,442$ ;  $p < 0,001$ ), with their maximal number per hour ( $r = 0,523$ ;  $p < 0,001$ ), with bigeminy ( $r = 0,339$ ;  $p < 0,001$ ) and early ( $r = 0,579$ ;  $p < 0,001$ ).

**Conclusions:** Electrical myocardial instability is noted to enhance in acute ischemic stroke, which is manifested in increased episodes of ventricular arrhythmias and QTc prolongation. The incidence of ventricular arrhythmias correlates with the severity of stroke, age and transient QTc prolongation.

## Modern preventive technology as a way to preserve the professional longevity of employees in organized team

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**Objective:** To assess the dynamics of the health of railway workers on the background of the implementation of modern preventive technologies within three years.

**Material and methods:** The machinists of locomotive and his assistant 20–55 years station Barnaul. In group 1 ( $n = 224$ ) from 2010 to 2012 conduct group prevention counseling in the workplace and in-depth individual preventive counseling in the clinic and fitness center locomotive depot; group 2 ( $n = 128$ ) was under regular medical supervision (pre-trip inspections, clinical examination and medical expenses). The groups were

comparable in terms of professional characteristics and risk factors for cardiovascular disease (CVD). Evaluated the dynamics of risk factors, temporary disability, primary morbidity, suspension from work on the train and professional impropriety from CVD employees in 2010 and 2012 (for 100 employees).

**Results:** After 3 years received positive dynamics in group 1, compared with the 2nd group in reducing the frequency of risk factors: smoking at 24,8% ( $\chi^2 = 19,2$ ;  $p < 0,001$ ), overweight at 10,2% ( $\chi^2 = 3,7$ ;  $p < 0,05$ ), abdominal obesity at 12% ( $\chi^2 = 3,9$ ;  $p < 0,05$ ), hypercholesterolemia at 24,6% ( $\chi^2 = 19,9$ ;  $p < 0,001$ ), physical inactivity at 46% ( $\chi^2 = 67,1$ ;  $p < 0,001$ ), excessive alcohol consumption at 25,3% ( $\chi^2 = 25,4$ ;  $p < 0,001$ ), inadequate intake of fruit and vegetables at 66,9% ( $\chi^2 = 135,7$ ;  $p < 0,001$ ). In the group where for three years in addition to conduct group prevention counseling in the workplace and in-depth individual preventive counseling, compared with the control group, there were fewer cases of temporary disability from CVD 1.7 times, days of temporary disability from CVD and hospitalization 1.4 times, the number of outpatient visits 2.7 times, the cases of primary morbidity arterial hypertension 5.8 times, diabetes 4 times, suspension from work on the train due to higher blood pressure and heart rate 4 times; revealed no cases of coronary artery disease and professional impropriety from CVD.

**Conclusion:** Thus, the implementation of modern preventive technologies in the workplace allows to take control of cardiovascular risk factors and to maintain professional longevity of workers.

## Economic benefit of the formation of preventive environment in the working team from the perspective of an employer

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**Objective:** To develop and implement preventive measures in the workplace and assess their relevance for the position of employer investment on the basis of identified priorities.

**Material and methods:** The workers of locomotive crews. At the first stage to identify economic priorities in the planning of preventive measures made the analysis «cost of illness». In the second phase developed preventive measures: 1) Increasing awareness and motivation of employees to control cardiovascular risk factors – information teleboard in the lobby of hospitals and departmental newspaper advertising a healthy lifestyle, sports corporate events, premium for smoking cessation and weight loss; 2) Providing a healthy lifestyle in the workplace – a gym and an office of psychological relief in the fitness center of the locomotive depot, the healthy food, including plenty of vegetables and fruits in the corporate dining room; 3) School of health in the workplace in the locomotive depot to leading risk factors; 4) Advanced individual prevention counseling to correct the identified risk factors with the issuance of a diary of self-control, and memos with the target values of risk factors; 5) Group preventive counseling in the cabinet prevention of

hospital with mandatory skills training emergency self and mutual assistance with life-threatening conditions. In the third stage the introduction of preventive measures carried out in the workplace (group 1), the control (group 2) was under regular medical supervision (pre-trip inspections, clinical examination and medical expenses). In the fourth phase evaluated the cost-effectiveness of preventive measures in the medium term (2010–2012).

**Results:** Analysis «cost of illness» determined that the CVD occupy a leading position in terms of total health care (direct and indirect) costs, accounting for 30.2%, which identified the economic priorities of preventive measures. After three years in group 1 decreased the cases of temporary disability for CVD by 32.8%, the days of disability and hospitalization by 34.6%, outpatient visits by 38.3%. In group 2 an increasing cases of disability for CVD by 18.2%, the days by 8.7%, the outpatient visits due to CVD by 34.6%, days of hospitalization by 11.1%. Respectively, in group 1 decreased losses from the employer passes on CVD 1.6 times, in the 2nd group after three years marked increase in losses from the employer passes on CVD 1.4 times, as a result, in 2012 in group 1 lost employer-skip workers because of CVD were 2.1 times less than in the 2nd group. When analyzing the economic feasibility of preventive measures from the perspective of the employer determined that ROI of the employer within three years was 3.9 Euros.

**Conclusion:** Formation of preventive environment in the working team is a clinically effective and economically feasible investment of the employer.

## **PREvalence and SENSivity for Cardiac Ischemic Arteriopathy of Frank sign (PRESENCIA-FRANK). Preliminary results**

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**Objectives:** Frank sign (FS) is a line in the earlobe related to ischemic heart disease (IHD). FS prevalence and sensitivity has not been established in Spanish population. It has been postulated that indeed FS is related with age instead of with IHD. The aim of this study was to establish FS sensitivity in IHD patients and analyze FS prevalence and utility in patients with IHD suspicion. **Methods:** Observational study of all patients with acute IHD suspicion (chest pain, unstable angina or acute myocardial infarction) who were admitted between 1 Dec 2014 and 1 May 2015 in Santa Tecla Hospital. FS presence, age, sex, classical vascular risk factors, laboratory tests, final diagnostic, and coronarography (if done) results were recorded. Confirmed IHD was assessed as final unstable angina or acute myocardial infarction. Data were analyzed using SPSS 20.0 for MAC.

**Results:** Preliminary results of PRESENCIA-FRANK study included 109 patients with IHD suspicion. IHD final diagnosis was confirmed in 72 (78%) cases while 37 (22%) had chest pain related to other causes. In these selected 72 patients with confirmed IHD, FS was present in 41 of them (56%). So sensibility

of FS to IHD diagnosis was 56%. In all 109 patients with IHD suspicion FS was present in 58 of them (52%) and absent in 51 (45%). Comparison of those with and without FS showed significantly older patients in FS group ( $68 \pm 9$  vs  $61 \pm 12$  years,  $p < 0,01$ ). No differences were found in troponin levels  $5,5 \pm 17,4$  vs  $8,3 \pm 14,1$ , urea  $48 \pm 25$  vs  $40 \pm 15$ , creatinine  $1.1 \pm 0.4$  vs  $0.9 \pm 0.1$ , glomerular filtration  $73 \pm 26$  vs  $81 \pm 21$ , total cholesterol  $159 \pm 36$  vs  $165 \pm 37$ , LDL cholesterol  $83 \pm 34$  vs  $95 \pm 34$ , HDL cholesterol  $45 \pm 15$  vs  $38 \pm 16$ , triglycerides  $159 \pm 85$  vs  $151 \pm 118$ , hemoglobin  $13.2 \pm 1.8$  vs  $13.2 \pm 1.4$ , albumin  $3.4 \pm 0.3$  vs  $3.4 \pm 0.2$ , uric acid  $5.4 \pm 1.7$  or LDH  $223 \pm 146$  vs  $267 \pm 191$ ,  $p > 0,05$  for all of them. Neither sex (% males) 50,7% vs 49,3%, nor arterial hypertension, diabetes, dyslipidemia or obesity differed between FS and non FS patients (60.5% vs 39.5%, 61.1% vs 38.9%, 52,2% vs 47.8 %, 52.9 % vs 47.1, respectively,  $p > 0,05$  for all of them). Both final confirmed IHD and pathological coronarography results were higher in FS patients (57% vs 43% and 56% vs 44%, respectively), but Odds ratio of them (1.5 (0.7–3.4) and 1 (0.2–3.9), respectively) was not higher for FS patients.

**Conclusions:** FS sensitivity for confirmed IHD is 56% in Spanish population. FS prevalence in patients with IHD suspicion is 52%. We confirm that FS patients are older than non FS ones. In this preliminary results, we can not corroborate that FS is associated with higher OR for IHD.

## **Mineral and bone disorder in chronic heart failure patients**

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**Objectives:** Mineral-bone disorders (MBD) are important prognostic factors in chronic kidney diseases (CKD), which are common in chronic heart failure (CHF). Our aim was to study MBD in CHF pts.

**Methods:** Serum phosphorus (P), calcium (Ca) corrected for albumin, calcitonin, intact parathyroid hormone (PTH), 25-OH-vitamin D (Vit D), markers of bone formation (osteocalcin-OC) and resorption (C-telopeptide of type I collagen-CTP, osteoprotegerin-OPG), glomerular filtration rate (GFR, CKD-EPI), urinary albumin excretion (UAE), Kansas City Cardiomyopathy Questionnaire (KCCQ) and bone mineral density (BMD) measured using dual-energy X-ray absorptiometry of lumbar spine (L1-4) and femur (Neck-N, Total-T) were evaluated in 207 CHF pts I-IV NYHA class without primary renal, endocrine, autoimmune, oncological and bone diseases [median (interquartile range) of age – 64 (57–70) years; left ventricular ejection fraction (LVEF, Simpson) – 30.8% (25.7–37.1), 86% males].

**Results:** Hypocalcaemia was in 48.3%, hypercalcaemia in 3.4%, hypophosphatemia in 10.3%, hyperphosphatemia in 6.8% of pts. Calcitonin was 4.67 (3.94–7.88) pg/ml. PTH [77.6 (38.2–136) pg/ml] was elevated (>62 pg/ml) in 59.8% (95% CI; 48–71.6). Vit D [47.3 (38.8–54.6) nmol/l] deficiency (<47.7 nmol/l) was in 53.8% (95% CI; 38.4–69.2). LVEF and GFR were decreased and UAE was elevated in high PTH pts compared to others ( $p < 0.05$ ). PTH correlated with CHF duration [53 (24–67) months:  $r = 0.62$ ,  $p = 0,002$ ] and Vit D ( $r = -0.5$ ,  $p = 0.01$ ). Osteopenia (T-score  $-1.2$ – $2.4$ SD) was in 40.5%

(95% CI; 22–59), osteoporosis (T-score  $< -2.5SD$ ) – in 32.4% (95% CI; 14.7–51.9) of pts. BMD correlated with KCCQ symptomatis (for ability of climbing stairs  $r=0.73$ ,  $p=0.027$  for N;  $r=0.68$ ,  $p=0.046$  for T), GFR ( $r=0.57$ ,  $p=0.039$  for N;  $r=0.7$ ,  $p=0.005$  for L1), UAE ( $r=-0.66$ ,  $p=0.036$  for N;  $r=-0.69$ ,  $p=0.026$  for T). T-score correlated with these parameters and PTH ( $r=-0.47$ ,  $p=0.033$  for N;  $r=-0.47$ ,  $p=0.033$  for T;  $r=-0.51$ ,  $p=0.019$  for L1;  $r=-0.53$ ,  $p=0.014$  for L4) and Vit D ( $r=0.63$ ,  $p=0.029$  for L4). OC was 17.8 (16–23.4) ng/ml; CTP – 0.41 (0.31–0.6) ng/ml; OPG–194 (151.5–244) pg/ml. OC correlated with PTH ( $r=0.39$ ,  $p=0.001$ ), L2 and L4 T-score ( $r=-0.35$ ,  $p=0.049$  and  $-0.41$ ,  $p=0.019$ ); CTP – with GFR ( $r=-0.76$ ,  $p<0.001$ ), Ca ( $r=-0.43$ ,  $p=0.045$ ), P ( $r=0.40$ ,  $p=0.046$ ); OPG – with PTH ( $r=0.34$ ,  $p=0.014$ ), calcitonin ( $r=0.28$ ,  $p=0.046$ ), BMD ( $r=0.42$ ,  $r=0.39$  for N,  $r=0.47$ ,  $r=0.017$  for T). Surviving was lower in group with higher levels of Ca\*P product ( $p=0.006$ ). Osteoporosis, hyperparathyroidism, calcitonin lower than median lead to poor survival ( $p<0.05$ ). There was a trend for adverse prognosis in lower Vit D and OPG and higher CTP concentration ( $p=0.05$ ).

**Conclusions:** Mineral and bone disorders are common and associated with severity of symptomatic, cardiorenal dysfunction and poor prognosis in CHF patient. Preventive strategies may be able to normalize mineral and bone metabolism, attenuate high bone loss and improve prognosis in CHF.

## Kounis syndrome – allergic angina after oral provocation test with metamizole

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**Introduction:** Kounis syndrome (KS) is potentially a life-threatening medical emergency with both an allergic reaction (AR) and acute coronary syndrome (ACS). The vasospasm of the coronary arteries and/or erosion or rupture of atherosclerotic plaques, induced by the release of inflammatory mediators in AR, have been suggested as the pathophysiological mechanism of this entity.

**Case report:** A 44 years old male without cardiovascular disease risk factors. The patient developed complaints of skin rash, generalized itching and angina, 10 minutes after oral provocation test with metamizole (143,75 mg). Electrocardiogram (ECG) demonstrated incomplete right bundle branch block and ST-segment elevation in V1 and V2 leads, de novo. Troponin I was negative, creatine kinase within normal range and IgE elevated (131 U/mL). Echocardiogram (ECHO) revealed hypokinesia of the apical segments of the inferior-septal and inferior walls. Coronary angiography revealed anterior descending artery with short, eccentric plaque in the middle segment, causing injury inferior to 30%. The patient was treated accordingly to the diagnostic hypothesis – KS secondary to oral provocation test with metamizole (nitrate 5 mg/24h, amlodipine 5 mg, prednisolone 0,5 mg/kg). There was normalization of ECG changes, the patient become asymptomatic and was discharged with scheduled follow-up visit. The ECHO was repeated 1 month later and no longer had the described changes.

**Discussion:** Incidence of KS is hard to delineate. It has been linked with several diseases, environmental exposures and a variety of drugs. In our case, oral metamizole acted as allergen,

triggering an acute AR accompanied by ACS. Three types of KS are recognized – our patient presented type I (normal coronary arteries, in whom the acute allergic reaction induces coronary artery spasm and consequently chest pain). There are no specific clinical practice guidelines for the KS treatment, so the current recommended treatment is the combined therapy of ACS and AR. Type I KS, characterized by coronary vasospasm, responds well to treatment with corticosteroids and H1/H2 receptor blockers in addition to coronary vasodilators, such as nitrates and/or calcium channel blockers, which was the strategy used in our patient.

**Conclusion:** AR could be the cause of ACS in patients with no cardiovascular risk factors so it should be taken into consideration in the differential diagnosis of ACS.

## Takotsubo cardiomyopathy – complications in clinical development

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**Introduction:** Takotsubo cardiomyopathy (TC) is unusual contributing for 1–2% of acute coronary syndromes (ACS).

**Case report:** 73years old female with hypertension and hypothyroidism resorted to the emergency department with acute onset chest pain at rest: electrocardiogram (ECG) – ST elevation in I, aVL, V5 and V6; troponin I and NT-proBNP elevated (3,61ng; 11612pg/ml); echocardiogram (ECHO) – hypokinesia of apical segments of the anterior and lateral walls; treated with acetylsalicylic acid, clopidogrel, enoxaparin, dinitrate, morphine, ranitidine and atorvastatin; coronary angiography and ventriculography – suggestive of TC (without coronary lesions, akinesia of apical segments of the anterior and lateral walls, good basal contractility). She was admitted and on 3rd day had an episode of atrial fibrillation, was treated with amiodarone and developed hemodynamic instability (HI), which conditioned brief hospitalization in intensive care. It was initiated hypocoagulation with warfarin. On the 13th day, new episode of arrhythmia, with asystole after amiodarone, reversed with cardiac massage. Posteriorly, developed chest pain radiating to left trapezius and aggravated on deep inspiration, pericardial friction rub, leukocytosis ( $14,3 \times 10^9/L$ ), elevated PCR and VS (29,9 mg/dL; 69 mm) and ECHO revealed circumferential pericardial effusion (22 mm), without HI, and recovery of ventricular function. It was established supportive therapy, with progressive improvement. She was discharged with scheduled follow-up visit. The ECHO was repeated 1 month later and no longer had the described changes.

**Discussion:** TC is characterized by the development of cardiac wall-motion abnormalities of the mid left ventricle and apex with relative sparing of the base, in the absence of coronary artery disease. The excess of catecholamines caused by physical or emotional stress may be at the root of this event, conditioning disturbance of ventricular contraction and function, by calcium overload. It stands out from ACS by more subtle elevation of cardiac markers, catecholamines and normalization of systolic

function in few weeks. The cardiogenic shock and arrhythmias are common, but pericardial effusion occurs only in some cases and acute pericarditis, as in this case, is rare, conditioning a poorer prognosis. Treatment is mainly supportive.

**Conclusion:** TC has similar clinical presentation to ACS, but different clinical outcome, whereby its timely recognition is crucial.

## Characteristics of patients in advanced stages heart failure

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**Objectives:** Hospitalizations represent deterioration in the quality of life of patients in advanced heart failure stages. The aim of this study is to analyze the epidemiology characteristics of hospital admissions of patients with heart failure and severe left ventricular dysfunction followed up in a heart failure unit during the last 12 months before the patient's death.

**Methods:** It is a retrospective study, that analyze qualitative and quantitative variables of the patients were followed in a heart failure unit from 2008 to 2013. It is described the kind of hospitalization, reason for admission and the features of it. It is compared to the same parameter in two different groups of survivor and dead patient.

**Results:** It was studied 599 patients: 45.7% diabetic, 18.2% COPD, 31.8% renal failure. 7.9% of the patients died. Average age was 70±9.9 years, 66% men and 34% women. The ventricular ejection fraction average was 30±11%. NTproBNP 283±537 mg/dL and uric acid 6±3.7 mg/dL. 27.3% of patients were in sinus rhythm with a heart rate 70±24 bpm. 70% of patients had an advanced functional grade (II–IV NYHA). The treatment was: angiotensin-converting-enzyme inhibitor (65%), angiotensin II receptor blockers (10%), b blockers (65%), aldosterone antagonist (70%), oral diuretic (95%), and antiplatelet therapy (45.5%). 72% of patients died from cardiac cause: 40.3% directly related to heart failure (multiorgan failure/cardiogenic shock) and 13.8% sudden death; and the rest of cause not heart. Patients who died in this period had a greater number of hospital readmissions (1.62 versus 0.2,  $p=0.001$ ) in relation to patients who were still alive and presented an average hospitable stay 2.24 times longer (29 days versus 12.7 days,  $p=0.03$ ).

**Conclusions:** Heart failure patients in advanced stages have a greater number of readmissions and hospital stays which represents an important consumption of healthcare resources, specially their last year of life. It is important to implement and promote palliative measures for the final phases of life in these patients.

## Lipid profile changes in familial hypercholesterolemia patients after their inclusion in the SAFEHEART follow up study

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**Objectives:** Heterozygous familial hypercholesterolemia (HeFH) increases the risk to develop premature atherosclerotic coronary heart disease. An adequate control of the lipid levels is necessary to reduce the incidence of cardiovascular events. However, it is unknown in clinical practice the lipid profile changes after HeFH diagnosis. The aim of this analysis is to describe the lipid profile changes in HeFH patients after their inclusion in the Spanish Familial Hypercholesterolemia Longitudinal Cohort Study (SAFEHEART follow up study).

**Methods:** Patient data were analyzed from the SAFEHEART follow up study, which recruited a total of 3745 subjects  $\geq 18$  years old from January 2004 to November 2013. The HeFH diagnosis was genetically confirmed in 2752 subjects. Follow-up data were obtained, including full lipid profile, in 2168 patients. Results: Median age was 44 years old (18–89 y.o). 1264 were male (45.9%). Median follow-up time was 1426 days (196–4418 days). Lipid profile data relating to the inclusion and at the last evaluation performed: total cholesterol (mg/dL) median 226 range (94–610) vs 206 (98–552),  $p<0.001$ , LDL-C (mg/dL) 156 (15.20–498) vs 133 (30–469),  $p<0.001$ , HDL-C (mg/dL) 50 (15–132) vs 53 (12–156),  $p<0.001$ , TG (mg/dL) 84 (10–582) vs 86 (21–721),  $p=0.049$ , non-HDL cholesterol (mg/dL) 175 (46–532) vs 150 (63–494),  $p<0.001$ .

**Conclusions:** HeFH diagnosis and its proper management are efficacious in a positive change of lipid profile. Therefore, an early FH detection program is crucial to reduce the incidence of cardiovascular events in this high risk population.

## Familial hypercholesterolemia: treatment and therapeutic targets in the SAFEHEART follow-up study (Spanish Familial Hypercholesterolemia Longitudinal Cohort Study)

Rubio-Marín P., Michán A., De Isla L.P., Alonso R., Fuentes-Jiménez F., Muñiz O., Díaz J.L., Andrés R., Hidalgo A.M., Miramontes P., Manjón L., López P.M.

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**Objectives:** Heterozygous familial hypercholesterolemia (HeFH) increases the risk to develop premature atherosclerotic coronary heart disease. An adequate control of the lipid levels is necessary to reduce the incidence of cardiovascular events. However, it is unknown if lipid control in HeFH patients follows the European guidelines (ESC/EAS). The aim of this study is to describe the changes in lipid lowering therapy (LLT) in HeFH patients and whether are achieving therapeutic goals (ESC/EAS).

**Methods:** Patient data were analyzed in a follow up study, which recruited a total of 3745 individuals from 18 years old. The HeFH diagnosis was genetically confirmed in 2752 individuals from January 2004 to November 2013. Follow-up data were obtained, including full lipid profile, in 2168 patients.

**Results:** Median age was 44 years old (18–89 y.o.). 1264 were male (45.9%). Median follow-up time was 1426 days (196–4418 days). Patients in treatment with maximum doses of statins (atorvastatin 40–80 mg or rosuvastatin 20–40 mg) 452 individuals (16,2%) follow up in 417 (15,7%) ( $p=0.14$ ). Patients taking maximum combined LLT (atorvastatin 40–80 mg or rosuvastatin 20–40 mg plus ezetimibe) 593 individuals (21,6%) follow up in 977 (36,8%) ( $p<0.001$ ). Patients in treatment with maximum tolerated LLT (at least a 50% LDL reduction treatment) 1329 individuals (48,3%) follow up in 1831 (69%) ( $p<0.001$ ). The percentage of subjects with a previous cardiovascular event achieving therapeutic targets (LDL-C  $<70$ mg/dl) at inclusion  $n=4$  (1.1%), follow up  $n=13$  (3.9%). The percentage of subjects without a previous cardiovascular event achieving therapeutic targets (LDL-C  $<100$  mg/dL) at inclusion  $n=89$  (3.7%), follow up  $n=182$  (7.9%).

**Conclusions:** Despite the improvement in LLT and in the achievement of LDL-C goals in the follow up, the percentage of individuals who achieve recommended lipid European Guide goals remains very low. This reality shows the need for new lipid lowering drugs more powerful to reduce LDL-C in FH patients.

## Inflammatory markers and adipokines in patients with metabolic syndrome in the presence or absence of coronary heart disease

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*Objective:* To study the inflammatory markers and adipokines in patients with metabolic syndrome in the presence or absence of coronary heart disease.

**Material and methods:** The study included 82 men at the age from 39 to 72. The first group (I) consisted of 40 men with arterial hypertension (AH) in combination with metabolic syndrome, the second group (II) included 42 men with coronary heart disease (CHD) and metabolic syndrome. All patients were examined to confirm or exclude CHD with the help of electrocardiogram, exercise testing, ultrasonic examination of the heart and coronary angiography.

**Results:** The patient groups under study were matched in age, sex, body mass index. Comparing the groups it was found that total cholesterol lipid profile and low density lipoprotein were increased in both groups, but significantly higher indices were in group I. The levels of apolipoprotein-B, the other marker of atherosclerosis of the coronary arteries raising the risk of cardiovascular diseases, was higher in patients of group II –  $114,6\pm 34,6$  mg/dL vs.  $90,5\pm 21,7$  mg/dL I group, ( $p<0,05$ ). The comparative analysis of plasma pro-inflammatory activity marker showed higher levels of interleukin-6 –  $6,35\pm 2,03$  ng/ml in group II vs.  $3,45\pm 1,12$  ng/ml, and C-reactive protein  $8,78\pm 2,79$  ng/ml vs.  $6,44\pm 2,75$  ng/ml ( $p<0,001$ ). The study also showed that the concentration of tumor necrosis factor (TNF- $\alpha$ ) was significantly higher in group II  $5,5\pm 2,38$  ng/ml vs.  $3,41\pm 1,29$  ng/ml in group I ( $p<0,001$ ). It confirms the role of these markers in the pathogenesis of coronary atherosclerosis. The level of cardioprotective protein apelin exceeded indices in patients with isolated AH in comparison with the group with CHD  $0,46\pm 0,17$  ng/ml vs.  $0,18\pm 0,15$  ng/ml ( $p<0,001$ ).

**Conclusion:** Obesity leads to the developing of chronic inflammation in adipose tissue as a source of pro-inflammatory hormones and cytokines, which serve as a basis for the development of secondary pathologies that accompany metabolic syndrome, primarily cardiovascular disease.

## Cardiac comorbidities in patients admitted in medical intensive care units for non-cardiac entities

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**Objectives:** Cardiovascular diseases are the main cause of death in the world. It is known that comorbidities impact negatively on prognosis, however it is still undetermined the specific importance of cardiac comorbidities. We aimed to identify the most common cardiac comorbidities in patients admitted in medical intensive care units for non-cardiac entities, and determine how these pathologies influence the clinical evolution of the patients.

**Material and methods:** Retrospective, observational case-control study. Two groups were selected: patients with known cardiac disease (Group A) and patients without cardiac diseases (Group B), from a population of intensive care patients, admitted for a non-cardiac entity. This study took place in Centro Hospitalar Cova da Beira and Hospital das Forças Armadas between December 2013 and January 2015. The clinical records were reviewed and the data was statistically analyzed.

**Results:** A total of 71 individuals were studied: 50 included in group A and 21 from group B. The mean age in group A was  $75,4\pm 9,2$  years versus group B  $56,8\pm 16,2$  years ( $p<0,001$ ). Patients from group A had a greater mortality rate (44% in group A vs 9,5% in group B;  $p=0,006$ ). Group A comorbidities included arrhythmic events, that increased by 47 times the risk of in-hospital death (56,2% of mortality vs 43,8% of survival,  $p=0,001$ ; OR=46,8; 95% CI 4,7–63,9). NYHA classification (OR=3,1; 95% CI 1,3–7,4) and APACHE II score (OR=1,1; 95% CI 1–1,2) have shown to be good mortality predictors. From the in-hospital complications, we emphasize atrial fibrillation, that increases by 8 times the risk of in-hospital death (47,4% of mortality vs 52,6% of survival,  $p=0,002$ ; OR=7,5; 95% CI 1,8–30,7), and shock (mainly septic), that results in a 9 times higher in-hospital mortality risk (40% of mortality vs 60% of survival,  $p=0,001$ ; OR=9,1; 95% CI 2–41,2). Group A patients prompted an increased use of inotropic agents in group A (30% group A vs 4,8% group B,  $p=0,027$ ).

**Conclusions:** Patients with cardiac comorbidities or complications, especially dysrhythmias, showed a higher mortality rate. This was mostly due to septic shock, what explains the higher use of inotropic agents in this group.

## Analysis of risk factors and structural features of patients with ischemic organ damage without stenosing arteriosclerosis

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**Objectives:** Heart and brain are interrelated target organs of vascular pathology, which clinical variants (ischemic heart disease, stroke) continue to lead in structure of death causes in developed countries. It is known that approximately 10–20% of patients undergoing diagnostic coronary angiography due to acute or chronic ischemic syndrome, have intact arteries. We will summarize risk factors, clinical and angiographic, genetic testing in patients with myocardial infarction or ischemic stroke, but without signs of atherosclerotic vascular damage. Genetic testing involves identifying the examined genetic polymorphisms of the following genes: lipid metabolism, structure and tone of the vascular wall, platelet coagulation and hemostasis, inflammation, histone deacetylase, CRP, epidermal growth factor receptor (VEGFR).

**Material and methods:** Pool for inclusion in the study was defined as all patients who have suffered myocardial infarction or stroke, under the supervision of the Hospital № 40 at the age of 20–59 years. The control group consists of healthy or practically healthy people. Each patient in the study start up map of the test, including the results of lipid profile with detailed indicators of coagulation, glycemic profile, ECG evaluation of possible focal changes, signs of coronary heart disease, echocardiography assessment of contractile ability of hypo-akinesia and ejection fraction, stress tests or Holter monitoring, ultrasound of cerebral arteries, the arteries of the lower limbs, measuring ankle-brachial index, coronary angiography and study of polymorphisms of genes predisposing to the development of coronary artery atherosclerosis and cerebral arteries.

**Results:** Mean age of studied contingent was 55 y.o.; 47 women (31%), 113 men (69%); 101 of which have a history of coronary artery disease (67%) and 17 (11%) revealed stroke; history of recurrent myocardial infarction had 9 people. Operations on the coronary arteries had 52 (35%) patients. The total duration of CHD was on average 1.2 years. Risk factors: smoking – 88 (59%) patients, obesity – 43 (29%) patients, dyslipidemia – 46 (31%), 89% had a history of hypertension, 77 (51%) – diabetes. In assessing lipid: average total cholesterol level was 5.2 mmol/l, LDL 3.2 mmol/l, TG 1.8 mmol/l.

**Conclusions:** Preliminary data suggest that there is a group of patients studied genotype and phenotype features in generalized atherosclerosis without evidence of stenosis, and identify a correlation between the severity of clinical manifestations and the degree of arterial injury with existing risk factors and structural features of DNA. The results will clarify the pathogenesis of fatal cardiovascular complications in patients regardless of the presence of atherosclerotic lesion.

### Role of different combined genes polymorphism (CYP4F2, VKORC1) on the dosing of phenindion in patients with valvular atrial fibrillation

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**Objectives:** The importance of predicting the patient's reaction on the anticoagulation therapy is well known. The reaction on the non-coumarine anticoagulants (AC) (phenindion) is different due to the individual variants of the patient's genotypes. Previously there were studied the influence of gene's polymorphism (VKORC1 and CYP4F2) on AC dosage (warfarin) separately. It was noticed that «wild» homozygote's genotypes needs the lower dosages of drugs and heterozygote's or pathological homozygote's types leads to disturbed dosing of drugs. The cooperative influence of gene's polymorphism of CYP4F2 and VKORC1, both involved in vitamin K metabolism, was in the interest of study.

**Material and methods:** 42 patients (20 male and 22 female), 27–78 years, valvular atrial fibrillation – were studied. The using of coumarin AC was impossible in all of them. All patients received phenindion in the dose of 30–130 mg daily with a target international normalized ratio (INR) of 2.0 to 3.0. Genotyping for polymorphism's marker V433M gen CYP4F2 and VKORC1 were designed using the PCR and RFLP (restriction fragment length polymorphism). Statistics were performed by Mann-Whitney U-test.

**Results:** Genotype GG («wild») of VKORC1 were found in 19 patients with achieved target levels in INR 2–3 (62%); phenindion dose – 83,8±4,2 mg (n=31). In GA type (n=7, 22%) – 75±3,1 mg and in AA type (n=5, 16%) – 60±0,0 mg. In the group of patients, that didn't achieve target levels of INR, the frequency referred to genotypes was the next: 64%, 27% and 9% respectively. Genotype CC (CYP4F2) was found in 26 patients (62%), so the dose of phenindion was 75±4,8 mg. Genotype CT – in 16 patients (38%) and the dose of phenindion was 60±3,7 mg. Genotype TT wasn't found at all. In the CC gr. (n=26) high dose of phenindion (>90 mg) was needed only in 2 patients (8%), versus 6 patients (37.5%) in the CT gr. (n=16), p=0.04 (significant statistically). The genes combination CT (CYP4F2) and GA/GG (VKORC1) resulted in summary phenindion dose 60±5,5 mg, combination of CC (CYP4F2) with GG (VKORC1) – 75±6 mg, so as in another gene's combination CC+AA\GA (VKORC) – 75±3,6 mg.

**Conclusion:** The revealed absence of suggested increasing of phenindion dose in the patients with CT genotype of CYP4F2 may be explained by the combination with another gene's polymorphism (GA and AA – VKORC1) in some cases; so as another gene's combination may change individual sensitivity to the drug.

### Carotid intima-media thickness and inflammation markers in individuals with cardiovascular risk factors

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**Objective:** To study the carotid IMT and inflammation markers in the individuals with cardiovascular risk factors (CV RF).

**Methods:** A cohort of 106 healthy individuals (44 men, 62 women,

average age 43.7±1.1) was examined for the following CV RF: smoking, the increased blood pressure, dyslipidemia, overweight, physical inactivity, family history of cardiovascular diseases. The level of high-sensitivity C-reactive protein (hsCRP) and cytokines: tumor necrosis factor alpha (TNF-α), interleukins (IL) -1, -8 have been studied by enzyme immunoassay test systems (SeroELISA, DSL, USA). The IMT and carotid atherosclerotic plaques were determined by ultrasonic scan (Vivid 5, GE, Germany) in B-mode. The correlation, factor and cluster analysis was used for statistical data processing.

**Results:** By means of cluster analysis all patients were divided into 3 groups (clusters) that significantly differed in the carotid IMT from each other (p=0.04–0.02). All groups were comparable in age and gender (p>0.05). The performed analysis revealed significant difference between these groups in the blood levels of hsCRP and cytokines (p<0.05). In group 2 correlation analysis revealed a close link between IMT and hsCRP (r=0.36; p=0.02), IMT and TNF-α (r=0.51; p=0.01). The study also found a direct correlation between IMT and CRP (r=0.41, p=0.01), IMT and TNF-α (r=0.54; p=0.01), IMT and IL-8 (r=0.59, p=0.01) in group 3. However, these significant correlations were not found in group 1.

**Conclusions:** The increase of IMT and blood levels of hsCRP and cytokines was detected in healthy individuals with CV RF. The presence of atherosclerotic plaques is associated with a significant increase in hsCRP and TNF-α levels.

## Relationship between intima-media thickness with blood pressure and vascular microinflammation

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**Objective:** To determine the carotid intima-media thickness (IMT) and inflammatory markers in healthy subjects with different levels of BP.

**Methods:** 194 subjects (93 men, 101 women, average age 43.2±0.9) were split into 5 groups according to the blood pressure level. Group 1 – 35 patients with BP level <110/70 mmHg, group 2 – 41 patients with BP level 110/70–119/79 mmHg, group 3 – 41 subjects with BP 120/80–129/84 mmHg, group 4 – 39 subjects with high normal BP (130/85–139/89 mmHg), and group 5 consisted of 38 patients with BP > 140/90 mmHg. All groups were comparable in age and gender (p>0.05). The carotid IMT was determined by ultrasonic scanning (Vivid 5, GE, Germany). The level of high-sensitivity C-reactive protein (hsCRP) and cytokines: tumor necrosis factor alpha (TNF-α), interleukins (IL) -1, -8 have been studied by enzyme immunoassay test systems (SeroELISA, DSL, USA).

**Results:** There was no difference in IMT in groups 1–3 (p>0.05), but in groups 4 and 5 its meaning differed significantly (p1,2,3-4,5=0,01-0,001). The significant difference in the levels of hsCRP and proinflammatory cytokines was detected between groups 1, 2, 3 and 4, 5 (p1, 2, 3 -4, 5=0,01-0,001). In groups 4 and 5 the correlation analysis revealed a direct link between systolic BP and hsCRP (r=0,49-0,57, p=0,02-0,01),

and between IMT and hsCRP, IL-1, IL-8, TNF-α (r=0,37-0,65, p=0,04-0,01).

**Conclusions:** The IMT increase is associated with BP level and proinflammatory cytokines concentrations. The vascular wall remodeling accompanied by vascular microinflammation is noted in subjects with high normal BP as well as in patients with arterial hypertension.

## Genetic predictors of calcific aortic valve disease in South Russia

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**Objective:** The aim of this study is to identify the genetic background of the degenerative aortic valve (AV) calcification. **Methods:** The study was an open non-randomized comparative (case-control) investigation involving 102 patients (48.5% males, mean age 72.5±7.5 years) with calcified AV (main group) and 92 patients with comparable clinical and biographical data and intact AV (controls). The population of the two groups underwent genotyping test through the PCR method with electrophoretic detection of the data (leukocyte DNA employed as the substrate). The procedure focused on the following genetic polymorphisms: Leu28Pro (rs80357266) of the apolipoprotein E (apoE) gene, Gln192Arg (rs662) of the paraoxonase 1 (PON1) gene, 8202A>G (rs1169732) of matrix metalloproteinase type 9 (MMP9) gene, 536C>T (rs11551797) of the tissue inhibitor of the matrix metalloproteinases type 1 (TIMP1) gene, 66T>G (rs28357094) of the osteopontin (OPN) gene, 138T>C (rs1800802) and 7G>A (rs1800801) of the matrix GLA-protein (MGP) gene, and TagIC>T (rs 731236) of the vitamin D receptor (VDR) gene. The predictive role of the variables was calculated via the odds ratios (OR) and their confidence intervals (95% CI). The significance of the differences was assessed through  $\chi^2$  criterion.

**Results:** The genotypes frequencies and alleles' distributions for the studied population lay within the Hardy-Weinberg equilibrium. The groups under investigation showed no difference in the frequencies of apoE, PON1, MMP, TIMP1 and 138T>C allele of the MGP gene. The patients with AV calcification revealed significantly higher presence (compared to the control) of the following alleles: 66G of the OPN gene (45 vs. 21, OR 2.82 (95% CI 1.51; 5.25), p<0.01), 7A of the MGP gene (52 vs. 35, OR 1.81 (95% CI 1.03; 3.2), p<0.05) and TagI t of the VDR gene (33 vs. 15, OR 2.58 (95% CI 1.3; 5.15), p<0.01). The subgroups with aortic stenosis (68 persons) and AV calcification without stenosis (34 persons) were identified. 66G allele of the OPN gene and 8202G allele of the MMP9 gene were significantly prevalent in patients with aortic stenosis (48 vs. 17, OR 2.4 (95% CI 1.02; 5.62), p<0.01 and 53 vs. 15, OR 4.48 (95% CI 1.84; 10.87), p<0.01 respectively).

**Conclusions:** Therefore, genetic polymorphisms of the OPN (rs28357094), VDR (rs 731236) and MGP (rs1800801) genes can predict the development of the calcific aortic valve disease. Genotyping of the said markers may be used to identify patients with the higher risk of AV calcification.

## Resistant hypertension and poor controlled dyslipidemia in severe obstructive sleep apnea

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**Objective:** To characterize the efficacy of combined treatment of patients with arterial hypertension (AH) and dyslipidemia in obstructive sleep apnea (OSA) of varying severity.

**Materials:** The study included 80 patients with OSA, AH and dyslipidemia in middle age 49.6 years. Cardiorespiratory monitoring using a screening system Breas SC 20 (Sweden) was performed. Patients with mild to moderate OSA were 44, with severe OSA – 36 patients. Combined antihypertensive therapy included lisinopril, indapamide, and bisoprolol. Correction of dyslipidemia was conducted with simvastatin 20 mg. Continuous positive airway pressure (CPAP) therapy was not performed. The treatment duration was 2 years.

**Results:** Marked the worst performance in patients with severe OSA was noted: systolic blood pressure was achieved only in 12% of patients with severe OSA. In mild syndrome similar figure was 72%. 17% of patients with severe and 64% in mild OSA reached the target diastolic blood pressure level. In all groups showed improvement in lipid profile. There were no significant differences in dynamics of high-density lipoprotein (HDL) cholesterol, triglycerides, atherogenic index ( $p > 0.05$ ) in the severe apnea group. Achieving target levels of low density lipoproteins in the mild apnea was 60%, in the group of heavy OSA – 12%, reaching the level of HDL cholesterol – 29% and 0%, respectively.

**Conclusion:** In severe OSA without CPAP therapy observed resistance of both hypertension and dyslipidemia to drug therapy.

## The correlation of uric acid levels with the occurrence of atrial fibrillation in patients with metabolic syndrome

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**Objectives:** Uric acid (UA) is a cardiovascular risk marker associated with oxidative stress and inflammation. There are some evidences that the prevalence of atrial fibrillation (AF) is increased in patients with metabolic syndrome (MetS). Both conditions seem to be associated with inflammation and oxidative stress. The aim of this observational study was to investigate the association between UA levels and AF in patients with MetS.

**Methods:** We evaluated 51 patients with MetS (group A) and 42 patients with MetS and AF (group B), mean age  $58.4 \pm 9.7$ , respectively  $68 \pm 8.8$  years, 65% F. We excluded subjects with coronary artery disease, congestive heart failure, valvular heart disease, congenital heart disease, cardiomyopathy, renal

failure, inflammatory conditions, thyroid dysfunction, respiratory diseases, and those who were taking drugs that affect UA metabolism (apart from diuretics). In the group B: 20 pts. had paroxysmal AF, 3 pts. persistent AF and 19 pts. permanent AF.

**Results:** After univariate analysis, age, duration of hypertension, serum creatinine, serum UA, left atrial diameter (LAD) and volume index (LAVI) were significantly increased in group B compared with group A, while the estimated glomerular filtration (eGFR) level was much lower in patients with AF than in those without AF. There was no correlation with left ventricular hypertrophy or the glycated hemoglobin levels. After multivariate logistic regression analysis, the independent predictors of AF were UA (OR: 1.005; 95% CI: 1.002–1.009,  $p = 0.005$ ), LAD (OR: 1.12; 95% CI: 1.071–1.19;  $p < 0.001$ ) and LAVI (OR: 1.1; 95% CI: 1.06–1.13;  $p = 0.002$ ).

**Conclusion:** We demonstrated an independent association between increased serum UA levels and the occurrence of AF in patients with MetS, suggesting the role of inflammation in the pathogenesis of AF.

## Diastolic heart failure – the enigma

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**Objective:** Heart failure with preserved ejection fraction (HFpEF) accounts for almost half of the cases of heart failure, and is associated with high mortality and short-term readmission. The authors intend to characterize the patients hospitalized with the diagnosis of HFpEF.

**Methods:** Observational retrospective study based on the collection of clinical data of 48 patients admitted in an internal medicine ward, during 2014, with the diagnosis of HFpEF. HFpEF is defined as: left ventricle ejection fraction  $> 45\%$ , atrial volume  $> 34 \text{ mL/m}^2$ , septal E wave  $< 0.08$  and lateral  $< 0.10$ . Statistical analysis in Statistical Package for Social Sciences v21.

**Results:** 1) The vast majority of patients of the sample studied is over the age of 65 years (93.5%), and most of them is above 80 years (54.3%); 2) The female gender (FG) is more frequent (60% vs. 32%); 3) 14% had been admitted last year; 4) The length of hospitalization is longer in FG ( $10.2 \pm 8.4$  vs.  $7.9 \pm 2.4$  days); 5) Comparing comorbidities between genders, there are no differences in hypertension, dyslipidaemia, obstructive lung disease, anemia and smoking, but there is a higher tendency to diabetes in males (64.3% vs. 35.7%,  $p = 0.08$ ); 6) Upon admission, the FG present less dyspnea (30% vs. 37.5%,  $p = 0.744$ ), less peripheral edema (12.5% vs. 20%,  $p = 0.694$ ) and lower NYHA class (class I, 63.3% vs. 56.3%); 7) FG present a lower readmission rate at three months (14.8% vs. 26.7%,  $p = 0.425$ ).

**Conclusions:** HFpEF is an understudied entity, but with high prevalence in the elderly and very elderly, causing frequent hospitalizations. The FG present more prolonged hospitalization, without any apparent connection with clinical severity, functional class or associated pathologies. Further studies are needed with larger populations.



## Survival of patients with congestive heart failure in the representative sample of Ryazan region

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**Objective:** To study the survival and adverse prognostic factors in CHF patients, revealed by screening of representative sample of Ryazan region population.

**Material and methods:** In 2002 as a part of Russian National epidemiological "EPOCH" study, a representative sample of Ryazan region population was evaluated with 95.3% response rate (2098 subjects, mean age 44.8±18.6 years). 233 respondents with suspected CHF were revealed (with any cardiovascular disease present combined with complaints for dyspnea while walking at own pace). In 167 of them the diagnosis was verified in cardiology hospital, 7.8% of subjects had signs of systolic dysfunction (LVEF < 50%). The respondents' vital status monitoring was carried out prospectively with annual analysis of endpoints.

**Results:** During the prospective 4-year follow-up of 167 patients with verified CHF, 39 patients have died. Annual mortality rate was 5.8%, 4-year mortality – 23.4%. The direct causes of death were: stroke (35.9%), decompensated heart failure (28.2%), sudden cardiac death (12.8%), myocardial infarction (10.3%), other CHF complications (5.2%), extracardiac causes (7.7%). As compared to survived CHF patients, the deceased ones were older (mean age 72.6±8.4 vs. 66.3±9.5, p=0.003), had more severe NYHA functional class, p<0.001, had signs of fluid retention (59.0 vs. 23.4%, p=0.001), more frequently had a history of stroke (33.3 vs. 10.9%, p=0.001), smoked (28.2 vs. 11.7%, p=0.013) and had signs of alcohol abuse (12.8 vs. 3.1%, p=0.033). The deceased had significantly higher linear and volume LV dimensions and lower LVEF as compared to survived, they also had grade 3 mitral regurgitation more frequently. In stepwise multifactor regression analysis by Cox proportional hazards model, only NYHA functional class (p=0.001) and age (p=0.01) were independent mortality predictors, and LVEF lost its prognostic significance, despite the results of single factor analysis.

**Conclusions:** 4-year survival rate of NYHA I-IV functional class patients, 92.2% of whom had preserved LV systolic function, was 76.6%. Age and NYHA functional class were independent predictors of all-cause mortality.

## A snapshot of blood pressure measurements in hospitalised patients: a missed opportunity for targeted intervention?

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**Objectives:** Ireland has a high burden of hypertensive illness with a prevalence of over 60% in adults over 45 years of age. In

this condition a large percentage of patients are not aware of the diagnosis and even when the diagnosis is clear a large percentage of patients are not adequately controlled. When patients are hospitalised regular blood pressure (BP) measurements are taken and a unique opportunity exists to identify and treat previously unrecognised hypertensive illness. In this study we sought to identify the number of inpatients who have uncontrolled and previously undiagnosed hypertension with the aim of identifying an obvious opportunity for screening.

**Methods:** A chart and bedside survey of all hospitalised patients was performed and the following data obtained: age, sex, weight, blood pressure (mean of last 3 readings). Hospital notes were reviewed to identify if there was a known history of hypertension and to establish if any cases of high blood pressure were in fact acted on and treated. Data was collected on the same day from all the wards in our hospital which is a level three district general hospital. For the purpose of this study uncontrolled blood pressure was defined as a blood pressure above 140/90 (mean of last 3 readings).

**Results:** A total of 92 patients were reviewed and the average BP was 128/72 mmHg (±17/10). Of these 92 patients reviewed 46% (n=42) were known to have hypertension. 23% (n=21) patients had a blood pressure above 140/90 mmHg. Of these patients with an uncontrolled blood pressure, 48% (n=10) were known to be hypertensive and 52% (n=11) were not on any antihypertensive medication.

**Conclusions:** This audit showed that half of the hospitalised inpatients had hypertensive illness and that in the remaining patients reviewed there were 10% with blood pressure in the hypertensive range. This was not noted by the medical teams and reflected a missed opportunity for optimal cardiovascular risk modification. In these patients with borderline hypertension it seems sensible to arrange 24h BP monitor and inform GP on discharge letter.

## Protein binding fatty acids in diagnosis of acute myocardial infarction (GIANT trial)

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**Objective:** To assess the practical importance of evaluation of the protein binding fatty acids (FABP) in differential diagnostics of an acute coronary syndrome.

**Methods:** The study included 1049 patients (671 men and 378 women) (middle age of 62,7±0,4 years) with suspected acute coronary syndrome and duration of clinical presentations between 1 and 12 hours. Thus the myocardial infarction was diagnosed in 69% of cases, unstable angina – in 24%, other cardiac diseases – in 5%, extracardiac diseases – in 2%. The FABP level was evaluated with immunochromatographic test "Cardio-FABP" (NPO Biotest, Novosibirsk) (sensitivity 15 ng/ml); troponin I – with usage of Troponin I WB-Check-1 test (VEDALAB, France) (sensitivity 1 ng/ml).

**Results:** The treatment was carried out according to standards. A balloon angioplasty and/or stenting of coronary arteries are

carried out 22% of patients, thrombolytic therapy – in 21%, the delayed endovascular intervention – in 10%, bypass grafting – in 2%. Complications within 72 hours after ACS occurrence: heart failure of the II–IV FC (Killip) became perceptible in 23% of cases, early post-infarction angina in 4%, recurrent myocardial infarction in 2%, pulmonary thromboembolism – in 0,3%, all-cause mortality was 4%. The FABP-test was positive in 53,5% of all cases (sensitivity – 73,8%, specificity – 92%, accuracy – 79,3%). Troponin I test was positive only in 33,4% (sensitivity – 46,7%, specificity – 97,2%, accuracy – 62,2%).

**Conclusions:** Express-test Cardio-FABP in combination with other traditional biomarkers of myocardial necrosis, allows to diagnose an acute myocardial infarction more precisely, especially in early period of the disease. The method will have the larger practical importance in the presence of difficult diagnostics of an acute myocardial infarction, for example, absence of permanent elevation of the ST segment, non-specific ECG changes, existence of intra-ventricular conduction disturbances or atypical clinical presentations of MI.

### **Influence of complex therapy with mexicor on restoration of coronary function in patients with myocardial infarction**

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**Objective:** To assess the efficiency of cardioprotective action of mexicor at various regimens of administration in patients with myocardial infarction.

**Methods:** 300 men with STEMI were enrolled in the study. Group 1 included 109 patients, mean age of 53±8,1 years, treated with thrombolysis in combination with intravenous administration of mexicor in dose of 200 mg, followed with mechanical recanalization and angioplasty of infarct-responsible coronary artery (IOA) with intracoronary injection of mexicor in dose of 200 mg. 101 patients of group 2, mean age of 54±9,1 years, were treated with the first administration of mexicor in dose of 200 mg intracoronary followed by endovascular intervention. In control group – 90 patients (mean age 58±11,1 years) angioplasty without usage of mexicor was carried out. In groups 1 and 2 the scheme of treatment with mexicor was: 600 mg/day intravenously 5 days, then 600 mg/day intramuscularly 9 days, then 300 mg/day per os during 1 year.

**Results:** In 12 hours after endovascular procedure concentration of troponin-I and myoglobin was less in the groups receiving mexicor. In 7 days left ventricle ejection fraction (LVEF) in the 3rd group (41±5%,  $p<0,05$ ) were lower, than in the 1st (49±8%) and the 2nd (47±6%) groups. In 10 days at a control ventriculography in groups 1 and 2 it is reliable above LVEF, final diastolic and systolic volume of LV. In 1 month indicators of an oxidizing stress were lower ( $p<0,05$ ) in groups with mexicor: diene conjugates (nmol/l): 10,1±0,3, 11,3±0,4, 14,0±0,5; malon dialdehyde (nmol/l): 9,8±0,3, 10,3±0,3, 12,5±0,2 (in groups 1, 2 and 3, respectively). In group 1 decrease of defects of perfusion in pools of the majority of coronary arteries was the most significant. In 1 year in groups 1 and 2 there were

more patients with low functional class of angina pectoris than in the 3rd one. At mexicor's users the risk of occurrence of acute coronary attacks was less on 8,5%, recurrent myocardial infarction decreased by 2,8%, death for 2,2%.

**Conclusions:** Complex treatment with mexicor is the most effective at early stages of myocardial infarction. It promotes prophylaxis of reperfusion damages and positively influences on ischemic myocardium, considerably increases clinical efficiency of methods of restoration of coronary blood flow, allows to prevent recurrence and transition of angina to higher functional classes.

### **Analysis of structure of a cardiac rhythm at patients with ACS and paroxysmal atrial fibrillation after carrying out electrical cardioversion**

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**Objective:** To estimate structure of a cardiac rhythm at patients with the acute coronary syndrome (ACS) and a paroxysm of atrial fibrillation by means of the analysis of RR-and RR-of intervals. Material and methods: The studied group – 70 men (mean age of 55,6±3,2 years) with ACS and a paroxysm of atrial fibrillation, group of comparison: 30 healthy men (mean age of 55,6±3,2 years). Patients of the studied group received a necessary standard pharmacotherapy. Cardioversion was carried out for 1–7 days according to the emergency or planned indications. Registration of intervals of RR-and RR was carried out by means of a 12-channel electrocardiograph, spectral components by means of the hardware-software complex «Dinamika-M» (St.-Petersburg, Russia).

**Results:** Right after cardioversion the analysis of RR-intervals appreciable depression of average values of the general spectral power in comparison with control group was established. The share of fast waves (HF range) – 13%, in control group – 27%. At a regimen of averaging of RR values in all frequency ranges the power augmentation at 12%, and also augmentation at 15% of slow waves was noted (VLF range) in the analysis of RR-intervals. In a day after cardioversion in the analysis of RR-intervals rising of average values of the general density of a range and spectral density in all frequency ranges was noted. Average values of indicators of RR intervals in the VLF range were also enlarged. The maintenance of the HF domain accrued to 31% for RR-intervals and to 33% for RR intervals. By 5–7 days the same indicators were much higher in comparison with control group: 23% for these RR-intervals (in control group – 11%), in the analysis of RR intervals – 36% (in control group – 17%).

**Conclusions:** The data of the analysis of RR-and RR-intervals received by means of the Dinamika-M complex characterize function of sinoatrial node and rhythmic activity of auricles. The method can be used wider in clinical practice for an assessment of variability of a heart rhythm and structure of a cardiac rhythm at patients with ACS and atrial fibrillation after carrying out a counter shock.

## FAR NHL – FARmacology and NeuroHumoral activation in heart failure registry

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**Objectives:** New ESC guidelines on heart failure were published in 2013. Our aim: to assess adherence to new guidelines for diagnosis and treatment of chronic heart failure in a big cardiology centre (University hospital) with specialized heart failure care.

**Methods:** Prospective data from stable out patients with chronic heart failure were collected.

**Results:** Data from 250 consecutive patients were collected in a 6 month observational survey. Mean age was  $67.8 \pm 8.7$  years, 78% were male. The diagnosis was based on sign and symptoms plus confirmed left ventricle dysfunction in all (100%) patients (EF < 50%). Mean ejection fraction was  $34.2 \pm 6.8\%$ . Ejection fraction < 35% was found in 125 (50%) of the patients. 169 (67.6%) were on sinus rhythm, mean heart rate was  $78 \pm 9$  beats per minute. 158 (63.2%) were NYHA class II, the etiology of heart failure was ischemic heart disease in 142 (57%) of the patients, dilated cardiomyopathy – 100 (40%), 7 – other diagnosis. Co morbidities were frequent – hypertension 71 %, dyslipidemia 67 %, diabetes mellitus 36%, abnormal renal functions 33%, anemia 37%. Mean AHEAD score was 2.2 (AHEAD score = A – atrial fibrillation, H – hemoglobin < 130 g/l for male and 120 g/l for female (anemia), E – elderly (age > 70 years), A – abnormal renal parameters (creatinine > 130  $\mu\text{mol/l}$ ), D – diabetes mellitus). Beta blockers (BB) were used in 88%, RAAS blockers in 92% (ACE-I 69%, AIIA 23%) and aldosterone blockers in 64%. But only 16% had the recommended dose of BB and 11% the recommended dose of ACE-I. The most frequent explanation for low doses was hypotension. More than one half (57%) were treated non-pharmacologically (8% pacemaker, 18% ICD, 31% ICD + biventricular pacemaker). Mean BNP and NT-pro BNP level will be available during the congress.

**Conclusions:** Patients with chronic heart failure followed in specialized heart failure departments are properly diagnosed and treated according to ESC guidelines. Maybe an attempt to increase the BB and ACE-I doses could be stressed. The long term prognosis will be evaluated using the AHEAD score classification.

## AHEAD score – long-term risk classification in acute heart failure

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**Objectives:** Acute heart failure is a wide clinical syndrome and prognosis depends on large list of factors. So far there is no widely used long-term simple prognostic scoring system. The aim of the study to determine the role of comorbidities for the

prognosis of patients hospitalized for acute heart failure using the AHEAD score system (A – atrial fibrillation, H – hemoglobin < 130 g/l for male and 120 g/l for female (anemia), E – elderly (age > 70 years), A – abnormal renal parameters (creatinine > 130  $\mu\text{mol/l}$ ), D – diabetes mellitus).

**Methods:** For the statistical analysis data from 5846 patients with prime hospitalization for acute heart failure (AHEAD registry; derivation cohort) were used to build AHEAD score. The Acute Heart Failure Database (AHEAD) Network registry comprises consecutive patients from 10 centers with 24-h catheter laboratory services and centralized care for patients with acute coronary syndromes and from five regional centers. Each risk factor of the AHEAD score was count as 1 point. The model was validated externally on international cohort of similar patients in the GREAT registry (n=6315).

**Results:** Mean age was  $72 \pm 12$  years, 61.6% of them were above 70 years, 43.4% were women. Atrial fibrillation was present in 30.7%, anemia in 38.2%, creatinine > 130  $\mu\text{mol/l}$  (abnormal renal parameters) – in 30.1%, and diabetes mellitus – in 44%. Mean AHEAD score was 2.1, the one year mortality for score 0 was 13.6%, for score 1 point 23.4%, for score 2 points 32.0%, for score 3 points 41.1%, for score 4 points 47.7% and for score 5 points 58.2% ( $p < 0.001$ ). The 90 month mortality for score 0 was 35.1%, for score 1 point 57.3%, for score 2 points 73.5%, for score 3 points 84.8%, for score 4 points 88% and for score 5 points 91.7% ( $p < 0.001$ ).

**Conclusions:** The AHEAD score system is a simple scoring system using comorbidities for estimating the short and long term prognosis in patients hospitalized for acute heart failure. Each comorbidity (age) increases the one year mortality by about 10%.

## From trivial to intricate

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**Case report:** A 59 years old male, with no previous medical history, was admitted in the emergency department for syncope (without sphincter relaxation or tonic-clonic seizures). Immediately after admission in our department, as well as on the 24h ECG monitoring, 2 episodes of non-sustainable ventricular tachycardia could be observed, indicating a probable arrhythmic etiology of the syncope (the EEG performed in the emergency department ruled out any neurological involvement). Considering the ECG changes (1 mm ST segment depression in DII, DIII, aVF, V5, V6, along with negative T waves) we decided to perform coronarography, which revealed multiple lesions: occluded LAD with recharging from collateral vessels, sub-occluded PDA, 75–90% stenosis of the RCA segment III, 50–75% and more distally 75–90% stenosis of the circumflex artery segment II, occluded postero-lateral branch. Echocardiography revealed a dilated LV (80/70 mm), with severe segmental hypokinesia. Echocardiography stress test with dobutamine expresses viability criteria for the inferior and lateral territory, so we decided to perform PCI on the PDA, followed by BMS implantation, which was carried out

successfully without any complications. The patient returned to our department after 3 months for ICD placement for secondary prevention of sudden cardiac death. The patient's evolution was favorable, with no angina or electric shocks to the present day.

**Discussion:** We should always be careful when approaching a patient with syncope, because what may seem very simple and trivial at a first glance could actually hide a more intricate pathology.

## Pericardial thickening: one single clue, several differential diagnoses

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**Introduction:** Pericardial tuberculosis is a rare condition presenting with nonspecific symptoms such as fever, chills, dyspnea, night sweats, friction rub and chest pain. It may be suspected if there is a pericardial thickening or effusion.

**Case report:** A 19-year-old male went to the ER complaining about fever (2 consecutive days, max. 42°C). He referred no relevant medical history, no hereditary familial diseases and no epidemiological risk factors besides unsafe sexual contact with a female. Functional inquiry revealed a 4-months history of right inferior limb pain, painful homolateral inguinal adenopathies and 1-month history of intermittent atypical chest pain, asthenia, vespertine sudoresis, anorexia and 5% weight loss in the previous week. Physical examination was significant for skin pallor and fever. Lymph node exploitation revealed soft, elastic, bilateral inguinal adenopathies. Laboratorial tests were positive for anemia of chronic disease, C-reactive protein (17.8 mg/dL) and sedimentation rate (100 mm/h) elevation. Autoimmune study was dubious: a single weakly positive ANA (1/160) and a borderline angiotensin-converting enzyme (65 U/mL). Serologies and blood cultures were negative and Mantoux test unreactive. Toracoabdominopelvic CT scan as well as ECG normal. Inguinal lymphadenopathy biopsy: "reactive process, no lymphoproliferative disorder". Under endocarditis suspicion, a transthoracic echocardiogram was performed and came upon a "thickened pericardium and no vegetations", confirmed by transesophageal. Cardiac MRI revealed: "dilated left ventricle, non constrictive, conserved systolic function and small pericardial effusion". After multidisciplinary discussion, once the patient maintained feverish, empirical doxycycline was initiated (failed) and pericardial biopsy/pericardiocentesis pondered. Due to the risks of the latter, they were postponed. Despite negative Mantoux test, pericardial tuberculosis remained suspicious; IGRA was done and proved positive. A trial of antituberculous drugs plus steroid was started. One week after, the inflammatory laboratory tests were significantly lower.

**Discussion:** Nonspecific signs like fever have broad range of diagnostic hypothesis. Even under exhaustive investigation, the diagnosis can remain presumptive. Pericardial tuberculosis remains the final diagnosis in our case, based on the pericardial

thickening, positive non-sensitive IGRA test and the good response to the antituberculous chemotherapy trial.

## Age-specific associations between obesity and sub-clinical cardiac or vascular changes in women

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**Objective:** To explore the association between obesity and sub-clinical measures of cardiac and vascular structure in women of different age.

**Methods:** Cross sectional comparison of female patients (pts) with obesity to normal weight females in three age groups. 382 Caucasian pts without known history of diabetes mellitus or CVD were included: 111 adolescents and young adults (15–20 y., 57 obese), 127 women of reproductive age (20–40 y., 65 obese), 144 postmenopausal women (44–65 y., 77 obese). Serum levels of lipids, glucose; intima-media thickness of common carotid artery (IMT), carotid-femoral pulse wave velocity (PWV), LV mass index (LVMI, g/m<sup>2</sup>), glomerular filtration rate (GFR EPI) were evaluated, 24-hour ABPM was performed.

**Results:** In all groups obese pts had higher rates of hypertension (HT) (39 vs 4; 48 vs 8; 70 vs 32%,  $p < 0,01$ ), metabolic syndrome (MS), higher night SBP, LVMI ( $p < 0,01$ ), IMT ( $p < 0,05$ ) than age-matched non-obese pts. In 1st group obese pts had higher day, night pulse pressure (PP) and rates of high night SBP ( $p \leq 0,01$ ), higher rates of left ventricular hypertrophy (LVH) and increased IMT ( $p < 0,01$ ). In 2nd group obese pts had higher night SBP, DBP, lower night-day BP ratio ( $p \leq 0,01$ ), higher GFR EPI ( $p = 0,04$ ), increased IMT ( $p < 0,05$ ). In 3d group obese pts had higher day SBP, day and night DBP, PP ( $p < 0,01$ ), higher rates of LVH ( $p < 0,01$ ),  $PWV > 12$  m/s ( $p = 0,01$ ). On univariate analysis, in total group there was a correlation between LVMI, IMT, PWV and age ( $r = 0,53; 0,66; 0,68$ ), BMI ( $r = 0,61; 0,32; 0,15$ ), WC ( $r = 0,59; 0,32; 0,21$ ); GFR and age ( $r = -0,78$ ). In 1st group there was a correlation between LVMI, IMT and BMI, WC, MS, smoking status, day SBP, night and day PP; IMT and HT. In 2nd group there was a correlation between LVMI, IMT and BMI, WC, MS; PWV and MS; GFR and age. In 3d group there was a correlation between LVMI and age, BMI, WC, HT, night and day SBP, MS; IMT and night and day SBP, PP; PWV and night and day SBP; GFR and age. Multiple regression analysis among age, BMI, WC, HT revealed that determinants for LVMI were age ( $\beta = 0,36$ ) and BMI ( $B = 0,52$ ), for IMT were age ( $B = 0,53$ ) and BMI ( $B = 0,2$ ), for PWV and for GFR was age ( $B = 0,57$ ,  $B = -0,82$ ). In 1st group determinants for LVMI was BMI ( $B = 1,18$ ), for IMT were BMI ( $B = 1,61$ ) and WC ( $B = 1,1$ ), for PWV was age ( $B = 0,51$ ). In 2nd group – for LVMI was BMI ( $B = 0,54$ ). In 3d group – for LVMI were age ( $B = 0,23$ ), BMI ( $B = 0,57$ ) and HT ( $B = 0,17$ ), for PWV were HT ( $B = 0,2$ ), ( $p < 0,05$ ).

**Conclusions:** There are age-specific associations between obesity and sub-clinical cardiac or vascular changes in women. Obesity is associated with increased LVMI and LVH in all age groups, with increased IMT only in young females, and is not associated with PWV and low GFR.

## Original physical rehabilitation program at patients with ST segment elevation myocardial infarction and percutaneous coronary intervention

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**Objective:** To estimate efficiency of the developed program of physical rehabilitation (PR) at patients with ST segment elevation myocardial infarction (STEMI) after percutaneous coronary interventions (PCI) according to spiro-bicycle-ergometry test (BET) data.

**Methods:** We randomized 69 patients with STEMI after PCI. The main group (MG) was made by 34 patients at the age of  $50,3 \pm 1,3$  years, they used the developed PR program taking into account completeness of a revascularization (according to TIMI scale) and myocardial perfusion (according to MBG). The control group (CG) included 35 patients at the age of  $52,8 \pm 1,2$  years, PR at them wasn't carried out. Therapy of STEMI was the similar and included aspirin, clopidogrel, heparin, beta-blockers and ACE inhibitors. Test I was performed at randomization on 6–14 days after STEMI and PCI (on the average  $12,1 \pm 1,2$  days), test II – after 3 month, III – 12 month.

**Results:** At the test I tolerance to physical activity (TPA) in MG was  $85,7 \pm 3,7$  W, in CG –  $77,1 \pm 6,5$  W ( $p > 0,05$ ), maximal oxygen consumption ( $VO_{2max}$ ) was  $15,4 \pm 0,7$  ml/kg/min and  $13,3 \pm 0,9$  ml/kg/min respectively ( $p > 0,05$ ). At test II we studied that TPA in MG significantly increased up to  $117,2 \pm 5,8$  W ( $p < 0,05$ ). In CG at test II TPA was  $88,5 \pm 5,1$  W that was not significantly differ in comparison to test I ( $p > 0,05$ ) and was less than TPA in MG at test II ( $p < 0,05$ ). We also revealed significant growth of  $VO_{2max}$  in MG at test II ( $17,4 \pm 0,9$  ml/kg/min) in comparison to test I ( $p < 0,05$ ). In CG at test II we noticed that  $VO_{2max}$  made  $14,6 \pm 0,8$  ml/kg/min that was comparable to revealed at test I ( $p > 0,05$ ). In 1 year after STEMI and PCI TPA in CG was  $105,8 \pm 1,7$  W that was higher than at test I –  $85,7 \pm 3,7$  W ( $p < 0,05$ ). In CG at test III TPA was  $93,5 \pm 5,9$  W – significantly didn't differ from taped at tests I and II ( $p > 0,05$ ).

**Conclusion:** Developed program of physical rehabilitation based on individual level of TRA, completeness of revascularization and character of myocardial perfusion promoted to improvement of physical capacity as well as maximal oxygen consumption in patients with STEMI after PCI.

## Non valvular atrial fibrillation at the department of internal medicine

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**Background:** Little is known about atrial fibrillation (AF) among patients hospitalized at departments of medicine.  
**Objective:** To explore the characteristics of these patients and their treatment during hospitalization, mainly anticoagulation.

**Methods:** A retrospective study, based on charts review of patients with non- valvular AF, hospitalized at the departments of medicine at Beilinson hospital, Rabin medical center, Israel. The following parameters were collected: age and gender; co morbidities; cause of index admission; mean hemoglobin, platelets and creatinine levels, CHADS2-VASC and HAS-BLED scores, INR level. Rhythm/rate control policy, anticoagulation and antiplatelets treatments at admission and discharge.

**Results:** The study group consisted of 404 subjects, who had 735 hospitalizations. Mean age was  $76 \pm 12$  years, 50% were males. The most common comorbidity was hypertension (73%). Most AF (90%) were documented previous to the current admissions. Most patients were at high risk for embolization (CHADS2-VASC  $> 3$  – 86%), with high risk for bleeding (HASBLED  $> 3$  – 79%). On admission, in three quarters of the cases patients with previously diagnosed AF were treated by rate control, 45% were not treated by anticoagulants. The therapeutic policy of rate control or anticoagulation treatment did not change significantly during hospitalization. The rate of anticoagulation treatment didn't differ significantly between CHADS2-VASC levels. The most predictive parameter for anticoagulants treatment at discharge was previous anticoagulation treatment.

**Conclusion:** The effect of hospitalization on AF treatment policy is poor. Future registries of hospitalized patients with AF as well as therapeutic interventions are needed.

## Sleep quality in young men with natural history of arterial hypertension is related with diastolic blood pressure, heart rate and heart rate variability

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**Objectives:** Sleep-disordered breathing (SDB) leading to complains on insomnia and daytime sleepiness is common in patients (pts) with arterial hypertension (AH). Nevertheless little is known about sleep habits in young men with mild essential AH. We aimed to investigate the association between subjective sleep quality, daytime sleepiness, blood pressure (BP) dynamics, heart rate variability (HRV) and thoracoabdominal excursion irregularity in young men with mild AH.

**Methods:** 24-h outpatient polyfunctional Holter monitoring was provided in 167 untreated young men (mean age –  $19,3 \pm 0,2$  yrs, body mass index (BMI)  $26,5 \pm 0,4$  kg/m<sup>2</sup>) during 2012–2015. Self-reported questionnaire to examine sleep quality and smoking status was completed in the same time.

**Results:** Mean systolic blood pressure (SBP) was 142.0 mmHg at day and 123.5 mmHg at night; mean diastolic blood pressure (DBP) – 72.6 and 58.8 mmHg, respectively; Nighttime decline was -12.6% for SBP and -19.1% for DBP. Mean apnea-hypopnea index (AHI) was 7.4 episodes/hour. Questionnaire results showed that "good" sleep had 45.5% of young men, "satisfactory" – 50.3% and "poor" – 4.2%. Association of sleep quality and BMI was not found. Young men reported "good" sleep had lower heart rate during day-time (83.3 bpm) than those with "satisfactory" (90.4 bpm,  $p < 0,01$ ) and "poor" sleep (93.6 bpm,

$p < 0.001$ ). Only DBP but not SBP has any differences between groups: DBP was lower at the day (70.6 mmHg) in men having good sleep than in the group with poor sleep (78.8 mmHg;  $p < 0.05$ ). At night DBP was also higher in poor sleepers (62.1 vs. 57.1 mmHg respectively,  $p < 0.05$ ). Day power of all frequency HRV bands (VLF, LF and HF) significantly progressively decreased from good sleepers to poor ones. Significant correlations were obtained between difficulty falling asleep, poor sleep quality and number of supraventricular premature beats ( $r = 0.29$ ,  $p < 0.05$ ;  $r = 0.69$ ,  $p < 0.001$ ). Young men having difficulties with falling asleep had higher heart rate at the day (93.6 bpm) than men without this problem (83.3 bpm). Pts with daytime sleepiness more frequently reported smoking (43.3% vs 21.7%) and snoring (83.3% vs 45.2%,  $p < 0.05$ ).

**Conclusions:** The increasing heart rate and DBP, lower total power spectrum of HRV (in all bands) and smoking status negatively influence on sleep quality in young men with mild AH. Lack of correlations between breathing irregularity, BMI and sleep quality in young pts requires further study.

### Long-term results of left main coronary artery PCI in STEMI setting

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**Objectives:** ST-elevation myocardial infarction due to the left main coronary artery disease is one of the most life-threatening conditions in daily clinical practice. Short-term and long-term clinical outcomes of unprotected left main stem PCI in STEMI patients were evaluated.

**Methods:** Of the 1127 PCIs performed in STEMI patients at our hospital from January 1, 2009 to December 31, 2011, the left main stem was the culprit lesion in 43 (3.8%) cases. A retrospective analysis of treatment of 43 patients (mean age  $64.7 \pm 6.5$  years, 74.4% males) presenting with STEMI due to the left main disease that underwent PCI at a single high-volume center was performed. The study end points included in-hospital mortality and the rate of major adverse cardiac and cerebrovascular events (MACCE), defined as composite of death, myocardial infarction, stroke and repeat revascularization at a mean  $26.7 \pm 9.2$  (range 13–43) months of follow-up.

**Results:** The median time from symptoms onset to balloon was 75 minutes with an interquartile range of 55 to 115 min. 16 (37.2%) patients presented with cardiogenic shock at admission, 21 (48.8%) patients had pulmonary edema. Angiographically, 7 (16.3%) patients had an acute occlusion of left main stem, 28 (65.1%) – distal left main disease, 6 (14.0%) – isolated left main disease, 8 (18.6%) – chronic total occlusion of the right coronary artery. Intra-aortic balloon pump was used in all cases. Drug-eluting stents were implanted in 39 (90.7%) patients. Multi-vessel PCI in acute phase was performed in 14 (32.6%) patients. TIMI III flow was achieved in 97.7% cases. The in-hospital mortality rate was 11.6%. At  $26.7 \pm 9.2$  months of follow up there were 3/38 (7.9%) deaths, 4/38 (10.5%) – new myocardial infarctions, 12/38 (31.6%) patients were performed CABG, 7/38 (18.4%) patients

had staged PCI of non-culprit lesions. One (2.6%) patient had a minor stroke after CABG. At  $26.7 \pm 9.2$  months of follow up the overall rate of MACCE was 62.8%.

**Conclusions:** Unprotected left main coronary artery PCI in STEMI is technically feasible in most patients and provides rapid reperfusion to critically ill patients with acceptable short-term and long-term outcomes. PCI of the non-infarct-related arteries in acute setting in patients with multi-vessel coronary disease should be considered in patients that remain hemodynamically unstable after left main stenting. The high rate of MACCE at  $26.7 \pm 9.2$  months of follow up is largely driven by the high incidence of repeat revascularization and can be explained by the intention to provide complete revascularization after stabilization of left main STEMI patients with concomitant multi-vessel coronary disease.

### Results of bioresorbable vascular scaffolds use for treatment of acute myocardial infarction with ST-segment elevation

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**Objectives:** Everolimus-eluting bioresorbable vascular scaffolds (BVS) have been shown to be safe and effective for stable coronary artery disease treatment. The current data on the use of BVS in ST-segment elevation myocardial infarction are very limited. Short-term and mid-term outcomes of PCI with bioresorbable vascular scaffolds in STEMI were evaluated.

**Methods:** The prospective single-center registry was initiated to evaluate feasibility and performance of everolimus-eluting bioresorbable vascular scaffolds in STEMI setting. From 1 October 2013 to 31 December 2014 a total of 107 STEMI patients underwent PCI with BVS implantation. The mean age of patients was  $52.5 \pm 6.1$  (range 27–66) years, 77.6% were males. The primary endpoints of the study were the device success defined as BVS implantation in the culprit lesion without intraprocedural complications and the rate of major adverse cardiac events (MACE) defined as all-cause death, myocardial infarction, repeat target vessel revascularization at 30 days and at a median 224 (range 30–441) days of follow-up.

**Results:** 5 (4.7%) patients presented with Killip class III-IV at admission. Multi-vessel PCI with BVS in acute phase was performed in 2 (1.9%) patients due to unstable hemodynamics after infarct-related artery intervention. 29% of patients received multiple scaffolds in the infarct-related artery. 34.6% of BVS implantations were IVUS-guided. All patients had successful scaffold implantation with TIMI-3 flow achieved in 94.4% of cases. The MACE rate at 30 days was 0%. At a median 224 (range 30–441) days of follow-up there was one (0.9%) non-cardiac death and one (0.9%) Q-wave myocardial infarction in non-target vessel. There was no scaffold thrombosis. The overall rate of major adverse cardiac events at follow-up was 1.9%.

**Conclusion:** PCI with bioresorbable vascular scaffolds in STEMI is technically feasible and safe with favorable short-term and mid-term outcomes.

## Long-term outcomes of different strategies of revascularization of STEMI patients with multivessel coronary artery disease

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**Objectives:** Multivessel coronary artery disease is found to be present from 41 to 67% of patients with STEMI. Contemporary guidelines recommend treating the infarct-related artery alone initially. The optimal strategy for further treating these patients is the subject of considerable controversy and uncertainty.

**Methods:** A retrospective analysis of treatment of 541 STEMI patients with multi-vessel coronary artery disease that underwent primary PCI during the period from January 1, 2009 to December 31, 2010 at a single center was performed. All patients were divided into 3 groups depending on strategy of revascularization: the first one – the group of PCI of infarct-related artery only in the acute phase and CABG within the first month following discharge (74 patients), the second one – staged PCI with the infarct-related artery treated acutely and other lesions treated later during the hospital stay (182 patients), the third one – primary PCI of only the infarct-related artery and subsequent medical therapy (285 patients). The primary end point used was major adverse cardiovascular and cerebrovascular events, defined as cumulative composite of death, myocardial infarction, stroke and repeat revascularization at 2 years of follow-up.

**Results:** At 2 years of follow up, 13/74 (17.6%) patients in the first group had at least one major adverse cardiovascular or cerebrovascular event, 49/182 (26.9%) patients in the second group and 116/285 (40.7%) patients in the third group,  $p < 0.05$ . The difference in death and stroke rates wasn't statistically significant among groups. The rate of myocardial infarctions was significantly higher in the group of medical treatment (20.4%) comparing to the PCI-CABG (14.9%) and staged PCI (15.4%) groups,  $p < 0.05$ . The rate of repeat revascularization was 2.7% for PCI-CABG group, 9.3% for staged PCI and 29.1% for primary PCI plus medical treatment group,  $p < 0.01$ .

**Conclusions:** Choice of treatment strategy for STEMI patients with multivessel coronary artery disease should be individualized and directed at the complete revascularization. Stenting of the infarct-related artery in STEMI is a default strategy. Staged PCI during the hospital stay is feasible and safe. Primary PCI of infarct-related artery in STEMI followed by CABG is the treatment of choice in patients with aneurysm of the left ventricle, diabetes mellitus, left main disease, a high Syntax score, high grade mitral valve insufficiency.

## Outcomes of pharmaco-invasive reperfusion strategy in STEMI patients

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**Objectives:** Primary PCI is the preferred strategy of reperfusion in STEMI. But in real life many STEMI patients present to non-PCI capable hospital and often cannot undergo timely primary PCI due to expected logistic delays and therefore receive fibrinolysis. Current guidelines recommend transfer of all STEMI patients to PCI-capable center for coronarography with a view to revascularization within 24 hours after lysis. But the place of such pharmaco-invasive strategy of reperfusion in STEMI management system is not well defined. Outcomes of STEMI treatment with these two strategies of reperfusion in real world settings were evaluated.

**Methods:** A retrospective analysis of treatment of 427 STEMI patients that underwent PCI at a single center from January 1, 2011 to December 31, 2011 was performed. All patients were divided into 2 groups depending on strategy of reperfusion: the 1st one – primary PCI (294 patients), the 2nd one included 133 patients that underwent PCI after fibrinolysis (rescue and routine early coronary intervention) at non-PCI capable referral hospital. All patients received heparin, loading dose of aspirin and clopidogrel. In the primary PCI group the median time from symptoms onset to balloon was 160 minutes with an interquartile range of 110 to 230 minutes, 77.9% of patients were delivered directly to our center, the rest were transferred from the nearest hospitals. In the pharmaco-invasive group the median time from symptoms onset to needle was 95 minutes (the interquartile range of 70 to 140 min), the median time from lysis to PCI – 11.5 hours (the interquartile range of 8.5 to 17 hours). The study endpoints included in-hospital mortality and the rate of major adverse cardiac and cerebrovascular events (MACCE), defined as composite of death, myocardial infarction, stroke and repeat revascularization at a mean  $38.3 \pm 6.1$  months of follow-up.

**Results:** The in-hospital mortality was 4.4% in the primary PCI group and 5.2% in pharmaco-invasive group,  $p = 0.805$ . There was no significant difference between the groups in the incidence of major bleeding. At  $38.3 \pm 6.1$  months of follow up the difference between the groups in the incidence of MACCE was also insignificant (15.3% patients in the 1st group and 21.1% patients in the 2nd group had at least one MACCE,  $p = 0.165$ ).

**Conclusions:** The study demonstrates that in real world settings when timely primary PCI is not possible due to long transfer times to PCI-capable hospital a pharmaco-invasive strategy combining fibrinolysis with an obligatory use of PCI has short-term and long-term outcomes that are comparable to those of primary PCI.

## Arterial hypertension relevance in a Portuguese active population in Portugal. Elvas study

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Introduction: High blood pressure (HBP) is a first cause of cerebral vascular accident, heart failure and 50% responsible of

all myocardial infarctions. Therefore, its knowledge and control are essential to decrease population cardiovascular risk.

**Objective:** To determine the prevalence of HBP in an active population of a rural area of Portugal, where the prevalence of cardiovascular diseases is higher than in this country.

**Methods:** We conducted a descriptive study in a working population of East Portugal. Blood pressure (BP) was determined in brachial artery, with OSROM sphygmomanometer validated. Three determinations spaced 10 minutes, were realized, at rest, following international recommendations.

**Results:** We analyzed a sample of 1883 individuals. The prevalence of hypertension was 39.3%. The prevalence of isolated diastolic hypertension was 3.8%. The prevalence of isolated systolic hypertension was 12.8%. The prevalence of diastolic blood hypertension was 4.6% in men and 3% in women. The prevalence of systolic blood hypertension was 15.3% in men and 10.1% in women. Diastolic hypertension distribution was following ESH-ESC guidelines: pre-HT 11.0%, 22.5% grade I, 2.8% grade II and 1.1% grade III. Systolic hypertension distribution was: pre-HT 23.8%, 27% grade I, 6.5% grade II and 2.2% grade III. By age, the HBP distribution was: 54.8% of <50 years had systolic HBP and 81% of group ≥50 years had systolic HBP. A 32.8% of <50 years had diastolic HBP, and a 60.8% of ≥50 years had diastolic HBP.

**Conclusions:** Both, systolic and diastolic HBP, are more prevalent in men older 50 y.o. The prevalence of hypertension was higher (about 20%) in men (48.5% vs 28.7%). The prevalence of HBP (systolic and diastolic) increases significantly with age, and it is higher (2 times) in group ≥50 years when compared with <50 y.o. group (66.1% vs 33.9%). This fact indicates that age and sex are 2 factors to influence blood pressure. But if we crossed sex and age, differences between men and women only are appreciated in group of <50 years ( $p=0.000$ ), but not in the group ≥50 years, in which differences among sexes are not significant ( $p=0.867$  and  $p=0.533$  to systolic and diastolic blood pressure, respectively).

### Prevalence of cardiovascular risk factors in a Portuguese rural area. Elvas study

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**Background:** Cardiovascular diseases are a major cause of morbidity and mortality worldwide. Early detection of cardiovascular risk factors and intervention may reduce consequential morbidity and mortality.

**Objective:** The aim of the present study was to investigate the prevalence of cardiovascular risk factors in a rural Portuguese area working population.

**Methods:** The study included 1883 working people (mean age 38 years, range 18–77 years, 54.1% male) undergoing routine medical check-up, which involved a structured questionnaire, physical examination, and standard serum biochemical analysis.

**Results:** Cardiovascular disease had been diagnosed previously in 1.2% of workers, hypertension in 13.8%, diabetes in 2.3%, and

dyslipidemia in 19.9%. Routine check-up showed that 38.7% (47.9% of males and 26.8% of females) were smokers, 39.3% (48.5% of males and 28.7% of females) had high blood pressure ( $\geq 140/90$  mmHg), 19% (17.2% of males and 21.3% of females) were obese (body mass index  $\geq 30$ ), 19.3% (22.8% of males and 15% of females) were hyperglycemic (blood glucose  $> 110$  mg/dL), 6.8% had total cholesterol  $\geq 240$  mg/dL (7.3% of males and 6.2% of females), 4% had LDL cholesterol  $\geq 160$  mg/dL (3.6% of males and 4.4% of females), 28.5% had triglycerides  $\geq 200$  mg/dL (30.5% of males and 22.6% of females), and HDL was  $< 40$  mg/dL in 5.0% of males and  $< 50$  mg/dL in 38.5% of females.

**Conclusions:** The prevalence of cardiovascular risk factors in the Portuguese rural area working population is high. Changes in lifestyles and early detection campaigns to prevent and control these risk factors are necessary.

### Analysis of oral anticoagulants application in real clinical practice in patients with non-valvular atrial fibrillation

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**Objective:** To analyze application of oral anticoagulants (OA) in real clinical practice in patients with non-valvular atrial fibrillation (AF).

**Methods:** There were analyzed 70 records of patients with non-valvular AF, who had undergone a cure in cardiovascular care unit of Nizhny Novgorod Regional Clinical Hospital named after N. Semashko during the period of 6 months. Attention was paid to the patients who had used OA in anamnesis. All patients had been rated by CHA2DS2-VASc score.

**Results:** The research indicated that male patients prevailed (41 case – 58,6%). Overwhelming majority (50 patients – 71,5%) had combination of ischemic heart disease and arterial hypertension (AH). In other cases the leading diseases were angina pectoris – 8 patients (11,4%), dilated cardiomyopathy – 5 patients (7,1%), AH – 4 patients (5,7%), myocardiodystrophy – 2 patients (2,8%), hypertrophic cardiomyopathy – 1 patient (1,5%). Acute ischemic stroke was detected in anamnesis of 3 patients (4,3%). Out of 70 patients, 11 (15,7%) had CHA2DS2-VASc zero score, 16 (22,8%) had CHA2DS2-VASc score not exceeding 2, 43 (61,4%) had CHA2DS2-VASc score over 2. The latter one serves indication for prescription of OA. OA had been taken by 23 patients (32,9%) with non-valvular AF before hospitalization. Overwhelming majority of patients were on warfarin (20 patients – 86,9%), 3 others used new OA (13,1%). International normalized ratio (INR) was monitored according to guidelines of Russian Society of Cardiology (2012) in 3 patients (13%). During the hospitalization OA were prescribed to 48 patients (68%). The other 22 abstained from taking OA for the following reasons: 4 patients (18,2%) had CHA2DS2-VASc zero score which excluded OA prescription, 3 patients (13,6%) had high risk of hemorrhage, 15 patients (68,2%) refused taking OA. The following OA were administered: warfarin (42 patients – 87,5%), rivaroxaban (5 patients – 10,4%), dabigatran (1 patient – 2,1%). OA were prescribed to the patients with AF



according to indications and risk of general thromboembolism after discharge from the hospital.

**Conclusions:** According to the fulfilled research the non-valvular AF patients even despite the high risk of general thromboembolism rarely use OA in the outpatient setting. Moreover, even the patients who used warfarin before hospitalization rarely came up to INR control. In addition one has difficulties with prescription of OA in hospital (contraindication, refusal of patients).

## Non-using of beta-blockers as a predictor of unfavorable cardiovascular events among heart failure patients

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**Objectives:** The studies show that prognosis depends on some risk factors, and it is known that they have not been well characterized. The most known predictors of high cardiovascular risk are smoking, history of coronary heart diseases, heart failure (HF) functional class, left ventricular ejection fraction (LVEF). It is well known that beta-blockers are one of the important components of heart failure treatment. We aimed to identify independent predictors of incident fatal and non-fatal clinical outcomes in heart failure patients.

**Methods:** We enrolled 175 HF patients (average age – 64,6±10,4 years, LVEF – 53,8±11,4%, II– III HF functional class – 88±10,3%) and analyzed 1 year fatal and non-fatal outcomes.

**Results:** At 1 year, all-cause mortality was 12%, cardiovascular mortality – 11%, and included myocardial infarction (84,6%), stroke (7,7%) and pulmonary embolism (7,7%). The frequency of atrial fibrillation occurrence was 62%, myocardial infarction – 46,2%. Significant predictors were identified by forward selection: hemoglobin level (95% CI, 0,6, p<0,05) and history of coronary heart disease (95% CI, 0,5, p<0,05). Non-fatal cardiovascular events was defined in 69 research participants (39,4%): myocardial infarction – 14,4%, stroke – 2,6%, incident HF hospitalization – 55,4%. We identified the predictors of non-fatal cardiovascular events: hemoglobin level (95% CI, 0,6, p=0,03), not using of beta-blockers (95% CI, 0,5, p=0,04).

**Conclusions:** Among research participants with II– III FC heart failure, there are several easily identifiable predictors of incident cardiovascular outcomes, including traditional risk factors such as hemoglobin level and history of myocardial infarction. Among non-fatal cardiovascular risk factors statistically significant is non-using of beta-blockers.

## The factors influencing effectiveness of different teaching methods in heart failure patients

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**Objective:** The aim of the study was to examine factors influencing the effectiveness of different teaching methods in patients with heart failure.

**Methods:** 120 patients with heart failure (NYHA II–IV, mean age 62.8±9.8 years) were randomized to three (two study and control) groups. In the 1st group patients were trained on the individual programs that took into account the initial level of patients' health literacy, patients from the 2nd group attended lectures, patients from the control group were not additionally trained. The duration of observation period was 6 months. The criterion of the teaching method effectiveness in patient was the absence of heart failure decompensation during follow-up period.

**Results:** Initially groups of patients were comparable on age, sex, severity and duration of heart failure, presence of comorbidity and treatment adherence. Individual self-control and self-care skills training programs that took into account the level of patients' health literacy in heart failure were more effective than group sessions. IV NYHA class (1.5: 1.3–1.6; p=0.005) and anxiety (1.4: 1.2–1.8; p=0.017) were associated with negative results in the 1st group. Lectures in the 2nd group were also ineffective in patients with IV NYHA class (3.54: 1.75–7.16; p<0.05) and anxiety (3.43: 1.59–7.39; p=0.022), but were successful in patients with high level of education (0.22: 0.06–0.88; p<0.05) and preserved left ventricular ejection fraction (0.47: 0.23–0.96; p=0.025).

**Conclusions:** Individual self-control and self-care skills training programs and group sessions don't prevent heart failure decompensation in patients with IV NYHA class and anxiety. So these categories of patients require additional support. Group lectures can be successful in patients with high level of education and preserved left ventricular ejection fraction.

## "To investigate or not to investigate: That is the question!" Investigation protocol for iron deficiency in chronic heart failure patients

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**Background:** Anemia occurs commonly in patients (pts) with chronic heart failure (CHF) and has been proposed as a new therapeutic target in this population. Patients with CHF who are anemic are often resistant evidence based CHF therapies resulting in repeated hospitalizations repeatedly and early death. There is evidence from clinical trials that early correction of the CHF anemia improves dramatically both symptoms and outcome by reducing hospitalization.

**Objective:** To analyze predictors of iron deficiency (ID) in HF pts and diagnostic causes of ID based on the findings in endoscopy and colonoscopy in order to create a protocol to approach the patient with ID with (IDA) or without anemia (IDW).

**Methods:** Prospective study of patients admitted consecutively in a heart failure unit during a year. Anemia was diagnosed according to WHO criteria, absolute iron deficiency (AID) when ferritin <100 ug/mL or functional (FID) when ferritin=100–300 ug/mL and transferrin saturation <20%.

**Results:** 163 patients were included: ID was diagnosed in 67,5% (49,1% with AID; 18,4% with FID); 31% with ID didn't show

anemia. Age, gender, ejection fraction, GFR<sub>e</sub>, oral anticoagulation, simple and dual antiplatelet therapy were included in the Cox regression model and female gender (HR 6,3; 95% IC [2,467-15,995]  $p < 0,001$ ) and single antiplatelet therapy (APT) (HR 4,5; 95% IC [1,342-15,343]  $p = 0,02$ ) were the only independent predictor of anemia. IDW diagnostic investigation: 10 upper GI endoscopies (UEND) – 3 normal; 6 gastropathies; 1 angiectasia; 1 flebectomy; 11 colonoscopies: 6 normal; 3 diverticulosis; 2 hemorrhoids; 2 intestinal polyps. IDA: 26 UEND – 1 Normal; 16 gastropathies; 1 comb erythema; 1 benign neoplasia; 1: bilious reflux; 2 gastric ulcers; 1 angiectasia; Colonoscopies: 11 Normal; 2 adenocarcinomas; 1 tubular adenoma; 8 diverticulosis; 1 angiodysplasia; 2 hemorrhoids.

**Conclusions:** There was a high prevalence of IDA in the HF population and the only independent predictors were female gender and single APT. Therefore these patients should be studied systematically with blood ferritin measurements and endoscopic exams. Those who only have ID don't need endoscopic exams but those with IDA should perform upper GI endoscopy and colonoscopy.

### Triglycerides in patients with acute coronary syndrome: clinical significance and risk for readmission

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**Objectives:** Recent studies suggest that fasting triglyceride levels were associated with both long-term and short-term risk after ACS in patients treated with statins. HDL-cholesterol and triglycerides have been more closely associated, in some studies, with cardiovascular risk in women. We aimed to examine the prevalence of elevated triglyceride levels among patients with ACS hospitalized in two emergency departments between June and December 2013.

**Methods:** 333 patients (123 women (W) aged 48–89 yrs and 210 men (M) 35–86 yrs) were included in the first sample. In hospital mortality rate was 2.7% (9 M). 44.7% of W and 25.7% of M were diagnosed with ST segment elevation myocardial infarction (STEMI); 31.7 and 23.3% – with non-STEMI and 23.6% of W and 51.0% of M – with unstable angina (UA). The most prevalent comorbidities were excessive weight (66% of W and 55% of M), chronic kidney disease (CKD; 39.8 and 14.0%) and diabetes mellitus (DM; 23.5 and 10.8%). The second study sample consisted of 116 pts aged 28–89 yrs.: 48 W (29.2% had STEMI, 25.0% – NSTEMI, 45.8% – UA) and 68 M (38.2% – STEMI, 16.2% – NSTEMI and 45.6% – UA). DM rate in W (39.6%) in this group was higher than in the first one, but in the M (11.8%) was the same. All pts were treated noninvasively.

**Results:** Fasting triglyceride levels is one of key points of metabolic syndrome. Elevated triglyceride level at admission was seen in 32.5% of W and 29.0% of M in the first and in 17.4% of W and 19.2% of M in the second sample tended to increase with age (50.0% W and 44.1% of M >80 yrs). W aged 60–70 yrs with DM had elevated triglyceride levels in 50% cases in the first and in 44.4% – in the second group; in the older group one half of W was diagnosed with CKD, predominantly – nephrolithiasis

and pyelonephritis. M with ACS and elevated triglyceride level more often had such comorbidities as gastric or duodenal ulcer disease, nephrolithiasis and peripheral arteries disease. Pts having elevated triglyceride levels presented more often with blood pressure rise (W and M) or decline (cardiogenic shock in M aged 61–70 yrs). 11 pts (3 W and 8 M) were re-hospitalized within 2 months. In 9 of 11 pts triglyceride level was >170 mg/dl at first admission.

**Conclusions:** Our findings confirm clinical significance of triglycerides. Elevated triglyceride level may be served as additional risk factor for readmission in patients with ACS.

### Relative lymphocyte count: a prognostic indicator of stress response in patients with acute coronary syndrome

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**Objectives:** A reduction in the relative lymphocyte count is a marker of the stress response; however, its prognostic value remains undetermined. Low lymphocyte count has been shown to be an independent prognostic marker in heart failure in the outpatient setting. The aim of this study was to investigate the clinical significance and predictive value of the relative lymphocyte count in patients with acute coronary syndrome (ACS).

**Methods:** 333 patients (123 women (W) aged 48–89 years and 210 men (M) 35–86 years) were hospitalized in the emergency department in 2013. 44.7% of W and 25.7% of M were diagnosed with ST segment elevation myocardial infarction (STEMI); 31.7 and 23.3% – with non-STEMI and 23.6% of W and 51% of M – with unstable angina (UA). In hospital mortality rate was 2.7% (9 M). The most prevalent comorbidities were excessive weight (66% of W and 55% of M), chronic kidney disease (CKD; 39.8 and 14%) and diabetes mellitus (DM; 23.5 and 10.8%). All pts were treated noninvasively. Thrombolysis before admission was provided in 20.3% of W and in 6.2% of M.

**Results:** 48 W (39%) and 59 M (28.1%) had a relative lymphocyte count  $\leq 20\%$ . The higher rate of stress response was seen in the oldest groups: in W >80 years (10/24, 41.7%) and in M aged 71–80 years (15/36, 41.7%). Comorbidity has been represented as factor increasing appearance of this pathophysiologic reaction. In pts having STEMI low lymphocyte count was detected in 74.5% of W and 40.7% of M, in pts with NSTEMI – in 23.7% ( $p = 0.0001$ ) and 34.7% ( $p > 0.05$ ), but only in 13.7% of W ( $p = 0.0001$ ) and in 18.7% of M ( $p = 0.002$ ) with UA. Low relative lymphocyte count was associated with mild anemia in 36.3% of W and in 50.9% of M, more often in W aged 71–80 years (52.3%) and in M aged 51–60 years (65%). 11 pts (3 W and 8 M) were hospitalized twice within 2 months. Low lymphocyte count at admission had 10 of 11 pts, 6 pts – in association with mild anemia. 50% of pts who died with lung edema had low relative lymphocyte count and 75% – anemia.

**Conclusions:** Relative lymphocyte percentage represents a simple, inexpensive, and widely available immunological marker with potential prognostic significance in patients with ACS and may help predict residual risk beyond currently used measures.

## A cardiac pleural effusion: is pacemaker insertion an innocuous procedure?

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**Objectives:** Post-cardiac injury syndrome (PCIS) is an inflammatory process involving the pleura and/or the pericardium following a variety of cardiac injuries, including pacemaker implantation. The clinical manifestations of PCIS develop days to weeks after the injury, are non-specific and may result in exudative pleural and pericardial effusions or even acute pericarditis. Most cases respond to medical treatment with non-steroidal anti-inflammatory agents (NSAIDs) or corticosteroids, reducing the need for a surgical procedure.

**Case report:** An 89 year old woman with no relevant past history was admitted for mental confusion, dyspnea and dry cough for 6 days. She had undergone pacemaker implantation one week earlier for 3rd degree heart block. On physical examination she was hypertensive and had decreased breath sounds in left hemithorax. Blood tests showed microcytic anemia, elevated D-dimer (3000 ng/mL) and C – reactive protein (CRP). Hypoxemic respiratory insufficiency was seen on blood gases. Chest x-ray (CXR) revealed a large left pleural effusion with associated atelectasis. A computed tomography angiography (CTA) of pulmonary arteries excluded pulmonary embolism. On echocardiogram no relevant changes were seen in pericardium. Thoracentesis was performed, with drainage of 1.8 liters of bloody fluid which was compatible with a sterile serosanguineous exudate. Control CXR with slight improvement of pleural effusion. In order to exclude malignancy, chest/abdomen/pelvis computed tomography, mammary ultrasound and colonoscopy were done and no suspicious lesions were found. Given the temporal link between the symptoms and the procedure, a diagnosis of PCIS was assumed and the patient initiated naproxen (500 mg twice a day). After 4 weeks of medical therapy, complete resolution of symptoms, laboratory abnormalities and pleural effusion. The patient remains asymptomatic until nowadays.

**Discussion:** Implantation of pacemakers is a safe procedure although complications can occur. The presence of pleural effusion in the setting of possible heart injury should raise the suspicion of a post-cardiac inflammatory process. However, before a definitive diagnosis, entities as heart failure, pulmonary embolism, parapneumonic effusions, tuberculosis and malignant tumors must be ruled out.

## Venous thromboembolism prophylaxis in the emergency department: a new score

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**Objectives:** Venous thromboembolism (VTE) prophylaxis is less frequent in emergency medicine (EM) than in internal medicine (IM) department. Statistically, such difference was substantial in case of immobilization and when was adopted the Padua Score that assigns a higher score at immobilization criterion. The aim of the present study is a critically review of thromboembolism criteria and score in the medical patient, in EM and IM department. Particularly we hope find a score more suitable for acute patient but with high sensibility and specificity. Methods: Double case-control observational study, with enrollment, for each case of VTE, of two consecutive patients without VTE, of equal sex and age group (18–50, 50–55, 55–60, 60–65, 65–70, 70–75, 75–80, >80 years). The study involved EM and IM department of 23 hospital/university of Lazio and Umbria, in Italy.

**Results:** We analyzed data pertaining to 1215 patients, 409 with VTE (50% – deep venous thrombosis (DVT), 9.9% – pulmonary embolism (PE), 40.1% – PE+DVT) and 806 case-control. 222 patients (30%) were in charge to EM department while 520 patients (70%) to IM department. The TEV risk factors at more statistical significance ( $p < 0.01$ ) were: previous VTE, active cancer, known thrombophilic condition, immobilization, chronic venous insufficiency, hyperhomocysteinemia, central venous catheter, recent hospitalization. Obesity, recent surgery, family history of VTE, hormone therapy and treatment with drugs that stimulate hematopoiesis were resulted at intermediate statistical significance ( $p < 0.05$  but  $> 0.01$ ). We proposed TEVere score (active cancer, previous VTE, hypercoagulability, recent surgery, drugs that stimulate hematopoiesis, central venous catheter, obesity, immobilization, hormone therapy, age  $> 70$  y.o.). This score show a good specificity and sensitivity, compared to Padua score.

**Conclusions:** The TEVere score, differently from Padua, assigns a low score to the immobilization criterion, but the predictivities keeps high. The criterion of immobilization, very important, but is difficult assignment in the departments of emergency medicine and short observation because there is often no time for the allocation of this risk criterion. The TEVere score could therefore represent the ideal score in the afferent patients to the EM department, even if the are necessary further validation studies.

## Concept of peripartum cardiomyopathy formation

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Manifestations of heart failure (mainly of the left ventricle) predominate among the symptoms of peripartum

cardiomyopathy (PPCM): a rapid reduction of the left ventricular ejection fraction (LVEF), enlargement of the heart chambers, and formation of intracardiac thrombi. The causes of this condition are unknown. The idea of viral myocarditis, hormonal disorders, physiological stress of pregnancy, oxidative stress of the late pregnancy and the role of other known causes are untenable, because they can not explain the frequent association of PPCM with complications of pregnancy, family and recurrent cases of the disease in the same patient, and, most importantly, catastrophically rapid development of the left ventricular failure with individual capabilities of cardiac function recovery in different patients. In view of these facts, relying on our own observations, we propose a concept of PPCM pathogenesis. Basic provisions of the concept are: 1) numerous cases of PPCM in women with complicated pregnancies, having, according to the modern concepts, thrombophilia basis (pre-eclampsia, eclampsia, gestational hypertension, spontaneous preterm labor, etc.) as a proof of a single – hemocoagulation mechanism of the development of these states; 2) the observed cases of adverse heredity on thromboembolic complications in PPCM women families and proved facts of the presence of genetic traits of combined forms of inherited (congenital) thrombophilia with polymorphisms of the genes responsible for various parts of hemostasis (plasmatic, platelet, metabolism of folic acid and methionine) in various combinations; 3) observation of intracardiac thrombosis and thrombosis of other locations in patients with PPCM in the terms of heart failure formation. The proposed concept admits the possibility of development of multiple distal (disseminated) microembolism of the coronary bed, its exclusion from the blood flow, the formation of acute thrombotic microangiopathy and myocytes energy deficiency as the causes of systolic heart failure in women with hereditary (often combined) thrombophilia in terms close to the pregnancy as a trigger of "coagulation stress". The outcome of this process: 1) regression, full or nearly full recovery of LVEF or 2) progression, dilatation of the heart chambers and a gradual reduction in systolic function until a terminal heart failure – it is determined by the severity of coagulation disorders, rates and prevalence of coronary embolism, the start time of anticoagulation therapy.

## Prevention of affective disorders in cardiovascular patients

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Objective: Prevention of cardiovascular and other noncommunicable diseases is an important part of the joint project of WHO and the Ministry of Health. It is established that the presence of comorbid affective pathology greatly aggravates the clinical course and prognosis of the disease. In 65% of patients hospitalized with acute myocardial infarction (MI) there are identified the symptoms of depressive spectrum disorders. We aimed to evaluate the impact of meditative technique of self-regulation on emotional and physical health in patients with CVD, to justify the application of this method in the basic programs of prevention and rehabilitation.

**Material and methods:** In a cardiological sanatorium there was conducted a study aimed at the evaluation of the positive effect of regular meditation practice on psycho-functional status of cardiovascular patients. The study involved 44 people aged 40 to 65, where 23 of them were the control subjects not practicing meditation or other techniques of psychic self-regulation and the 21 were an experimental group of meditators who the technique was introduced to and who began practicing Sahaja Yoga meditation regularly. The main clinical effects of meditation practice are the following: regression of anxiety and depressive symptoms, recovery of the integrative processes of the central nervous system, enhancement of adaptive reactions of the organism. The fact of positive therapeutic dynamics is also important: there is a gradual decrease in the level of sympathicotonia. At the beginning and at the end of the study (in 3 weeks) both groups were assessed by levels of trait anxiety (STAI-t), alexithymia (TAS-20), depression (BDI) and extroversion/introversion, neuroticism and psychotism (EPQ).

**Results:** According to the psychometrics, the patients who were practicing meditation, in spite of greater introversion, had higher emotional stability. The control subjects, on the contrary, were characterized by lower values of neuroticism, psychotism, trait anxiety and depression and they also had a better ability to identify and express emotions. These data are consistent with the results of other authors about lower levels of anxiety, neuroticism, expanded the spectrum of positive emotional experiences and quality of life in the individuals who practice meditation on a regular basis.

**Conclusion:** Meditation eliminates violations of the mental-emotional sphere of anxiety and depressive disorders, it influences somatic condition and it is an effective method to increase the resistance of the organism to the effects of psychosocial stress.

## Vascular endothelial growth factor-D mediates fibrogenic response in myofibroblasts

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**Objectives:** Vascular endothelial growth factor (VEGF)-D serves as a mediator of angiogenesis and lymphangiogenesis. We have recently reported that cardiac VEGF-D and VEGF receptor (VEGFR)-3 are upregulated following infarction. Furthermore, VEGFR-3 is strongly expressed in myofibroblasts, key cells for fibrous tissue formation in the infarcted myocardium, implicating the potential role of VEGF-D in cardiac fibrogenesis. The current study is to further explore the role of VEGF-D on fibrogenic response in myofibroblasts.

**Methods:** Myofibroblast proliferation, migration, collagen degradation and synthesis were detected in cultured cardiac myofibroblasts subjected to VEGF-D with/without VEGFR antagonist or ERK inhibitor. Untreated cells served as controls. Myofibroblast proliferation and migration were detected by BrdU assay and Boyden Chamber method, respectively. Expression of type I collagen, metalloproteinase (MMP)-2/-9, tissue inhibitor

of MMP (TIMP)-1/-2 and ERK phosphorylation were determined by Western blot.

**Results:** Our results revealed that compared to untreated cells: 1) VEGF-D significantly increased myofibroblast proliferation and migration; 2) VEGF-D significantly upregulated type I collagen synthesis in a dose and time dependent manner; 3) VEGF-D stimulated MMP-2/-9 production, which was accompanied with activated TIMP-1/-2 synthesis; 4) VEGFR antagonist abolished VEGF-D-induced proliferation and type I collagen release; 5) VEGF-D activated ERK phosphorylation; and 6) EAK inhibitor abolished VEGF-D-induced proliferation and type I collagen synthesis.

**Conclusions:** Our study implicate that VEGF-D serves as a fibrogenic mediator and stimulates myofibroblast growth and collagen deposition. Further studies are underway to determine the regulatory role of VEGF-D in fibrous tissue formation and cardiac remodeling following infarction.

### Acute myocarditis: case report

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**Introduction:** Myocarditis is defined as the inflammation of the myocardium. It can occur at any age or gender, but the young men are most affected. Viral infections are the most common causes of acute myocarditis. In Brazil, the major viruses implicated are adenovirus, parvovirus and herpes virus.

**Case report:** A 24 years old male was admitted with the chief

complaint of breathlessness. He initiated five days before with retrosternal pain associated with progressive dyspnea, dry cough and measured fever, the highest 39,3°C. He had been to another hospital at the first day of symptoms, from where he was discharged with levofloxacin. Instead of the correct use of the antibiotic, the symptoms progressively get worst; then he started with orthopnea, nocturnal paroxysmal dyspnea and decreased urine output. He denied other complaints, allergies, or comorbidities. Her mother reported that he had flu symptoms 2 weeks earlier. Physical examination: patient somnolent but well oriented, dyspneic, acyanotic, anicteric. Vital signs: BP 100x60 mmHg, HR 136 bpm, T 38,4°C, SpO2 86%, RR 38 rpm. Presence of jugular turgescence. Cardiac auscultation: regular gallop rhythm, presence of systolic murmur at the mitral area. Lungs auscultation: absence of vesicular murmurs on the lower third of the right hemithorax, presence of diffuse rales. Laboratory: leukocytosis, hypoxemia, elevated C-reactive protein, elevated troponin. Hemocultures and serologies: negative. Eletrocardiogram: sinus tachycardia. Echocardiogram: LVEF 40%. Left ventricular diffuse hypokinesis. Cardiac magnetic resonance: presence of late gadolinium enhancement on mesocardial topography of the lateral and inferobasal walls. Presence of a little pericardial effusion. This patient had a clinical suspicion of myocarditis, which was corroborated with the result of the cardiac resonance. He had an optimal response to supportive clinical management.

**Conclusions:** Myocarditis course is unpredictable, ranging from mild symptoms that resolve without specific therapy to cardiogenic shock and death. This diversity on clinical presentation demonstrates the importance of a high level of suspicion early in the course of this disease with the aim not to delay its diagnosis and treatment.

### Therapeutic hypothermia after cardiac arrest: effects of a protocol implementation with emergency medical services

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**Objectives:** Cardiac arrest is a leading cause of mortality, with significant social and economic impact. Therapeutic hypothermia is a key intervention with demonstrated benefit in reducing mortality and improving neurological outcome. Recommended since 2003 in out-of-hospital comatose patients with ventricular fibrillation, later studies have shown benefit in its use immediately after restoration of spontaneous circulation and in other rhythms which led to the beginning of the cooling in the pre-hospital environment. This study was made in order to evaluate the implementation of a new hypothermia protocol including emergency medical services, emergency room, coronary care unit and our intensive care unit.

**Methods:** We conducted a prospective cohort study between May 2012 and June 2014 of the consecutive patients submitted to the new hypothermia protocol. The control group was formed by the patients that undertook the previous protocol at our intensive care unit since January 2005 until April 2012.

**Results:** The study group included 70 patients of which 67 concluded the hypothermia protocol. The average age was  $62.6 \pm 13$ , with 73% male. The control group included 102 patients of which 97 concluded the hypothermia protocol. The average age was  $60.7 \pm 16.0$  with 67% male. These two groups were similar in what concerns age, sex, APACHE II, SAPS II, SAPS 3, SOFA 24, 48 and 72h and SOFA variation within the first 72h. CPR time was significantly higher in the study group ( $p=0.001$ ), and time from ROSC until beginning of hypothermia and time until attaining target temperature significantly lower ( $p=0.047$  and  $p<0.001$  respectively). There was no difference in time until CPR, hypothermia duration and re-warming duration between groups ( $p=0.45$ ,  $p=0.82$  and  $p=0.07$  respectively), despite the different maximum rates of re-warming between the groups. Despite lower times of hypothermia beginning and attaining target temperature, there was no difference in mortality at 8 days and 6 months ( $p=0.48$  and  $p=0.36$  respectively) and also in neurologic outcome between groups ( $p=0.44$ ).

**Conclusions:** Despite the beneficial effects previously demonstrated by therapeutic hypothermia and the assumption that patients would benefit from an earlier beginning of hypothermia, in view of our results we consider that new controlled randomized trials are needed to define which patients will effectively benefit from it.

### Retrospective analysis of risk factors associated with relevant pathological findings in head MRI in medical walk-in patients with acute headache

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**Objectives:** Acute headache is a leading reason for emergency consultations. A major goal in the work-up of such patients is to distinguish patients with secondary, symptomatic and potentially dangerous causes of headache from those with primary headache syndromes. Here we tested, whether a score could predict subjects with relevant pathological findings on MRI in patients from a medical walk-in clinic.

**Methods:** All medical outpatient referrals for brain magnetic resonance imaging (MRI) between June 2010 and November 2014, with the main symptom 'acute headache' (<4 weeks) were analyzed. A retrospective chart review was performed and all MRI scans not considered completely normal underwent a second read by a neuroradiologist. MRI findings were classified by relevance regarding need for additional work-up and whether the findings explained the headache. Validity of a clinical 9-point score consisting of D-dimer/CRP positivity (1 point); nausea (1 point); pathological neurologic exam (2 points); sensitivity/vision abnormality (2 points) and fever/meningism (3 points) to predict a relevant finding explaining the headache was determined.

**Results:** For the total of 513 MRI, acute headache was the second most common reason for referral, accounting for 82 exams (16%). 42 of these 82 (51%) had a completely normal MRI. Of the remaining 40 patients, 16 (19%) had no relevant findings and no identifiable cause of headache, 9 (11%) had a 'non-relevant' finding potentially explaining the headache (e.g. sinusitis), 8 (10%) a 'relevant' finding likely explaining the headache (e.g. meningitis), and 7 (8%) a 'relevant' finding likely not causing headache (extensive microangiopathy). Patients with a relevant finding explaining the headache had a median score of 4, compared to a score of 3 in those with a relevant finding not explaining the headache and a score of 1 in all non-relevant findings; reflecting a sensitivity of 100% and a specificity of 51% for the score (cut-off  $\geq 2$  points).

**Conclusions:** Among walk-in clinic patients with acute headache, we found a relevant pathological finding in 1 of 5 patients. Applying a score based on history, clinical findings and lab-values allowed identifying those patients with pathological findings with high sensitivity. If prospectively validated, this score might be useful in selecting patients requiring immediate neuroimaging.

## Impact of education based on problem and cases solving in medical emergencies training of first-year medical residents at GMGH. June 2015

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**Introduction:** First-year medical residents (MR1) start a crucial period of their training in medical emergencies. In recent years the medical education has implemented different methodologies to improve the training of graduate students; however there are few studies that analyze the importance of these methodologies in the initial formation of the MR1 in the specific area of medical emergencies. PBL (Problem Based Learning) and CBL (Case Based Learning) have been implemented as learning tools to improve the academic field of graduate students but few studies have been conducted in undergraduate and MR1.

**Objective:** Analyze the level of improvement in training given by the grade obtained in the final test case of MR1 LBL (Lecture Based Learning) courses compared with MR1 PBL-CBL course of Gregorio Marañon General Hospital (GM GH).

**Material and methods:** Study type – cohorts. Based courses PBL-CBL vs LBL score in the final test case. Inclusion criteria: all new MR1. Exclusion criteria: MR1 on external rotations, prior learning courses or those on re-enroll in the first year of training. The score were collected on final test. For data analysis Excel and SPSS statistical analysis were used. Universe of work and sample: the total number of MR1.

**Results:** In total 107 MR1 were collected of whom, 92 (86%) met inclusion criteria. The range of ages was between 24-60 years, with an average of 25.9 years. 26 (24.3%) MR1 from the GMGH receive the course PBL-CBL method. And 81 (75.7%) MR1 receive the course LBL. From those in PBL-CBL group: 11.5% – suspended, 7.7% – approved, 23.1% were remarkable, 53.8% were outstanding and 3.8% earned honors qualification, in contrast with LBL course in which 49.4% suspended the final test, 38.3% approved, 4.9% were remarkable, 7.4% were outstanding and none earned honors qualification. 49.4% of LBL group suspended the test, compared to 11.5% of the PBL-CBL group. 80.7% of MR1 in the PBL-CBL group obtained remarkable, outstanding or honors qualification, compared with only 12.3% in LBL group, being the difference statistically significant ( $p < 0.0001$ ).

**Conclusion:** There is statistically significant difference in the percentage of MR1 who obtained remarkable, outstanding or honors qualification rating between the group who received PBL-CBL course compared to LBL at GMGH in June 2015.

## Viral pneumonia in a patient with chronic antibiotic treatment

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**Introduction:** Nosocomial viral pneumonia remains a common disease associated with significant morbidity and mortality. It is

the second most common nosocomial infection and accounts for 15–20% of the total patients in the intensive care unit. Patients with nosocomial pneumonia with influenza virus are older and more commonly have simultaneous health problems (such as previous stroke, heart failure and diabetes).

**Case report:** A 60 years old female patient is addressing the emergency department presenting dyspnea, anterior chest pain with posterior irradiance, cough with expectoration for two days. The disease occurred after waiting for about 4 hours at the general practitioner for a drug prescription and she went into progressive respiratory failure, because she could not administer herself oxygen. She is unstable and has a history of stroke, COPD, asthma, arterial hypertension stage III, diabetes type II insulin resistant, chronic kidney disease stage III, mitral stenosis, congestive heart failure class III NYHA, tricuspid valve disease and aortic valve disease. The patient admits to have had acute rheumatic fever as a sequel of streptococcal infection in her early life. As a complication of rheumatic fever, the patient develops mitral stenosis, for which she had surgery. Because her valves were affected and predisposed to other conditions, the surgeon suggested the patient to take at home a chronic antibiotic treatment to reduce the risk of serious illnesses over time. The patient is brought to the intensive care unit at the Clinical Emergency Hospital in Bucharest presenting severe dyspnea, moderate hyperkalemia (potassium level 5.88 mEq/L), and moderate anemia syndrome. Before being admitted to the hospital, oxygen pressure 68.4 mmHg, the blood pH was 7.26 indicating respiratory acidosis. Her blood tests revealed chronic infection with hepatitis B virus. After 8 days of hospitalization, the patient contracted nosocomial pneumonia due to the airborne transmission. The patient's symptoms were: dry cough, chest pain, myalgia, wheezing. Both lungs presented crepitations from top to bottom. The chest X-ray showed an increase in heart size and basal pulmonary stasis. The patient was treated with: oxygen therapy, sintrom, ceftriaxone, miofilin, algocalmin, arnetin, furosemide, nifedipine, and her evolution were favorable with the disappearance of the dyspnea and the anterior chest pain.

## Caval Index – Pulmonary Embolism Severity Index correlation. CAPESI study: comparative analysis with Student's test for continuous variables in 30 patients with VTE. Three-year experience

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**Objective:** The CAPESI study, acronym of "CAval index – Pulmonary Embolism Severity Index" (PESI), enrolled 30 patients with venous thromboembolism during the 2012-2014 period. The PESI was measured pre-lysis and the Caval index was measured pre-lysis in all the patients (IVCd exp-IVCd insp/IVCd exp, VN at rest in inspiration from 0 to 14 mm, at rest in exhalation 15 to 20 mm). A comparative analysis for continuous variables with Student's "t" parametric test was performed. The CAPESI study has the following objective: to verify any relationship between the values of pre-lysis Caval Index and pre-lysis PESI; verify the statistical significance observed by applying Student's "t"

parametric test as a benchmarking test to determine whether the relationships of the variables considered are due to chance.

**Methods:** The pre-lysis Caval Index values were compared with the pre-lysis PESI values in the 30 patients enrolled. Therefore, the test calculates the relative value (RV) of the t index to be associated with the difference found by the following formula:  $t = (M1-M2)/\sqrt{DS12/DS22+N1/N2}$ . Therefore, the value of "t" obtained with degrees of freedom (DOF) = 29 is 6.94. Being 3.659 the critical value (CV) of "t" with DOF = 29,  $p=0.001$ , the relative value (RV) of "t" equal to 6.94 expresses an absolute positive correlation of the co-variation between the values of the two variables considered (pre-lysis Caval Index and PESI), which is highly significant with  $p<0.001$ .

**Results:** Student's "t" test shows a highly significant correlation ( $p<0.001$ ) of the two variables examined (pre-lysis Caval Index values and Miller Score) and, therefore, cannot be attributed to chance. In fact, the value of "t" obtained is 6.94 and the CV (critical value) of "t" for  $p=0.001$  is 3.659 with DOF=29. The data obtained suggest that the inverse co-variation of the pre-lysis Caval Index and pre-lysis PESI values expresses a highly significant difference, the clinical significance of which lies in the overload of right-side heart sections, in the presence of high pressure regimes attributable to the embolic pulmonary condition, evaluated with the pre-lysis PESI, which results in a decreased collapsibility of the inferior vena cava, evaluated with the pre-lysis Caval Index.

**Conclusion:** The CAPESI study has shown that there is a highly significant correlation between the two variables considered: pre-lysis Caval Index and pre-lysis PESI.

## Do we order too many blood cultures in the emergency department?

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**Objective:** Bacteremia is a frequent (140-160 per 100.000 persons per year) and severe condition, with high mortality rate. Blood cultures analysis often results in low rates of pathogen detection (4-8% of blood cultures yield growth), therefore ordering blood cultures inappropriately may be wasteful and expensive. A promising and validated decision rule for predicting bacteremia in patients with suspected infection was established by Shapiro et al, with high sensitivity and negative predictive value (97 and 99%, respectively), despite low specificity and positive predictive value (29 and 11%, respectively). It includes "major" and "minor" criteria, and blood culture is indicated if at least one major or two minor criteria are present, otherwise patients are classified as "low risk" and cultures may be omitted. We decided to perform a study in order to understand if this prediction rule applied to our emergency department (ED) had the same results in predicting true bacteremia.

**Methods:** Retrospective study including adult patients (18 years or older) admitted to the ED of our hospital, a Portuguese Median Community Hospital, from 2014 January 1st to December 31th, and for whom blood cultures were obtained. The outcome was

true bacteremia. Features of the clinical history, co-morbidities, physical observations and laboratory tests were registered. Statistic analysis was performed using Excel 2007.

**Results:** 673 patients were included, of which 38 had true bacteremia (5.6%). The median age of our patients was 78 years, with a slight majority of men (59%). 60% of our patients had one major or at least two minor criteria, but even in this group the number of true bacteremia was small (37 out of 404). The number of true bacteremia was even smaller in the group of patients with one or less criteria for bacteremia (1 out of 269). This resulted in a sensitivity of the prediction rule of 97.4% with a negative predictive value of 99.6%. The specificity was lower, as well as the positive predictive value (42.2% and 9.2%, respectively).

**Conclusion:** The clinical decision rule applied in our ED setting, highlights that we, indeed, order too many blood cultures. Up to 40% of the requested exams could be avoided using this score.

## Effects of weather conditions on emergency ambulance calls for hypertension in Surgut

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**Objective:** To investigate the effect of monthly air temperature (T), barometric pressure (BP) and relative humidity to detect the risk areas for low and high monthly volume (MV) of emergency ambulance calls for hypertension.

**Methods:** The study included data on 54419 patients who called the ambulance for hypertension. We used the classification and regression tree method as well as cluster analysis. The clusters were created by applying the k-means cluster algorithm using the standardized monthly weather variables. The analysis was performed separately during cold (October-May) and warm (June-September) seasons.

**Results:** During the cold period 33353 emergency ambulance calls were registered. The greatest MV was observed on months of high T and on months of high BP. Low DV was associated with high BP. During June-September, a lower DV was associated with low BP, and high T. During the warm period, the greatest DV was associated with increased BP and decrease T.

**Conclusion:** These results suggest that monthly T and BP on the month of the ambulance call may be prognostic variables for the risk of hypertension.

## The assistance to the emergency room in a tertiary hospital in Spain is influenced by the football matches played

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**Objective:** The aim of this study is to analyze the differences in the emergency room assistance between days when important football matches are played and a normal day.



**Methods:** Retrospective study. We selected the dates of the most important football matches were played in Spain on the first semester of 2015. We selected 4 important football matches dates and we compared it with the same day of the week before or after that there wasn't a football match. The following variables were analyzed: number of subjects who attended the emergency room, sex, age, disease severity and the number of admissions in hospital.

**Results:** The total number of subjects who attended the emergency room in game days was 924 patients (mean 231, 208-252), 419 men (45.7%), days with no football match: 1034 subjects, (mean 258.5, 194-304), 496 men (48%). During the time that football matched was played (9p.m to 11p.m): Football match days: 143 subjects (mean 35.8 subjects, 24-43), 70 men, 73 women. The minimum number of assistance was on the Real Madrid vs Atletico de Madrid (n=24). During the same period (9 p.m to 11 p.m) in a day that no football matches were played: n=207, 108 men vs 99 women, mean 51.8 subjects (43-68). There were no statistically significant differences in age, severity of illness and hospital admissions.

**Conclusions:** Football is the most popular sport in Spain which is reflected in the emergency room assistance that is diminished in the days when an important match is played. The number of men who come to the emergency room decreased the most because they are the most fanatics. These data suggest indirectly that emergency room assistance in a public health service is influenced by external factors, this shows that in most cases is used improperly.

## Community-acquired pneumonia in intensive care – a single center's 4-year experience

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**Objectives:** Community-acquired pneumonia (CAP) is a common diagnosis in an intensive care unit, being the main cause of sepsis. We made retrospective analysis of patients admitted in an intensive care unit (ICU) of a Portuguese hospital with CAP, from February 2010 to February 2014.

**Methods:** Retrospective study of patient files: demographic data, comorbidity, antibiotic therapy, microbiologic isolates, organ dysfunction (OD), duration of invasive mechanical ventilation (IMV), re-infection, severity scores, and mortality.

**Results:** 118 patients with CAP (78 male; 66.1%), mean age 63.7±17 years; mean length of stay 12±11.7 days. Mean SAPS II 49.9±19.2, with predicted mortality 47.2±29.9%. Bacteria were isolated in 46 patients (39%), most commonly Streptococcus pneumoniae (n=25; 54.3%). There were positive urinary antigens in 88% of S. pneumoniae and Legionella pneumophila infections. Influenza A was detected in 9 patients. Empiric antibiotic scheme: ceftriaxone and azithromycin were used in 62 patients (52.5%); in 9 of them oseltamivir was added. The empiric antibiotic approach was adequate in 87% of patients. 96.6% had OD; 84.7% needed IMV (mean length of 10.8±9.6 days); of these 34.3% had PaO<sub>2</sub>/FiO<sub>2</sub> ratio <100. Re-infection occurred in 31.4% (75.7% respiratory). ICU mortality was 41.5% (55.1% attributed to re-infection); in-hospital mortality was 44.1%.

In univariate analysis age, SAPS II, respiratory OD, renal OD, renal replacement therapy, hematological OD, and re-infection affected mortality. In multivariate analysis only SAPS II retained independent impact on mortality.

**Conclusion:** Empiric therapy was suitable. Mortality was lower than predicted but SAPS II retained discriminative power regarding mortality.

## Neurologic outcome after cardiac arrest: a prospective study

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**Objectives:** Determination of the prognosis of patients after cardiac arrest has clinical, ethical and social implications. Since therapeutic hypothermia the utility of biochemical markers, imaging and neurologic examination need to be evaluated. This study was designed to assess the validity of different markers which can be used in the detection of patients with bad prognosis under hypothermia protocol in order to reduce the uncertainty on the decision of treat or no to treat and improve the dialogue with relatives.

**Methods:** Data from adult patients of both sexes, admitted after cardiac arrest in our Intensive Care Unit for hypothermia protocol were recorded prospectively in order to perform a descriptive and analytical study to analyze the relationship between clinical, neurophysiological, imaging and biochemical parameters and the outcome at 6 months determined by in-person consultation or by phone using the Glasgow-Pittsburgh Cerebral Performance. Besides descriptive analysis, continuous variables non-normally distributed were analyzed with Mann-Whitney U test and Pearson's chi-squared was utilized to test categorical variables. A p<0.05 was regarded as statistically significant. Receiver operating characteristic analysis was performed to define a cut-off value with 100% of specificity for neuron specific enolase (NSE).

**Results:** Were included 67 patients of which 12 had good neurological outcome. Ventricular fibrillation was associated with increased likelihood of survival (p=0.03) and improved neurological outcome (p=0.01; OR 0.17 [CI 0.04-0.76]). The presence of teta activity in electroencephalogram had improved neurological outcome (p=0.01; OR 0.11 [CI 0.01-0.75]). Shorter time to reach target temperature had higher mortality at 6 months (p=0.04) and worse neurologic outcome (p<0.01). Hypoxic-ischemic brain injury in MRI had poor neurologic outcome (p<0.01) and 19 times higher risk of bad neurological prognosis (OR 19.8 [CI 1.7-229.6]). NSE>58ng/mL was associated with poor neurological outcome (p=0.02) and had a sensibility of 79% and a specificity of 100% to poor neurological outcome

**Conclusions:** Hypoxic-ischemic brain injury on MRI and NSE were strong predictors of poor neurological outcome. Although there is the belief that early achievement of target temperature improves neurological prognosis in our study there was increased mortality and worse neurological outcome with its earlier achievement.

## Hyponatremia in the elderly among the population of a Spanish third-level hospital

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**Objective:** To describe the special features of the population over 65 years of age with hyponatremia (HN) in our hospital's health care area.

**Methods:** A descriptive study was designed. All first HN found within January 2015 were included. Patient data were collected from electronic health records. SPSS 15.0 was used in order to make a statistical description. We separated the population over 65 years of age from the rest and analyzed this subpopulation's own distribution by age (over and under 80 years), gender, origin (nursing home, own residence), type of patient (healthy elderly, fragile elderly or geriatric patient) serum sodium at admission, etiology, days of hospitalization, days until correction of serum sodium, mortality (general and related to hyponatremia) and fulfillment of at least one STOPP criterion for inadequate prescription in the elderly related to HN or drugs known to favor the development of HN.

**Results:** From the total of 207 patients recruited, 138 (66%) were over 65 years old, and 83 among them were over 80 (60.1%). Male and female proportions were respectively 47.8% and 52.2%. 28 (20.3%) came from a nursing home, 102 (73.9%) came from their own domicile and 8 (5.8%) from other origins (e.g. other hospitals). 24 (17.4%) were healthy elderly subjects, 64 (46.4%) were fragile and 50 (36.2%) were geriatric patients. Up to 37% fulfilled at least one STOPP criterion directly or indirectly related to hyponatremia. The mean sodium at admission was  $130.6 \pm 4.0$  mmol/l; 41 patients (29.7%) had sodium values  $\leq 130$  mmol/l ( $126.2 \pm 5.1$ ), whereas 97 (70.3%) had values  $> 130$  ( $132.4 \pm 1.1$ ). The most common causes of HN among the elderly in our sample were thiazide use (27 out of 138, 19.6%), acute gastroenteritis (17; 12.3%) and heart failure (14; 10.1%). The mean hospitalization days were  $6.2 \pm 7.2$ , the mean days until correction  $3.0 \pm 3.7$ ; and the general mortality was 13.1% (no-one case related to HN). In addition, nobody died suffered any complication due to hyponatremia correction.

**Conclusions:** As the proportion of elderly subjects in the population is constantly increasing and they are the main health care users in internal medicine hospitalization wards, their peculiarities should be taken into account when managing HN. Numerous comorbidities and prescriptions, some of them may be inadequate, can favor and even worsen HN. A significant part of our elderly sports some degree of dependence, which poses an extra difficulty in their management, as well as an extra risk of additional morbidity and death.

## Chronic conditions and admission to intensive care: the relevance of a shared decision

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**Objectives:** The prevalence of chronic diseases is increasing in all countries of Europe. For this, greatly contributes to increasing

incidence of risk factors such as better health care for these patients. The chronic conditions such patients when associated with acute illness, may experience exacerbation that lead to the need for admission to intensive care. To evaluate whether patients were duly informed by their doctor about the possible need for admission to intensive care and, if that happened, what invasive procedures they would accept (oro-tracheal intubation (OTI), mechanical ventilation (MV), tracheotomy).

**Methods:** Cross-sectional study cohort of patients with chronic disease, as defined by the World Health Organization, admitted to an ICU or Internal Medicine Service due to exacerbation of it. Were recorded sociodemographic characteristics, cause of exacerbation of the chronic condition, personal history, knowledge about the reality of an ICU, it possible admission and in that case, what invasive procedures (OTI, MV and tracheotomy) would be accepted by the patient.

**Results:** 100 surveys were carried out: 44% to women and 56% to men; mean of age 60.9 years old. Of these, 18% reported knowing the reality of an ICU however only to 14% had been explained the possibility of admission. Of the patients informed about the possibility of admission on ICU, 78.6% had been informed about OTI, 64.3% about mechanical ventilation and 35.7% about tracheotomy. Of the patients surveyed 96.7% said they would like to have more information about their chronic condition and the possible exacerbations that require admission in ICU.

**Conclusions:** The natural evolution of many of the chronic diseases, usually treated by internal medicine doctors as are the heart failure, COPD and others, have great chances at an advanced stage to need ICU cares. The respect of the patient right to autonomy, obliges that the natural evolution of the disease should be discussed with the patient in a timely manner. Autonomy is to inform the patient and do not blame him by clinical decision. This study concluded that patients with chronic disease are not mostly informed about the possibility of admission in ICU, or the procedures inherent in this relocation. Medical assistants have an ethical obligation to clarify patients about their illness, the possible evolution of the need for invasive means of advanced life support, so that patients can have a more active and informed role of decision.

## Neurological impairment, hyperthermia and multiorgan failure as a manifestation of heat stroke. Importance of normothermia as initial treatment

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**Introduction:** Body temperature is result of balance between production and heat loss. Heat disorders are end result of failure of physiological mechanisms that maintain body temperature to a major overload internal or ambient heat. We report a case of multiorgan failure by heatstroke and importance of normothermia as one of initial steps.

**Case report:** A 60 years old man, who was found comatose (Glasgow 3 points) in greenhouse where he worked. Emergences

service proceeded to his orotracheal intubation. Physical examination showed 42°C of temperature and 150 ppm. Laboratory test showed: creatinine 1.64 mg/dL, myoglobin >40330 ng/ml, GOT 291 U/L, sodium 124 mEq/L, potassium 6.6 mEq/L, platelets 77000/L and metabolic acidosis. Differential diagnosis was made with patient clinic and laboratory test, between: infectious disease (meningitis, sepsis, encephalitis), hyperthermia syndromes (malignant hyperthermia, neuroleptic malignant syndrome, heat stroke), diseases of the CNS (brain hemorrhage, acute hydrocephalus, cerebral ischemia), endocrine diseases (diabetic coma, pheochromocytoma, thyroid crisis). Cranial-CT was normal. Lumbar puncture for CSF unaltered cytochemical, pathological anatomy and cultures were negatives. Therapy with normothermia with Artic Sun was begun for 12 hours, due to patient maintained hyperthermia, with good control of body temperature. Mannitol bolus was started by myoglobinuria. After 24 hours, he presented worsening of his hemodynamic situation starting vasoactive drugs, with worsening of renal function, lactic acidosis and severe liver disorders with severe thrombocytopenia and coagulopathy with onset of petechiae in pressure zones. Despite measures taken, he died 24 hours later. After testing, environmental factors (50°C and humidity 75%) and evolution, multiorgan failure by heat stroke was established as a final diagnosis.

**Discussion:** Heat stroke can cause a number of complications, respiratory and cardiac dysfunction, hypotension, seizures, rhabdomyolysis, acute renal and hepatic injury, and disseminated intravascular coagulation. Severe heatstroke carries a high mortality rate. Mortality correlates with the degree of temperature elevation, time to initiation of cooling measures, and the number of organ systems affected. Normothermia therapy would be of interest as a tool of cooling in them, getting a temperature regulation body in a short time, important to avoid complications 2nd to maintenance of a high body temperature.

## Air below the diaphragm

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**Introduction:** Chilaiditi sign, first described by the Greek radiologist Chilaiditi in 1910, refers to the radiological observation of segmental interposition of the colon between the liver and the diaphragm. With an incidence of 0.025-0.28% worldwide, it may be asymptomatic or accompanied by clinical symptoms, causing Chilaiditi syndrome. Under normal circumstances, suspensory ligaments and fixation of the colon impede its interposition between the liver and diaphragm. Intestinal, hepatic and/or diaphragmatic etiologies have been described, as absence, laxity or elongation of the suspensory ligaments of the transverse colon or the falciform ligament, chronic constipation, aerophagia, cirrhosis or diaphragmatic paralysis. Also, chronic lung disease, increased intra-abdominal pressure or adhesion caused by widespread tumor metastasis or previous surgery are associated with anatomic abnormalities that can result in Chilaiditi sign.

**Case report:** A 93 years old man was admitted to the emergency department of Hospital de Braga presenting cough and sputum

for 3 days. During the evaluation, the patient undergone a chest and abdominal X-ray, which showed elevation of the right hemidiaphragm by a distended bowel and the superior margin of the liver depressed below the level of the left hemidiaphragm. This is called Chilaiditi sign.

**Discussion:** Important differential diagnoses of this radiographic sign include pneumoperitoneum and subphrenic abscess. The finding of haustral folds or valvulae conniventes between the liver and the diaphragmatic surface can rule out those more serious entities. Moreover, the position of the radiolucency will not change by altering the posture of the patient, unlike free air. It is important to identify Chilaiditi sign in order to prevent complications occurring during a percutaneous transhepatic procedure, liver biopsy or colonoscopy. Chilaiditi sign is usually an asymptomatic radiologic sign – the treatment is usually conservative. When accompanied by symptoms, usually gastrointestinal (ranging from mild abdominal pain to acute bowel obstruction) or respiratory distress, less frequently angina-like chest pain, it is called Chilaiditi syndrome, which can evolve to volvulus or perforation. In conclusion, although Chilaiditi sign is a rare entity, it should be considered when a patient presents with abdominal and/or respiratory symptoms and has a radiologic finding of air below the right diaphragm.

## Incidence and etiology of hyponatremia within emergency wards in a third-level hospital

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**Objectives:** Hyponatremia (HN) is the most common hydroelectrolytic disorder and it is a relevant topic, not only because of its frequency, but also because of the complexity its diagnosis and right treatment poses. The goal of this study is to describe the features of patients and causes of HN in a third-level hospital.

**Methods:** Revision of patient data records of adults admitted into the emergency ward within January 2015, whose serum sodium values were found to be  $\leq 133$  mmol/l.

**Results:** Among 207 analyzed cases (incidence 0.03%), 56% were male with a mean age of  $72 \pm 16$  years [29-98]. 14% came from nursing homes. The most common reason for referral was dyspnea 19%, followed by fever 15%. Medical history: diabetes mellitus 30%, heart failure 28%, neoplasia 21%, renal failure 13%, cirrhosis 9%, IADHS 4%. 51% took hyponatremia-inducing drugs: 28% loop diuretics and 21% thiazides. 65% had normal, 23% increased and 12% decreased extracellular volume. The mean serum sodium in the first analysis was  $130.6 \pm 3.8$  mmol/l, the median was 132 mmol/l. 3% had HN  $\leq 120$  mmol/l, 19% had 120-129 mmol/l, 78% had 130-133 mmol/l. 87% were considered unknown temporality, 8% acute and 5% chronic. Mean glycemia was  $281.7 \pm 18.6$  mg/dL [71-574]. Analysis of urinary ions was performed in 23 patients (11%), TSH in 37% and cortisol in 4%. HN was among the diagnostics at discharge in 20% and was the main cause of admission in 4.3% (9 cases). 43% of patients

were discharged from the emergency ward. 29.5% were admitted into the internal medicine hospitalization. The causes for HN were: heart failure 16%, gastrointestinal losses 14%, thiazide 12%, hyperglycemia 9%, cirrhosis 6%, multifactorial 6%, renal failure 5%, furosemide 3% and IADHS 3%.

**Conclusions:** It is interesting to know the incidence (0.03%), baseline clinical characteristics and the causes of HN in our population in order to improve the management of this common disorder. Most of them are mild, and up to 26% of the times the cause of HN in our environment remains unknown. Only few times were complementary tests performed, which are nonetheless simple and available in the ambit of the emergency ward, such as plasma osmolality and urinary ion analysis.

## Management and evolution of hyponatremia in a Spanish third-level hospital

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**Objective:** To describe the management of hyponatremia (HN) in our hospital and to analyze the treatments initiated and their impact in the patients' clinical and analytical evolution.

**Methods:** A descriptive study was designed. All first HN found within January 2015 were included. Patient data were collected from electronic health records. SPSS 15.0 was used in order to make a statistical description. The sample was divided by cause of HN, by the presence or not of follow-up laboratory exams and by persistence of HN at discharge. These groups were

furthermore divided into mild (>130 mmol/l) and moderate ( $\leq$ 130 mmol/l) HN. Mean days until correction of HN and mean days of hospitalization were analyzed. We also analyzed general and hyponatremia-attributable mortality within the following 5 months, as well as readmission due to HN.

**Results:** 207 patients were included. The most frequent causes were heart failure (16%) and acute gastroenteritis (14%). HN due to heart failure was most frequently mild (79%), was most frequently treated with diuretics (57% among mild and 69% among moderate HN) and serum sodium initially improved thereafter most of the times. Fluid restriction was never used on its own, but in combination with diuretics. Among patients with acute gastroenteritis, the majority had mild HN (70%). 44% among moderate and 52% among mild HN due to dehydration had no follow-up and were not treated. The most frequent therapy was intravenous normal 0,9% saline (33% among mild and 56% among moderate HN), and most of them subsequently improved. Inadequate ADH secretion (IADHS) was only confirmed by criteria in 7 out of 207 (3%). Among them, mild HN was most frequently treated with hypertonic 3% saline fluid (50%), whereas moderate HN was treated of the times with fluid restriction (60%). 27 patients died within the following 5 months; no-one due to HN. In addition, nobody suffered any complication due to hyponatremia correction.

**Conclusions:** HN, especially in mild cases, is usually overlooked by hospital clinicians. Although most of them develop satisfactorily, only a minority of them is completely evaluated, which leads in many cases to suspected diagnosis and empirical treatment instead of confirmation and etiologically directed therapy. Although guidelines exist, there is little unity in the management, probably out of lack of awareness or attention to other major problems in patients' acute processes.

## Microalbuminuria as a cardiovascular risk factor in obesity

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**Objectives:** Obesity is a risk factor for renal failure and pathologies leading to renal failure, independent of related diseases. Microalbuminuria (MAU) is the first stage of those pathologies and has been shown to reflect higher probability of cardiovascular disease. In this study, we aimed to search for microalbuminuria and undiagnosed cardiac pathologies in metabolically healthy obese patients to assess the cardiovascular risk related to MAU.

**Methods:** 100 obese patients (body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>) without accompanying diseases, present medication or smoking history were included in the study. They were screened for any signs of acute/chronic inflammation and those having any were excluded. Blood glucose, HbA<sub>1c</sub>, urea, creatinine, total cholesterol, LDL, HDL, triglyceride and 24-hour-urine microalbuminuria levels (30-300 mg/24 hours) were studied. Two-dimensional Doppler echocardiography (ECHO) and 12-lead-electrocardiography (ECG) were performed. Data was statistically analyzed using SPSS Windows 11.5.

**Results:** 93 female and 7 male, totally 100 patients were included in the study. Mean age was 39 years and mean BMI was 39.9 kg/m<sup>2</sup>. None of the patients had metabolic syndrome according to ADA 2005 criteria. All patients had normal ejection fraction (EF) in ECHO and normal serum urea, creatinine levels. 14% (n=14) of the patients had MAU (146 mg/24 hours mean excretion). 43% (n=6) of patients who had MAU had positive ECHO findings (diastolic dysfunction, left ventricular hypertrophy and mitral valve thickening) and 36% (n=5) had non-specific ST-T wave changes in ECG.

**Conclusions:** Microalbuminuria found in obese patients can be related with subclinical cardiac damage. Thus, it would be possible to predict cardiovascular risk of the obese patients with a simple and non-invasive method in advance and prevent/delay further cardiovascular damage by taking the necessary precautions.

## Aging and obesity

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**Objectives:** Obesity is a global epidemic and an uprising problem. Treatment is usually difficult, long-term and expensive and it is affected by multiple different factors. In this study, we aimed to search how aging affected weight loss.

**Methods:** 20 patients with the age between 20-40 years and 20 patients with the age between 40-60 years, totally 40 patients who had matching body mass indexes (BMI) and achieved to lose weight in any degree in 6 months after admission to our obesity outpatient clinic were included in the study. They were all non-smokers and none of them were on any kind of anti-obesity drugs. Their BMI, metabolic syndrome (MS) and insulin resistance (IR) rates, accompanying diseases (diabetes mellitus, hypertension, hypothyroidism, hyperlipidemia), medication usage and treated depression rates were recorded. They were prescribed diet and exercise according to international guidelines. The weight loss amount after 6 months was calculated for 2 groups and compared using SPSS statistical analysis method. The study was approved by the Ethical Committee of our hospital.

**Results:** In younger group; the mean age was 32.9 years, the mean BMI was 39.3, MS rate was 45%, IR rate was 80%, accompanying disease rate 85%, medication usage was 75% (2.6 drugs/patient) and depression rate was 30%. In older group; the mean age was 50.2 years, the mean BMI was 40.7, MS rate was 55%, IR rate was 75%, accompanying disease rate 95%, medication usage was 70% (3.4 drugs/patient) and depression rate was 20%. At the end of 6 months, younger group achieved statistically significant better weight loss than the older group (mean weight loss 4.5 kg in younger group and 3.1 kg in older group).

**Conclusions:** Our study showed that higher percentage of weight loss is achieved in younger ages even with similar BMI, metabolic state, accompanying diseases, medication and depression rates. Weight loss gets more difficult by aging even though presenting the same effort by both the patient and the physician. Decreased energy expenditure due to decreased basal metabolic rate, limited exercise capacity, changes in body fat and muscle mass percentages are contributing factors. Genetics also play an important role. Thus, it is vital to take the needed precautions in advance to aging when reversal of the disease is easier, more rewarding and encouraging for continuation of healthy life style.

## Amiodarone-induced hyperthyroidism: a retrospective study

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**Objectives:** Amiodarone is a commonly used antiarrhythmic drug mainly in Europe. Its use results in a large iodine load increasing the risk of thyroid dysfunction, ranging from 2 to 30%, depending upon an individual's thyroid status and iodine intake. Though hypothyroidism is more frequent, affecting 5-22% of treated patients, amiodarone induced hyperthyroidism (AIH) is also an important side-effect due to its high morbidity, occurring in 2.0-9.6%. Considering the high frequency of amiodarone treatment and its side-effects, the authors decided to study AIH and its clinical features in a local hospital population.

**Methods:** We studied retrospectively all the patients diagnosed with hyperthyroidism, between January 2014 and June 2015.

**Results:** We found 242 patients, 42 of which had history of amiodarone therapy (24 female, mean age 75 years). 30 patients (71%) presented with clinical manifestations of hyperthyroidism the majority being cardiovascular symptoms (59%); 16 (38%) had tremors and 14 (33%) weight loss. We found 4 (9,5%) patients with positive thyroid auto-antibodies titles. A thyroid ultrasound (US) was performed in 20 patients (48%), 12 (60%) showing multinodular goiter, 9 (45%) with enlarged gland and 6 (30%) with low echogenicity. In 23 (55%) patients therapy for AIH was introduced, all of them with anti-thyroid drugs, 6 (26%) also needed corticotherapy and 2 (9%) required surgical thyroidectomy due to severe thyrotoxicosis.

**Conclusions:** In our casuistic, 16 (38%) patients had abnormal tests consistent with previous thyroid dysfunction, which favors type 1 AIH and 6 (14%) thyroid US was compatible with thyroiditis suggesting type 2 AIH. However 52% of the diagnosed patients didn't perform an US rendering it impossible to make an accurate differentiation. Since distinction into AIH two types wasn't possible, the therapy wasn't chosen considering that information. Thus, all treated patients received anti-thyroid drugs, despite it is generally recommended for type 1 AIH. AIH is an important cause of morbidity and often an unrecognized diagnosis which may lead to unsuitable therapeutic choices. When approaching a patient with hyperthyroidism, it is important to investigate previous or current amiodarone therapy so that therapeutic approach can be individualized. When electing amiodarone as an antiarrhythmic drug one should always have in account its relation with thyroid dysfunction considering its use in restricted situations and when strictly necessary.

## Lipid metabolism and testosterone status at men with type 2 diabetes mellitus at the religious fasting

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**Objective:** To assess the lipid metabolism and testosterone (Tst) status as the important component of the type 2 diabetes mellitus (T2DM) management at the religious fasting (RF).

**Material and methods:** In the observational clinical study 62 men with T2DM and visceral obesity (medians of body mass index (BMI) 32,2 kg/m<sup>2</sup>, waist circumference (W) 103 cm) were included. We studied interventional and control groups: RF(+) (n=30) and RF(-) (n=32) correspondently. The dynamics of the lipidogram parameters (total cholesterol (CHOL), triglyceride (TG), lipoproteins high (LPHD) and low (LPLD) density); the levels of glycosylated hemoglobin HbA<sub>1c</sub>, Tst had been investigated during the Lent and the Navity religious fasting. The physical activity (PhA) was assumed as high, mild and low in depending of profession and fitness. The total Tst (tTst), free Tst (fTst), PSA and AMS-index (without IIEF-5 due to sex deprivation during a religious fasting) were assumed before and after the RF. The processing data was made using Statistica6.0, and the differences were with statistical significance if p<0,05.

**Results:** The safety of RF for patients with T2DM was demonstrated. The maximal improvement of the metabolic parameters and Tst-status had been associated with adequate PhA. In the interventional group RF(+)PhA(+) the dynamics was -0,3% for HbA<sub>1c</sub>, -0,4 mmol/L for TG, -0,4 mmol/L for CHOL, -0,5 mmol/L for LPLD, +0,2 mmol/L for LPHD. Meanwhile tTst rised from 13,4 to 15,1 mcmol/L, and fTst – from 13,4 to 15,1 pg/ml. AMS-score reduced from 33 to 28 were observed (p<0,05). In other interventional group RF(+)PhA(-) the dynamics of those parameters was neutral as in the control group RF(-)PhA(+). The worst dynamics was in the control group RF(-)PhA(-). BMI was changed from 33,4 to 34,1 kg/m<sup>2</sup>, W – from 105 to 107 cm, and the median AMS-score – from 35 to 37 (p<0,05). PSA was constant in all groups (p<0,05).

**Conclusions:** The physical activity at the men with T2DM and visceral obesity is the key modified factor for the good T2DM management during religious fasting. The high and mild PhA at the men with T2DM, visceral obesity and androgen deficiency is positively correlated with the improvement of the lipid metabolism and enhancement of the Tst-status.

## Can liraglutide improve the renal function in type 2 diabetes mellitus?

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**Objectives:** Glucagon-like peptide 1 (GLP-1) is an incretin hormone secreted by the small intestine that increases insulin secretion and reduces glucagon release. Its secretion is triggered by nutrient ingestion and it is degraded by the enzyme dipeptidyl peptidase-IV (DPP-IV) and neutral endopeptidase. Acts through a G-coupled protein receptor expressed in the gastrointestinal tract, nervous system, heart, vascular smooth muscles and kidneys (proximal tubules and glomerulus). Liraglutide is a GLP-1 receptor agonist known to improve glycemic control and promote weight loss with minimal hypoglycemia in patients with type 2 diabetes mellitus (T2DM). Animal studies show that GLP-1 receptor agonists may protect from diabetic nephropathy. This effect may represent new ways to improve or prevent diabetic nephropathy. The present study aims to characterize single center 1-year results concerning the impact of liraglutide on renal function.

**Methods:** The authors prospectively evaluated the outcomes on patients with T2DM under treatment with liraglutide. Creatinine, albuminuria/creatininuria ratio and eGFR (CKD-EPI creatinine equation) were the endpoints of interest.

**Results:** 25 patients, 55% male, median age 58 [54-67] years old. T2DM diagnosis for 13.5 [6-20] years. Over 90% of the patients presented baseline eGFR >60 mL/min. Baseline creatinine level (mg/dL) was 0.80 [0.67–1.06] and there was no significant change over time: 0.83 [0.64–0.96], 0.80 [0.68–1.01], 0.69 [0.63–1.01] and 0.89 [0.55–1.13], respectively at month 3, 6, 9 and 12 (p>0.05). Albumin/creatinine ratio (mg/g) presents high variability over time, but without significant statistic value: 44.5 [12.7–158.6], 16.1 [4.68–116.9], 64.1 [23.7–244.7], 39.4 [7.55–244.7] and 44.4 [8.03–89.7]. Two patients stopped the medication due to GI symptoms. None presented acute kidney failure.

**Conclusion:** In this single center study liraglutide had no impact on renal function in patients with T2DM (>5 years duration) and no previous chronic kidney disease.

## **A case of acromegaly presenting with peripheral neuropathy**

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**Introduction:** Acromegaly is a rare disease characterized by secretion of excess growth hormone (GH). In these patients, arthropathy resulting from soft and bone tissue growth, carpal tunnel syndrome and peripheral neuropathy are frequently observed. These symptoms can even be the first manifestations of the disease. Acromegalic patients, especially those with peripheral neuropathy, consult first to orthopedic and/or physical therapy clinics, which leads to delayed diagnosis of acromegaly. Here, we would like to present a case of acromegaly, which has been diagnosed late since patient initially consulted to different clinics due to neuropathy.

**Case report:** A 22 years old male patient with symptoms of numbness, burning and tickling sensation in hands for 2 years applied to neurology clinic. Related examinations revealed bilateral peripheral neuropathy, and then B-complex vitamin and non-steroid anti-inflammatory drug (NSAID) were prescribed. The patient's complaints have lessened and, then he applied to physical therapy clinic. NSAID was prescribed once again. Since his complaints have not improved, more detailed biochemical tests have been conducted and elevated level of GH was found. The patient has been referred to our department and detailed medical history showed that there was a growth in hands and increase in shoe size, in addition to the existing complaints in hands. His basal levels of GH and IGF-1 were found to be increased to 22.6 ng/ml (reference range: 0-3 ng/ml) and 1131 ng/ml (reference range: 116-358 ng/ml), respectively. Oral glucose loading showed no GH suppression. Pituitary MRI showed a sellar mass, measuring 10x13x9 mm. Examinations of visual field, colonoscopy and echocardiography were all found to be normal. The patient was referred to the neurosurgery department, where they performed transsphenoidal pituitary adenomectomy. At the second month after operation, his serum levels of GH and IGF-1 were in normal limits and he was advised to have regular checks-up.

**Discussion:** Since acromegaly is a very insidious disease, the diagnosis is often late. As seen in our case, acromegaly should always be kept in mind in case of growth signs in soft and bone tissues. Acromegaly should be investigated carefully especially in cases with neuropathic complaints, and do not benefit from the treatment.

## **A case of metastatic pulmonary carcinoid associated with ectopic ACTH-dependent Cushing's syndrome**

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**Introduction:** Hypercortisolism due to ectopic ACTH production is one of the rare causes of Cushing's syndrome. General therapeutic approach is to remove the ACTH secreting tumor foci. In order to manage these patients properly, it is very important to evaluate comorbidities associated with Cushing's syndrome and to refer patients to surgery on time. We present here a case of metastatic pulmonary carcinoid admitted to clinic with ectopic Cushing's syndrome.

**Case report:** A 38 years old male patient presented with the complaints of excessive weight gain, blue-purple skin striae, chronic fatigue and shortness of breath. There was no known disease in his medical history and he seemed morbidly obese. He had moon face appearance, wide blue-purple striae in the abdomen, arms and legs, buffalo hump. There were crackles up to the middle zones during lung auscultation. Pretibial edema ++/+++. Tests conducted due to obvious cushingoid appearance: basal cortisol, cortisol in 24-hour urine and 1-2 mg dexamethasone suppression test (DST) were consistent with hypercortisolemia. Patient's basal ACTH was 165 pg/ml, and there was no cortisol suppression in 8 mg DST which is conducted for differential diagnosis. Thoracoabdominal computed tomography was performed to the patient who is suspected of ectopic ACTH-dependent Cushing's syndrome (EADC), showing a 2x1 cm nodular density increase in the right lower lung lobe, which could be compatible with pneumonia or tumor. Gallium 68 somatostatin receptor PET imaging was performed for differential diagnosis. Somatostatin receptor activity of the above-mentioned nodular areas was observed. Patient with ectopic Cushing focus was referred to surgical treatment. He underwent wedge resection and the pathology was consistent with metastatic pulmonary carcinoid tumor. In the postoperative follow-up period, patient who developed cardiac decompensation in intensive care, died due to myocardial infarction.

**Discussion:** Despite of rare occurrence, EADC is quite aggressive compared to other causes of Cushing's syndrome. The reason for this is usually underlying malignancies. Therefore, it is primarily important to consider the possibility of ectopic ACTH production in rapidly progressive Cushing cases which develop over weeks and months. In this way, malignancies which cause EADC can be detected at an earlier stage and it may provide a significant contribution in terms of survival. In our case, if the patient had consulted earlier, we believe that more positive contribution could be provided to this patient with metastatic cancer and improved in major cardio-metabolic affects in terms of survival.

## **A case of secondary hypertension completely cured with adrenalectomy: importance of investigation of secondary causes of hypertension in a young patient**

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**Introduction:** Secondary conditions such as endocrine, renal, cardiac, etc. disorders are responsible for only 5-10% of hypertension (HT). Since correcting the underlying cause in secondary HT (SHT) can completely cure HT itself, early diagnosis is very important for morbidity and mortality. Here,

we would like to present a case of a young hypertensive patient with hypokalemia and HT.

**Case report:** A 23 years old male-patient using amlodipine and valsartan in the previous 5 months for HT was referred to our clinic since he has been found to harbor a 3x4 cm right adrenal mass while being screening for SHT. In routine tests, nothing special was detected other than low serum potassium level (K 3,7 mEq/l). Hormone panel, 1 mg dexamethasone suppression test, and 24-hour urine catecholamine levels were all normal. Antihypertensive medication was replaced with an alpha blocker to measure more accurately aldosterone and plasma renin activity. Three weeks after medication exchange, basal aldosterone level was high (48 ng/dL) and so was aldosterone-PRA ratio (aldosterone/PRA >30). Based on these findings, saline infusion test was performed. In the 4th hour of the test, there was no meaningful suppression in the aldosterone level (28,5 ng/dL). In order to validate primary hyperaldosteronism (PA) diagnosis, adrenal venous sampling (AVS) was done, showing an increased level of aldosterone in the right-side compared to contraletal side. In early preoperative period, blood pressure was under control only by multiple antihypertensive drugs (amlodipine, spironolactone, hydrochlorothiazide, carvedilol). Later, no complication was observed in the patient who underwent right-adrenalectomy. In follow-up, there was no need to continue any antihypertensive drug.

**Discussion:** PA is one of the most important causes of secondary HT. Classic manifestation of PA includes hypokalemia and HT. The most commonly observed types are aldosterone producing adenomas (APAs) and bilateral idiopathic hyperaldosteronism. In addition to hypertensive patients with HT and hypokalemia, PA should be investigated in the following conditions: resistant hypertension, adrenal incidentaloma plus HT, HT with family history of early HT or cerebrovascular disease, first degree relatives of patients with PA. This case of PA shows the importance of keeping in mind and investigation of secondary causes of HT in young cases.

## Diabetes mellitus and patients with severe disability – a retrospective observational study

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**Objectives:** In 30 years the number of old people in Portugal almost doubled. Portugal is the second country from European Union with the highest rates of severe disability among older people. 26,3% of Portuguese people between 60 and 79 years old has diabetes. The latest researches suggest that diabetes treatment should be individualized. However there are still some difficulties at establishing adapted therapeutic programs for this population in particular. The aim of this study is to characterize the glycemic control, treatment and complications of the diabetic population with severe disability. We pretend to evaluate the need of establishing local guidelines for this particular group of patients.

**Methods:** Clinical process of hospitalized patients in an internal medicine department between January 2014 and February 2015. The Modified Ranking Scale (mRS) was used to measure the disability grade. The data was processed using the IBM SPSS Statistic™.

**Results:** Total of 162 patients, 110 females and 52 males. Average age of 80±8,7 years old. 84 patients scored 4 in the mRS and 78 scored 5. The average HbA<sub>1c</sub> was 7,5%, with a minimum of 4,9% and maximum of 12,1%. 62 patients had HbA<sub>1c</sub> <6,5% and 30 had HbA<sub>1c</sub> >8,5%. 95 patients were on insulin. 81 patients were on oral antidiabetics (OAD) – 43 on metformin, 26 on sulfonylureas and 49 on DPP4i. 39 patients were on insulin plus OAD. 6 patients had previous hospitalizations due to hypoglycemia and 9 due to hyperosmolar syndrome.

**Conclusions:** There's still a significant proportion of patients in which antidiabetic therapeutic seems to be too aggressive with increased risk of hypoglycemia – 1/3 of patients had HbA<sub>1c</sub> <6,5% and 16% were on sulfonylureas although its hypoglycemic potential. Only 6 hypoglycemic episodes were identified, however all the episodes that didn't lead to hospitalization were not taken into account. For terminal patients, the glycemic control is the one that doesn't cause symptomatic hyperglycemia. However, 9 episodes of hyperosmolar syndrome were identified. The severely disabled patients have some particularities, like hypoglycemic risk, that makes imperative the need for some special measures concerning their diabetes's treatment, different from the treatment for general population. To correctly apply these special measures it is necessary to establish local protocols that take into account the characteristics and needs of this population.

## Diabetes mellitus, cardiovascular risk and macrovascular complications – retrospective observing study

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**Objectives:** Cardiovascular diseases such as stroke and acute myocardial infarction (AMI) are still the main cause of death in Portugal. Diabetes mellitus (DM) is, by itself, associated to a high cardiovascular risk (CVR), but often, patients with DM has other factors of CVR such as hypertension and dyslipidemia. The purpose of the study is to characterize CVR, the way it is managed and the consequent macrovascular complications in a sub-population of patients with DM. This study aims to identify the main problems and hindrances felt on the management of these patients so that new strategies can be defined in order to improve the given care.

**Methods:** Clinical Process Consultations of patients with DM hospitalized in the Internal Medicine Service between January of 2014 and February of 2015. Data was processed using IBM SPSS Statistic™.

**Results:** Sample composed by 382 patients, 237 female and 145 male with an average age of 77,2±9,6 years. The average value of HbA<sub>1c</sub> was of 7,8±1,8%. 87.2% of the patients had



hypertension. 79.1% of patients had dyslipidemia. From these, 28.7% were not on statins and inside this group 85% had LDL cholesterol >70 mg/dL. In total, 54% of the sample had LDL >70 mg/dL. 71% of patients presented with hypertension, DM and dyslipidemia, 23,3% with DM and hypertension or DM and dyslipidemia and 5% with only DM. In total, 16,4% of the patients had history of AMI and 38,1% had already suffered a stroke. These values rise to 19,3% and 35%, respectively, for the group of patients with the 3 CVR factors. Global mortality during hospitalization was 16%.

**Conclusions:** The obtained results agree with available literature: diabetic population has a higher prevalence of hypertension and dyslipidemia when compared to the general population. When associated to the 3 CVR factors, the incidence of macrovascular complications further increase, namely AMI and stroke, which shows it, is of utmost importance the close control of all risk factors in these patients. However, there still exist a significant percentage of patients in which the values of LDL cholesterol were above the wanted levels and/or were not medicated with statins, increasing the risk of thrombotic events. It is necessary a greater sensibilization of the clinical staff to the importance of aggressive control of RCV factors in the diabetic patients, who already have a high risk on their own, in order to decrease the rates of AMI and stroke.

## Elevation in carcinoembryonic antigen levels, sometimes it's thyroid!

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**Introduction:** The carcinoembryonic antigen (CEA) blood test is not reliable as screening test for early detection of cancer. It is usually used as a tumor marker to monitor colorectal carcinoma treatment. CEA levels may also be raised in gastric carcinoma, pancreatic carcinoma, lung carcinoma and also medullary thyroid carcinoma.

**Case report:** The authors present the case of a 67 years old Caucasian male patient, with history of type 2 diabetes mellitus, arterial hypertension, cerebrovascular disease and dyslipidemia. In a routine blood checkup ordered by his family doctor, a CEA elevation was detected – 208 µg/L (reference range <5 µg/L). To investigate this finding the patient was submitted to a colonoscopy which only detected a benign polyp that was resected. Abdominopelvic computed tomography (CT) scan did not detect relevant alterations. Thoracic CT scan detected a thyroid nodule with calcifications. The patient was then sent to hospital consultation. The blood tests revealed CEA 198 µg/L, calcitonin 3387 pg/ml (reference range <8.4 pg/ml), normal thyroid function tests and negative antithyroid antibodies. The neck ultrasound showed a 3cm thyroid nodule in the left lobe. Fine needle aspiration cytology (FNA) was benign. He also had an abdominal ultrasound that excluded hepatic metastasis. Despite the benign result of the FNA, since the calcitonin levels were diagnostic, the patient was submitted to total thyroidectomy and lymph node dissection of the central compartment. Histology confirmed medullary carcinoma (4 cm

in the left lobe without vascular invasion, but with secondary deposition in 3 of 8 isolated ganglia.

**Discussion:** The authors aimed to highlight that although tumor markers should not be used as screening tests for cancer, it's important to keep in mind that not all elevations of CEA are related to gastrointestinal or lung cancer – medullary thyroid cancer, although rare, is an important cause.

## Cerebral venous thrombosis during diabetic ketoacidosis: case report

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**Introduction:** Cerebral venous thrombosis (CVT) is an uncommon disease with mortality rates. We report two cases with type 1 diabetes without underlying thrombotic tendency but having concomitant diabetic ketoacidosis (DKA) which may contribute CVT.

**Case reports:** Case 1: A 22 years old woman with known history of type 1 diabetes for 14 years. She was found unconscious at her house and had a history of fatigue, headache and anxiety for a week. On admission she was dehydrated, tachycardic, not responding to painful stimuli. In laboratory tests revealed blood glucose of 850 mg/dl, ketonuria, with a metabolic acidosis (pH 7.2, HCO<sub>3</sub> 13 mmol/l). A diagnosis of DKA with dehydration was made. Over the next 24 hours she was treated with a normal maintenance fluid rate (0.45% saline, 5% dextrose) and IV insulin (0.1 U/kg/h). Her laboratory values improved. She was still unconscious, only responding to painful stimuli and was found to have right sided hemiplegia. She transferred to an intensive care unit (ICU). She had a score of 11 from Glasgow coma scale (GCS). Brain computed tomography, magnetic resonance imaging (MRI) and venography scans were made. Examinations revealed left transvers and sigmoid sinus thrombosis. ASA 300 mg/day and anticoagulation therapies were started. She made a good recovery at ICU after 4 weeks. One month later her illness she had no motor deficit. Case 2: A 30 years old woman with known history of type 1 diabetes for 8 years. The last 2 weeks she has complained of nausea, vomiting, headache. She started skipping her insulin injections. She presented to the emergency department with worsening nausea and vomiting. In the first examination, the GCS was 15. She was dehydrated, tachycardic, and exhibited Kussmaul breathing. Blood gas examination results were pH 7,2, HCO<sub>3</sub> 13; blood sugar was 584 mg/dl, we were detected ketonuria in the urine. Patient was hospitalized with diagnose of DKA. Insulin infusion of 0.1 U/kg/h, fluid treatment were administered. During the follow-up, oral route was opened, plasma glucose was partly regulated. However, pH declined to 7.17 due to persistent nausea and vomiting. The patient history indicated a headache activated with position for 2 months, therefore a brain MRI was obtained and an occluded left transverse sinus was seen. Shortly after her vomiting declined. She recovered from DKA. She was discharged to outpatient monitoring with intensive insulin and anticoagulant therapy. In both cases there was no abnormality to coagulation studies, and rheumatologic examinations and laboratory tests.

**Discussion:** Our cases show the importance of neuroimaging in DKA when the cerebral edema is suspected. The treatment and management of other pathologies is often different to the management of cerebral edema.

### **A case of ACTH-independent Cushing's syndrome: which patients should be screened for Cushing's syndrome?**

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**Introduction:** Cushing's syndrome (CS) is an important disease, characterized by hypercortisolism and systemic symptoms. Diagnosis of the CS is mostly very challenging and management involves following steps: 1) the presence of classical CS symptoms and signs; 2) to demonstrate hypercortisolism; 3) to determine the main cause of the syndrome. Before starting diagnostic process, it must necessarily be excluded to steroid use for iatrogenic Cushing's. Here we report a missed ACTH-independent CS case, which has a cushingoid features for years.

**Case report:** A 34 years old female patient was admitted to the clinic because of weight gain. She has gained constant weight in the last 5 years. Except horseshoe kidney disease, she has no noticeable history, also hasn't used steroids or any other drug. Family history was negative too. In her physical examination: he was in obese habitus and BMI was over 30 kg/m<sup>2</sup>. She has developed purple-colored abdominal striae, moon face, buffalo hump, and has increased supraclavicular fat pads. Routine biochemistry evaluation was unremarkable. Basal ACTH was lower than 5 pg/mL and cortisol was 19 mcg/dL. With respect to cushingoid features, 1 mg dexamethasone suppression test (DST) was performed and cortisol suppression was not succeeded (18 mcg/dL). To verify hypercortisolism, 2 mg DST performed for 2 days and cortisol suppression was not succeeded (20 mcg /dL) again, 24-hour urinary cortisol was found more than 2 times normal (839 µg/24h). After hypercortisolism and ACTH suppression, initial diagnosis of ACTH-Independent CS was proven and adrenal MRI was performed, CT was avoided because of horseshoe kidney disease history. In right adrenal, 23x41 mm adenoma, which has shown diffuse suppression in out of phase sequence, has been observed. After the diagnosis of adrenal CS, patient was referred to urology clinic for surgical evaluation.

**Discussion:** In CS, the presence of certain findings (obesity, hypertension, glucose intolerance, etc.) is important, but they are nonspecific. In our previous study, we confirmed that only obesity is not important enough for CS screening. Thus, in the presence of suspected disease (not only obesity but also other findings), it should be focused on the detection of hypercortisolism. Basically, hypercortisolism should be evaluated in following cases: 1) in younger patients with hypertension or osteoporosis; 2) presence of multiple clinical findings related to CS (e.g. proximal myopathy, central obesity, facial plethora, easy bruising and striae (> 1 cm wide and red/purple); 3) presence of adrenal incidentalomas. Also in our case, CS related findings like obesity, purple-colored striae and subcutaneous fat tissue growth was observed. After verifying hypercortisolism, the main reason of the disease was

determined. As a result, in the differential diagnosis of patients with particularly obesity and other metabolic disorders, CS should be kept in mind.

### **A rare combination: Graves' disease with incidental papillary thyroid cancer**

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**Introduction:** The prevalence of palpable thyroid nodule in patients with Graves' disease (GD) is 3-fold higher compared to the general population. Thyroid nodule in GD patients is associated with an increased risk of thyroid cancer. However, the risk of thyroid cancer in GD without thyroid nodules is controversial. We present here a GD patient with papillary thyroid cancer identified after total thyroidectomy without preoperative thyroid nodule.

**Case report:** A 30 years old male patient had complaints of sweating, palpitations and weight loss for a month. The patient's scintigraphy showed a diffuse increased uptake and hyperplasia. Thyroid USG revealed an increased blood flow and diffuse enlargement of thyroid with no nodules. Laboratory exam showed an overt thyrotoxicosis with significantly increased titers of TRAb. The treatment was started by methimazole and propranolol. The patient was underwent total thyroidectomy after no remission and increased severity of Graves' ophthalmopathy despite of a 12 month-long antithyroid treatment. Postoperative pathologic exam revealed a single 8 mm focus of papillary thyroid cancer. Levothyroxine in a dose of TSH suppression was started.

**Discussion:** The association of thyroid malignancy and Graves' disease is very rare, making its therapy challenging. There are some studies showing an increased incidence of thyroid cancer among GD cases observed without thyroid nodules. In our case, although not seen preoperatively, PTC was detected in the thyroidectomy material. It may be concluded that, before applying ablative treatment for GD, the patients should be thoroughly reassessed for nodules. In such patients, if a thyroid nodule is encountered, we believe that surgery would be more appropriate option, particularly in terms of the possibility of PTC.

### **A case of idiopathic hypogonadotropic hypogonadism with monostatic fibrous dysplasia mimicking McCune-Albright syndrome**

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**Introduction:** McCune-Albright syndrome (MAS) is a genetic disorder, characterized by the classical triad of fibrous dysplasia of bone, café-au-lait spots and hyperfunctional endocrinopathies, and two of these findings are sufficient for the diagnosis. While polyostotic fibrous dysplasia (POFD) characterized by

fractures is more common, monostatic fibrous dysplasia (MFD) is less common. Main clinical features of MAS are precocious puberty, hyperthyroidism, acromegaly, hyperprolactinemia and hypogonadism. Due to its widespread involvement of the body, the disease requires a systemic approach and evaluation. We present here a case of idiopathic hypogonadotropic hypogonadism (IHH) with MFD mimicking MAS.

**Case report:** A 21 years old male patient was admitted to the neurosurgery clinic because of back pain. X-ray examination revealed a mass in the 12th thoracic vertebrae. Bone biopsy showed fibrous dysplasia. No other skeletal involvement was detected in the bone scan. The patient was referred to our clinic since his symptoms were consistent with hypogonadism. Patient stated that his secondary sex characteristics underdeveloped and he had ejaculation problems. There were no treatments or follow-up for these complaints. Examination showed his secondary sex development has lagged far behind and he had G1-P1 Tanner stage. Laboratory findings were consistent with IHH and other endocrine hormones panel was normal. Pituitary MRI was normal. Scrotal US showed bilateral testicular atrophy. The patient was placed on chorionic gonadotropin therapy. Alive sperm cells were available in the sperm analysis, performed after the 9<sup>th</sup> month of treatment. In addition to the current treatment, routine follow up were recommended to the patient at 3-6 month intervals.

**Discussion:** Since MFD of bone is a rare involvement form, hypogonadism was not due to hyperprolactinemia and the absence of café-au-lait spots, we didn't diagnose our patient as MAS. When we searched the literature we found two other cases associated with fibrous dysplasia and IHH which mimics MAS. We conclude that it is very important to conduct the differential diagnosis correctly especially in this kind of cases for appropriate diagnosis and treatment at the beginning. Also we think that we should follow the case for other components of the MAS.

## Clinical and laboratory features of the metabolic syndrome of patients from Khakassia

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**Objective:** To rationalize personalized approach to the prevention of metabolic syndrome in residents of Khakassia.

**Material and methods:** 266 patients with metabolic syndrome (MS), 188 women and 78 men, average  $42,2 \pm 0,46$  years were examined in the Republic clinical hospital in Abakan. All subjects were divided into groups of indigenous (Khakas) and new-comers (Caucasians) of the population of Khakassia. The diagnosis of MS according to the criteria was established by joint preliminary statement [JIS 2009]. Complex clinical and laboratory examination of two ethnic populations living in Khakassia was conducted. Statistical analyses were carried out using SPSS version 13.0 for Windows.

**Results:** The most common abnormalities in our population (Khakas) study were high blood pressure (100%), high blood

glucose (76.4%), high triglycerides (68.6%) and increase waist circumference (57.9%). In the group of indigenous patients with metabolic syndrome hyperfiltration in 52,2% of patients was revealed with increasing body weight. Using standardized serum creatinine values in the modification of diet in renal disease (MDRD) showed a slight decrease in GFR in 58,8% of patients, from 6,8% of patients had a moderate decrease in GFR and it was associated with high blood pressure and hyperglycemia in men (odds ratio 2.51,  $p < 0.001$  for both) as well as women (odds ratio 3.54,  $p < 0.001$  and 3.24,  $p = 0.0047$  respectively), and weakly with central obesity in men (odds ratio 2.05,  $p < 0.02$ ). Higher mean levels of CRP (7.34 vs 1.36,  $p < 0.001$ ) were observed in indigenous patients with MS. Also, mean C-reactive protein (CRP) levels were significantly higher in patients with central obesity (5.45 vs 1.24,  $p < 0.001$ ), high blood pressure (1.76 vs 1.12,  $p < 0.001$ ), hypertriglyceridemia (2.17 vs 1.32,  $p < 0.001$ ) and high fasting glucose (1.96 vs 1.46,  $p = 0.032$ ).

**Conclusion:** The differences prove the necessity of development and implementation of personalized approach in residents of Khakassia with MS for diagnostic, preventive and therapeutic measures taking into account ethnicity.

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## Daily dynamics of blood pressure and heart failure in patients with acromegaly

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**Objective:** To study the characteristics of the daily dynamics of blood pressure and cardiac morphofunctional characteristics and their relationship in patients with acromegaly.

**Material and methods:** 46 patients with acromegaly (mean age  $48,8 \pm 1,9$  years old) in the active phase were examined. Duration of the disease, according to history, was  $8,6 \pm 1,8$  years. For evaluation of disease activity levels were determined somatotropin and IGF-1. Control group included 30 patients. All patients underwent ambulatory blood pressure monitoring. To determine the structural and functional state of the myocardium all the patients underwent echocardiography with Doppler. Statistical analysis was performed using the program «Statistica 6.0».

**Results:** According to ABPM hypertension was recorded in 75%. In assessing circadian identified: insufficient degree of nocturnal SBP reduction of 50%, 45% DBP, increased night SBP DBP 35% to 40%. Obtained statistically significant correlation enough reduction SBP night with process activity (IGF-1) ( $r = 0,64$ ), average levels of SBP and DBP at night with the disease duration ( $r = -0,56$  and  $r = -0,6$ ). According echocardiogram ejection fraction in all patients was 50%, while all the patients was detected diastolic dysfunction type 1. Intensity changes (the ratio of peak E to peak A) correlated with average levels of SBP and DBP at night ( $r = 0,73$  and 0.63, respectively). In assessing the morphological and functional parameters of the heart muscle was an increase in the anterior-posterior left atrial size, end-diastolic left ventricular

size, thickness of the posterior wall of the left ventricle compared with the control group, a statistically significant correlation of the RIC and the average diastolic blood pressure at night (0.6), as CEB and IGF-1 ( $r=0,6$ ).

**Conclusions:** Acromegaly patients in the active phase characterized by the presence of diastolic heart failure with preserved ejection fraction, the formation and expression which is defined as the activity and duration of acromegaly, and the severity of hypertension. Daily dynamics of blood pressure is characterized by the predominance of nocturnal hypertension.

## A curious case: what is behind this hyponatremia?

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**Introduction:** Hyponatremia is defined as a serum sodium level below 135 mEq/L. Patients may be asymptomatic, present unspecific symptoms, such as nausea, malaise or, in severe cases, neurologic disturb. As it's associated with many different conditions that sometimes overlap, the differential diagnosis is sometimes complex.

**Case report:** The authors describe a clinical case of a 72 years old woman, with arterial hypertension and chronic osteoarthropathy, medicated with amlodipine, lisinopril, hydrochlorothiazide, gabapentin and mebeverine, presenting to the emergency department with nausea, vomiting, dizziness for 2 days and an episode of loss of consciousness the day before. No pathological features were found on physical examination. The lab results showed a serum sodium level of 115 mEq/L and a serum potassium level of 3.09 mEq/L. The cranial computer tomography had no ischemic, hemorrhagic or space occupying lesions. It was first assumed iatrogenic etiology for the ionic deficits. All medication was suspended and correction began with slow hypertonic saline and potassium infusion. As hyponatremia didn't resolve, further workup showed low levels of adrenocorticotrophic hormone, prolactin, gonadotropin, serum cortisol and free thyroxine, pointing to a hypopituitarism. A cranial magnetic resonance imaging revealed a probable cystic meningioma invading the cavernous sinus and sella turcica, determining marked deviation of the pituitary gland, with no compression of the optic chiasm. The patient began hydrocortisone and levothyroxine hormonal reposition with rapid improvement of the sodium levels. Neurosurgery proposed complete tumor excision.

**Discussion:** Hypopituitarism has an estimated incidence of 4.2 cases per 100 000 per year and extrinsic tumors account for less than 13% of all causes – approximately 0.54 cases per 100 000 per year. In elderly patients, with several comorbidities and overmedicated, ionic disturbances are often attributed to iatrogenic effect, decompensated chronic disease or poor nutritional intake and further investigation is often limited. Searching for potentially treatable conditions can improve survival and life-quality for these patients.

## Chronic kidney disease prevalence in diabetic patients admitted in an internal medicine ward

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**Objectives:** In Portugal, chronic kidney disease (CKD) is common among diabetics, affecting up to 40%. It's important to recognize the impact of having both diagnoses, since there's a higher risk for cardiovascular events. Their glycemic control is essential, but medication may need dose adjustment or even be contraindicated. With this study we strive for better knowledge of how our patients are being treated.

**Methods:** Review of clinical processes for a retrospective study in an internal medicine ward, between January 2014 and February 2015. The glomerular filtration rate (GFR) was calculated using MDRD4 formula. CKD is defined as  $GFR < 60 \text{ ml/min/1.73m}^2$  for  $\geq 3$  months. To stage CKD was used the "kidney disease outcomes quality initiative" (KDOQI) classification.

**Results:** Sample with 321 patients, 195 female and 126 male. Average age of 77 years old. 97.5% were type 2 diabetics. 53% of patients ( $n=170$ ) had a previous diagnosis of CKD. 39% were KDOQI stage 3, 12.8% stage 4 and 0.61% stage 5.  $HbA_{1c}$  average of 7.8%. 61.5% had  $HbA_{1c} \leq 8\%$  and 38%  $\leq 7\%$ . 67% ( $n=114$ ) were treated with insulin, 38.2% ( $n=65$ ) with DPP4-I, 23.5% ( $n=40$ ) with metformin (MET), 11.8% ( $n=20$ ) with sulfonyleureas and 1.8% ( $n=3$ ) pioglitazones. Of the 40 patients on MET, 7.5% ( $n=3$ ) had a  $GFR \leq 30$ , and 45% ( $n=18$ ) a  $30 < GFR < 45$ . Of this 18 patients, 44.4% were treated with daily doses  $> 1000 \text{ mg}$ . 40% treated with DPP4-I and  $GFR < 50\%$  weren't on CKD adjusted dose. 60% were on an angiotensin converter enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARBs).

**Conclusions:** With this study we're able to avouch the high prevalence of CKD in diabetics. Even so, we can't forget that in order to achieve it, aggressiveness may end in adverse effects. Notice the 45% of patients using high doses of MET, despite indication to lower it when  $GFR \leq 45$ , due to the risk of lactic acidosis. No 1st generation sulfonyleurea were prescribed, which is fit, and also, that the majority was on gliclazide, that doesn't need adjustment. The high rate of insulin use was expected, although doses should be reduced by 25-50% as the CKD progresses. Almost 40% were on high doses of DPP4-I, which is concerning. Depending on the severity of the CKD, drug regimens may require adjustments. Multidisciplinary care may provide the optimal system for maximizing the care of these patients; as well the creation of pre-discharge protocols, to standardize dose adjustment for oral antidiabetics, especially with MET, and increases ACEI/ARBs use.

## Retrospective study of diabetic patients admitted in an internal medicine ward

Canelas M.A., Machado C., Barbosa A.R., Pipa S., Rigor J., Fonseca T., Mondragão A., Silva J., Andrade L., Suarez E., Dias V.P.

**Objectives:** In Portugal the diabetes mellitus type 2 prevalence is 11.7%, affecting 26% in an age range of 60-79. The aim is to characterize the diabetic population admitted in an internal medicine ward, to better know them and improve health care.

**Methods:** Internal medicine ward admitted patients, between January 2014 and February 2015, clinical processes review. The glomerular filtration rate was calculated using MDRD4 formula. To measure the degree of disability in the daily activities was used the mRankin scale.

**Results:** sample with 382 patients, 62% female and 38% male. Average age of 77.6. 4% had more than 75 years old. 97.9% were type 2 diabetics. 42.4% had an mRankin >4. 372 patients were admitted through the emergency department (ER): 39 diagnosed with hyperosmolar hyperglycemic state, 5 hypoglycemia and 4 ketoacidosis. The main cause for primary decompensation was an infectious process (66.7%), followed by therapeutic failure (6.3%). The rest were admitted with secondary diagnosis of diabetes, 111 – for respiratory infections, 51 –cardiac failure, 19 – stroke and 2 – acute myocardial infarction. 87.4% were hypertensive, 37% had dyslipidemia, 40.5% hyperuricemia and 52.9% chronic kidney disease. 307 had end organ disease, being retinopathy the most frequent (49%). 45.9% had vascular brain disease and 17.1% had coronary disease. The HbA<sub>1c</sub> average was 7.8%. 207 patients used insulin, and 97 of these used oral antidiabetics (OAD) as well. 125 were only treated with OAD.

**Conclusions:** With these data we acknowledge an advanced age average that matches aging population projections. The main cause for admission was respiratory infections, for both primary/secondary diagnosis of diabetes. The therapeutic failure, common among these patients, was uncommon to motivate admission, so maybe this tells us we're being able to adjust their therapeutic in the ER. As expected, hypertension and dyslipidemia prevalence was high. Out of the 382 patients it was possible to know the HbA<sub>1c</sub> in 358, which demonstrates that health care professionals use this tool often to acknowledge glycemic control. Not so expectable was the high rate use of insulin, and a rate around 50% of patients only treated with OAD, when it was expected to be higher. This study allow us to know better our population, and the impact that a high prevalence of diabetes has, in order to improve health care, create a multidisciplinary group to approach all complications related and avoid readmissions.

### Short-term parenteral nutrition in an Internal Medicine Unit of a Tertiary Hospital: descriptive and economic analysis

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**Objectives:** Short-term parenteral nutrition (STPN) isn't generally recommended because its complications and costs are most of the time more common than clinical benefits. The main aim of this study is to describe the clinical characteristics of patients

receiving parenteral nutrition (PN) in a Tertiary Hospital Internal Medicine Unit focusing on the impact of STPN on clinical evolution and economic costs.

**Methods:** It is a retrospective study in adults that were hospitalized and dispensed PN in a Tertiary Hospital Internal Medicine Unit from June 2014 to February 2015. Data related to PN prescription, were recorded from Kabisoft™ software database. Clinical data was collected from Electronic Medical Record software. STPN is defined when PN duration last ≤5 days (according to Spanish Society of Enteral and Parenteral Nutrition [SENPE] guidelines). A cost accounting model, including nutrition solutions and additives only, was used to perform cost analysis.

**Results:** 1,940 admissions were registered. PN was prescribed in 35 episodes (1.8%). Unavailable or inappropriate enteral access was the most frequent cause of PN (54.3%). The most frequent cause of PN discontinuance was the transition to oral nutrition (54.3%). STPN was prescribed in 25.7% cases. Time from admission to first day of PN was shorter in STPN group (5.8±1.7 vs 12.8±2.5 days, p=0.028). Though hyperkalemia was frequently observed in STPN group, there wasn't significant difference between both groups (25% vs 4.2%; p=0.08). 33.3% of STPN prescriptions didn't follow the guidelines indications. If an optimal adequacy of PN prescriptions is taken, costs savings would be 1,648.65 €.

**Conclusion:** In some cases PN duration cannot be predicted therefore prescription according to guidelines could reduce PN costs by one-third and PN-related complications.

### Nutritional risk screening in HIV-infected patients: usefulness of a method based on analytical parameters

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**Objectives:** CONUT system (nutritional control) is a completely automatic method based on analytical parameters such as albumin, total lymphocytes and cholesterol whose validity is confirmed in diverse clinical scenarios. The usefulness of CONUT hasn't been studied enough in HIV patients. The main aim of this study is to clarify its utility in a population with high prevalence of albumin and lymphocytes disturbances.

**Methods:** Nutritional status was classified, according to CONUT score, as "normal" or "low, moderate or high nutritional deficiency" and a positive "nutritional alert" was generated when moderate or high nutritional deficiency was detected. All patients underwent full and independent nutritional evaluation and were classified according to this evaluation as "nutritional intervention needed" (moderate or high nutritional risk) or "not needed" (low risk or not nutritional risk). The stage of concordance between both results was evaluated.

**Results:** 111 HIV-infected patients (57.6% HIV/HCV co-infected) were included. According to CONUT score, all patients were classified as having nutritional deficiency (82% as "low", 17% as "moderate" and 1% as "high"). A positive alert was generated

in 20 patients (18% of the cohort). Only 1 patient (3.3% of all alerts) was considered as "nutritional intervention needed" so, 96.7% patients in whom alert was generated, did not need nutritional intervention. 2 patients did not generate CONUT alert and were classified as "nutritional intervention needed" (2.2%).

**Conclusions:** CONUT system in HIV-infected patients, overestimates nutritional risk and can lead to additional evaluations. Nevertheless, the natural history of HIV-infection, in developed countries, has changed (including nutritional status) in the last decades. Other nutritional screening tools or analytical parameters may be also bear in mind in HIV population.

### Relationship between body mass index and intraocular pressure in men and women. A population-based study

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*Rabin Medical Center, Beilinson Campus, Petah Tikva, Israel*

**Objective:** To assess a possible relationship between body mass index (BMI) and intraocular pressure (IOP) in both men and women.

**Methods:** A retrospective cross sectional analysis of database from a screening center in Israel assessed 18575 subjects, age range between 20-80 years.

**Results:** The mean ( $\pm$ SD) age of the study sample was  $46\pm 10$  years, 68% were men. Mean IOP ( $\pm$ SD) was found to be higher in men than in women;  $13.4\pm 2.5$  vs.  $13\pm 2.2$  mmHg respectively ( $p<0.001$ ). A positive linear correlation was found between BMI and IOP for both men and women. For each increase in 10 units of BMI, the IOP increased by 1 mmHg ( $r=0.17$ ,  $p<0.0001$  and  $r=0.20$ ,  $p<0.0001$  for men and women respectively). Mean (95% CI [confidence interval]) IOP in subjects with BMI  $<25$  kg/m<sup>2</sup> was 12.8 (12.7-12.9) mmHg and increased significantly to 13.4 (13.3-13.5); 13.9 (13.8-14.0) and 14.3 (14.1-14.5) mmHg for BMI subcategories 25-29.9, 30-35,  $>35$  (kg/m<sup>2</sup>) respectively ( $p<0.0001$ ). These differences remained significant after multivariate adjustment for age, gender, hypertension and diabetes mellitus ( $p<0.0001$ ).

**Conclusions:** This study clearly shows obesity as an independent risk factor for increasing IOP in both men and women. We consider this finding particularly pertinent in the context of the current obesity epidemic.

### Relationship between serum glucose levels and intraocular pressure in men and women. A population-based study

*Cohen E., Kramer M., Shochat T., Goldberg E., Garty M., Krause I.*

*Rabin Medical Center, Beilinson Campus, Petah Tikva, Israel*

**Objective:** To assess a possible relationship between serum glucose levels and intraocular pressure (IOP) in both men and women.

**Methods:** Data were collected from medical records of individuals examined at a screening center in Israel between 2000 and 2013.

Cross sectional analysis, was carried out on 18406 men and women aged 20-80 years.

**Results:** The mean ( $\pm$ SD) age of the study sample was  $46\pm 10$  years, 68% were men. Mean (95% CI [confidence interval]) IOP in subjects with impaired fasting glucose (IFG) and diabetes mellitus was significantly higher than IOP levels in subjects with normal glucose levels: 13.7 (13.6-13.8) mmHg and 14.3 (14.1-14.4) mmHg vs. 13.1 (13.0-13.1) mmHg respectively,  $p<0.0001$ . Those differences remained significant after adjusting for age, body mass index (BMI) and hypertension and ( $p<0.0001$ ). A positive linear correlation was found between serum glucose levels and IOP for both men and women. ( $r=0.13$ ,  $p<0.0001$  and  $r=0.17$ ,  $p<0.0001$  for men and women respectively). Multivariable adjustment for age, BMI and hypertension revealed that the coefficient factors for fasting glucose (95% CI) for men and women were 0.009 (0.007, 0.012)  $p<0.0001$  and 0.012 (0.009, 0.160)  $p<0.0001$  respectively. This meant that in men and women, the change in IOP associated with a 10mg/dl increase in fasting serum glucose was 0.09 mmHg and 0.12 mmHg respectively.

**Conclusions:** This study is the first to show that apart from diabetic patients, subjects with IFG have higher IOP levels compared to subjects with normal glucose levels. Moreover, we also show the direct correlation between fasting serum glucose and IOP. Those points add to the importance of controlling serum glucose levels.

### Behavior of liraglutide in a type 2 diabetes population with several cardiovascular risk factors

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**Objective:** We proposed to check the changes in the anthropometry, analytical and pharmacological parameters, and perform the descriptive analyze of patients diagnosed with type 2 diabetes with poor metabolic control treated and followed at least one year with liraglutide.

**Material and methods:** The vascular risk unit in Salamanca treats hypertensive, diabetic, dyslipemic and other comorbidities patients. Patients with the diagnosis of type 2 diabetes followed for a year and treated with a GLP-1 (liraglutide) were recruited from the database. The epidemiological characteristics (gender and age), body mass index (BMI), prevalence of hypertension, degree of chronic kidney disease (CKD), number of antihypertensive drugs, oral hypoglycemic agents (ADOS), doses of insulin and liraglutide, variation of the glycated hemoglobin (HbA<sub>1c</sub>), presence of dyslipidemia, number of lipid-lowering drug and the behavior on LDL and triglycerides levels.

**Results:** 18 patients were analyzed: 61% male and 39% female. The average age was 60 years old. The average BMI was 31.8 kg/m<sup>2</sup> at baseline and 29 kg/m<sup>2</sup> at the end. 11% of patients had CKD and microalbuminuria was detected in 40%. 100% were hypertensive. A decrease in blood pressure was achieved in 78% and antihypertensive drugs were discontinued in 11% of them. The 100% of patients were under ADOS thought the entire study.

The average of ADOS remained the same (2 drugs/patient). 55% of patients received treatment with insulin at baseline, reducing by 10% at the end. 61% were dyslipidemic. The dose of liraglutide was 1.8 mg in 78% of patients. The values of HbA<sub>1c</sub> were 8.2% at baseline and 7.4% at the end. The averages of HbA<sub>1c</sub> were analyzed at different times, detecting a significant decrease from the initial value (p= 0.048).

**Conclusions:** Type 2 diabetes patients starting treatment with GLP-1 had significantly decreased their BMI, LDL cholesterol, and insulin dose. The number of ADOS was unchanged. The decrease of HbA<sub>1c</sub> was statistically significant, especially in the group's reduced BMI and only at the beginning of treatment. The number of antihypertensive drugs dropped and the degree of hypertension improved not significantly. The improvement achieved in the lipid profile was poor in a group of patients considered at high cardiovascular risk. The profile of liraglutide showed in our study was excellent with effects not sustained (an increase in HbA<sub>1c</sub> compared to the levels of the 1st and 2nd consultation was observed at the end of study). The results are probably due to the heterogeneity of the study population and the small size of the sample.

## **A case of giant parathyroid adenoma displacing trachea in patient with primary hyperparathyroidism**

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**Introduction:** Primary hyperparathyroidism (PHPT) is often caused by a single parathyroid adenoma (80-85%). Parathyroid adenoma greater than 2 cm is very rare. The great majority of PHPT is asymptomatic and detected routine biochemical tests. Here we present a primary hyperparathyroidism case, in which trachea was deviated by giant parathyroid adenoma due to delayed surgical treatment.

**Case report:** A 50 years old female patient was diagnosed with multinodular goiter (MNG) about 1 year ago. During follow up, neck ultrasonography (USG) showed 6x3 mm smooth-edged hypoechoic nodule in thyroid right lobe. In the inferoposterior region of the left thyroid lobe, a second nodule of 40x25 mm size, with regular margins, cystic and solid components, and rough calcifications, was also seen. But boundaries between this nodule and thyroid gland were not clarified. No other abnormalities were observed in routine biochemical examinations except hyperparathyroidism and hypercalcemia (PTH: 492.3 pg/ml, Ca: 12.5 mg/dL, 24-hour urinary Ca: 511.4 mg/day). Parathyroid scintigraphy showed nodular lesions consistent with parathyroid adenoma in the left side of thyroid gland, pushing trachea to the right, with increased uptake. Patient's medical history included urinary stone complaint for a long time. Bone mineral density (BMD) showed osteopenia. He was referred to the general surgery section in order to be operated for hyperparathyroidism.

**Discussion:** Previous literature reports that the size of parathyroid adenomas is mostly less than 2 cm. Our case shows that, though a parathyroid adenoma reaches to a gigantic size, it remains asymptomatic and may not be detected for a long time.

## **Klippel Trenaunay syndrome: a rare cause of extremity overgrowth**

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**Introduction:** Klippel Trenaunay syndrome (KTS) is a rare mesodermal abnormality. It has the classical triad including (1) vascular nevus, (2) soft tissue hypertrophy/bony overgrowth, and (3) varicose veins. KTS has a broad clinical spectrum ranging from truncular to extratruncular vascular malformations, or from infiltrating to limited forms. The principal abnormality is capillary-lymphatico-venous malformation, which may lead to widespread geographic patches on the skin. Gigantism results from the accelerated bone or soft tissue overgrowth. The lower limb is affected more frequently than the upper limb, and the left side is involved more commonly than the right side. However, either the whole limb or only one bone in an extremity may be affected.

**Case report:** A 21 years old male was admitted to our clinic with an initial diagnosis of acromegaly. His physical examination revealed overgrowth of the left upper and lower limbs, and extensive vascular malformations on the skin. The inspection of the head and neck was not consistent with an acromegaly phenotype. His complaints gradually and progressively worsened since childhood. The biochemical analysis was not consistent with acromegaly and no additional laboratory abnormality was detected. Radiographs of the involved limbs revealed no pathognomonic appearance. The dermatology service was consulted to evaluate the rashes, which were found to be indicative of KTS.

**Discussion:** KTS is a rare syndrome usually characterized with an asymmetrical overgrowth of the soft tissues or bones. It often presents with advanced limb deformities, but also may affect all four extremities with left side predominance, as seen in the present patient. Regarding the fact that overgrowth of the hands and feet is a common presenting complaint in the endocrine practice, KTS must be kept in mind as a differential diagnosis in those presenting with both limb hypertrophies and characteristic skin rashes.

## **Heart rate variability and circadian index in patients with type 2 diabetes**

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**Objective:** Assessment of heart rate variability and circadian index in patients with type 2 diabetes, identifying violations due to the duration of diabetes and certain metabolic indicators.

**Material and methods:** We studied 40 patients with type 2 diabetes (20 men and 20 women). All patients underwent clinical and instrumental examination included anthropometric survey (measurement Quetelet index, waist circumference), biochemical studies (plasma lipids, blood sugar, glycated hemoglobin).

All patients underwent Holter ECG monitoring with complex "Myocard-Holter" (Russia). By statistical processing calculates time analysis of heart rate variability (SDNN, SDNNi, rMSDD, pNN50) and circadian index (CI). Determined by the average heart rate (HR) in the daytime and night-time, minimal and maximal heart rate.

**Results:** In patients with type 2 diabetes without concomitant coronary artery disease and arrhythmias showed a reduction in temporary HRV parameters. Temporary HRV/SDNN was higher in men and amounted to 118,8 versus 106,9 ms in women ( $p < 0,05$ ), SDNNi was also higher in men, than in women (48,9 and 38.8 respectively,  $p < 0,05$ ). Indicators that reflect the activity of the parasympathetic division of the ANS (RMSSD, pNN50) were also higher in men. Spotted rigidity circadian index circadian profile of heart rate in the majority of cases – 25 (62,5%) was rigid ( $CI < 1,2$ ), in 6 (15%) – normal ( $CI = 1,24 - 1,42$ ) and in 9 (22.5%) – slightly decreased ( $CI = 1,2 - 1,23$ ). During the correlation analysis revealed that with increasing levels of glycated hemoglobin had greater declines in TI, SDNN, rMSDD, pNN50, which indicates the severity of denervation of the heart in patients with a severe form of diabetes.

**Conclusions:** In patients with type 2 diabetes without concomitant coronary heart disease temporary HRV parameters are decreased. These changes are probably related to the development in the studied group of patients of cardiac autonomic neuropathy. In the group of patients with small prescription diabetes need to increase adherence to treatment in order to prevent the development of cardiac autonomic neuropathy.

### **Pure state of obesity: endocrine, hematologic, gastrointestinal, and other complications**

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**Objectives:** Obesity is correlated with multiple endocrine, hematologic, and morphological alterations, the majority being secondary to obesity. The primary causes of these abnormalities are due to insulin resistance, which leads to many complications including type 2 diabetes mellitus (T2DM). Other features such as hypertension, dyslipidemia, insulin resistance, and abdominal obesity contribute to the development of metabolic syndrome. These disturbances lead to clinical complications and a higher risk of developing cardiovascular complications. The authors of this study attempt to identify the main disturbances and complications in patients with obesity.

**Methods:** A retrospective observational study was performed, by evaluating medical records of all patients with obesity (defined as body mass index (BMI)  $\geq 40$  or  $\geq 35$  in patients with comorbidities) considered for bariatric surgery, evaluated through pre-surgical consultation during a two-year period (January 2013 to December 2014).

**Results:** A total of 201 patients were evaluated in the pre-surgical consultation, 164/201 (81.6%) were females with BMI average of 43.5% and 37/201 (18.4%) were males with BMI

average of 43.5%, with a mean age of 41.74 and 41.97 year old, respectively. The most common symptom associated with obesity was artralgiias in 121/201 (60.2%). The main comorbidities presented in these patients were: hypertension 109/201 (54.2%), dyslipidemia 95/201 (47.3%), and type 2 diabetes mellitus 63/201 (31.3%). Many patients presented endocrine dysfunction such as: high levels of vitamin D 1,25 in 93/201 (46.3%), hyperuricemia in 64/201 (31.8%), hyperinsulinemia in 37/201 (18.4%) and hyperparathyroidism in 23/201 (11.4%). We also identified hematologic disturbances such as iron deficiency in 50/201 (24.9%), vitamin B12 deficiency in 20/201 (10%), and folic acid deficiency in 18/201 (9%). We observed a strong correlation between the amount of visceral adipose tissue with specific comorbidities, namely, obstructive sleep apnea hypopnea syndrome (OSAHS) in 82/201 (40.8%) and urinary incontinence in females was seen in 37/164 (22.6%) patients with an average BMI of 45.2%. The majority of patients with obesity suffered from gastrointestinal related complications: 175/201 (87.1%) patients identified, had gastroenterology related complications such as gastroesophageal reflux disease (GERD) in 77/201 (38.3%), Helicobacter pylori infection in 95/201 (47,3%), and non-alcoholic fatty liver disease (NAFLD) in 98/201 (48.8%).

**Conclusions:** Obesity is associated to numerous endocrine disturbances and if not treated, potential severe consequences may arise. There was a higher prevalence of obesity in female patients. Majority of complications such as obstructive sleep apnea hypopnea syndrome, as well as, female urinary incontinence has a direct correlation to the amount of visceral adipose tissue accumulated in these patients. Metabolic syndrome should be identified such that vascular risk reduction strategies can be implemented. Early diagnosis and direct treatment can optimize the health of the individual.

### **Pituitary incidentaloma – a case report**

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**Introduction:** Prolactinomas and nonfunctioning adenomas are the most common types of pituitary incidentalomas. Concerning the latter, the clinical presentation may vary from asymptomatic to hypothalamic/pituitary dysfunction and visual changes.

**Case report:** The authors present the case of a 52 years old Caucasian male patient, with a history of meningoencephalitis at 11 years of age, with mild cognitive impairment and epilepsy sequelae. He was admitted through the emergency department due to community-acquired pneumonia. He also presented with left conjunctival hyperemia and unspecified visual changes. Physical examination revealed left VI cranial nerve paresis. The CT scan of the skull and orbits revealed an expansive sellar and suprasellar lesion. A head MRI confirmed the location of the lesion, which extended to the cavernous sinus and Meckel's cave to the left, and contacted inferiorly the optic chiasm and the pre-chiasmatic segment of the optic nerves without significant compression, which suggested a pituitary macroadenoma diagnosis. Laboratory findings included macrocytic anemia, normal sodium and



potassium, thyroid-stimulating hormone 0.36 uU/mL, free triiodothyronine 1.67 pg/mL, free thyroxine 0.5 ng/dL, testosterone <20 ng/dL, adrenocorticotrophic hormone <5 pg/mL, cortisol 0.5 ug/dL, insulin-like growth factor 45.1 ng/ml, luteal hormone 0.19 U/L; follicle stimulating hormone, prolactin and growth hormone were normal. Supplementation with levothyroxine, prednisolone and testosterone was initiated, with improvement of overall status and in hormone dosing. Neurophthalmology evaluation confirmed left VI pair paresis and reduction of both of central visual acuity and thickness of peripapillary nervous fibers layer bilaterally. However it remained difficult to determine the degree of visual impairment exclusively due to the lesion, given the previous history of meningoencephalitis.

**Discussion:** The authors aimed to highlight the diagnostic and therapeutic challenges of pituitary incidentalomas, particularly in a patient with previous cerebral damage and limited capacity of cooperating in both physical examination and functional testing. After a multidisciplinary discussion and neurosurgery evaluation, the patient was considered eligible for surgery, which he awaits.

### Poor sleep quality is a risk factor for the development of obesity

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**Objectives:** Recent evidence confirms previous findings of an association between sleep loss and increased risk of obesity. Sleep loss has been shown to result in metabolic and endocrine alterations, including decreased glucose tolerance, decreased insulin sensitivity, increased levels of ghrelin, decreased levels of leptin, increased evening concentrations of cortisol, and increased hunger and appetite. Besides sleep length, its quality must play a major role in the development of obesity. Low quality of night sleeps, in other words, inability to sleep deeply and frequent waking-ups at night, may also increase risk of obesity and this was our main concern in the planning of this study.

**Methods:** 450 obese patient between 15 and 75 years old (142 male, 308 female) who admitted to our obesity out-patient clinic, were included in the study. After detailed medical history and systemic investigation, patients' weight and height measurements were taken and their BMI were calculated. Patients' total sleep time, number of wake-up periods, medication for sleep disturbances and co-existing illnesses were recorded. Day-time sleeping patients were not included.

**Results:** Total sleep time was less than 6 hours in 32 patients, between 6 to 7.9 hours in 320 patients, and over 8 hours in 98 patients. 365 patients woke-up several times during sleep, while 85 patients stated that they had continuous high quality sleep at night. Patients that slept less than 6 hours were primarily obese and morbid obese patients (100%). There was a significant statistical correlation between less sleep time and degree of obesity ( $p=0.016$ ). There was no correlation between normal sleep time and BMI ( $r=0.002$ ,  $p=0.958$ ). Most of the morbid obese patients woke up at night (92,4%). 83.6% of obese patients woke up at night, while there was 58.1% of night waking-up in overweight patient group. There was a significant relationship between BMI of

irregular sleepers and BMI of regular sleepers ( $r=0.260$ ,  $p=0.001$ ).

**Conclusions:** In the etiology of obesity, there are roles of many different factors. Among those factors, life-style occupies an important part. According to our study, there is a correlation between obesity and sleep quality besides sleep length.

### Developing additional autoimmune disorders in 20 years follow-up of a young Addison patient

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**Introduction:** Multiple autoimmune diseases have association with each other but it is very rare to see multiple autoimmune diseases in one patient. Multiple autoimmune syndrome (MAS) is a condition in which patients have three or more separate autoimmune disorders.

**Case report:** Our case is a 35 years old female patient, which we diagnosed Addison's 20 years ago when she was only 15. It was found to be a very early autoimmune disease and she was put on glucocorticoid and mineralocorticoid treatment. In her follow up, when she was 25 years old, she had sudden attack of palpitation, sweating and weight loss with high thyroid hormones (TSH 0.04 (N: 0.4-4), FT4 1.65 (<1.12), FT3 3.5 (<3.9) antibodies (Anti TPO, Anti TSH), scintigraphy for Graves' thyroiditis. When she was 32 years old, she had irregular menstrual cycles and was diagnosed as early menopause because of primary ovarian insufficiency. At 33, she developed severe muscle and joint pain with ANA positivity and was diagnosed as autoimmune inflammatory arthritis. Afterwards, she had osteoporosis with low vitamin D levels. As she was on vitamin D treatment she had hypercalcemia. Further investigation with parathyroid scintigraphy and hormone levels, revealed that she also had primary hyperparathyroidism. In 20 years we diagnosed Addisons', Graves', primary ovarian insufficiency, inflammatory polyarthritis, osteoporosis and hyperparathyroidism.

**Discussion:** An autoimmune disease in a patient can be an indicator for the possibility of another one. The occurrence of MAS in our case shows the need for continued surveillance for the detection of new multiple autoimmune syndromes in predisposed patients.

### HCV/HIV co-infected patients with severe liver fibrosis have glucose metabolism alterations even in the absence of diabetes

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**Objectives:** Type 2 diabetes mellitus (T2DM) is a well known independent prognosis factor associated with cirrhosis. Nevertheless, few studies are focused on the association between glucose metabolism and liver fibrosis in HCV/HIV patients.

The conclusions of those studies are contradictory. The aim of our study is to investigate the relationship between glucose homeostasis and liver fibrosis in co-infected HCV/HIV patients.

**Methods:** In a cross-sectional study, we compared the prevalence of glucose disorders and the data related to its homeostasis, according to the liver fibrosis stage. Liver stiffness was measured by transient elastography. Severe liver fibrosis was defined as  $\geq 14$  kPa liver stiffness. Insulin resistance was defined as Homeostasis Model for Assessment (HOMA-IR)  $\geq 2$ .

**Results:** 65 HCV/HIV co-infected patients were included. Prevalence of prediabetes and T2DM was higher (40% and 24%, respectively) in patients with severe fibrosis compared to 37% and 3.7% in those with less severe stage of fibrosis ( $p=0.005$ ). Among parameters related to glucose metabolism, levels of fasting glucose, HbA<sub>1c</sub> and HOMA-IR were significantly higher in patients with severe fibrosis ( $p=0.006$ ,  $p=0.048$  and  $p=0.001$ , respectively). Also, there was a positive correlation between HOMA-IR and liver fibrosis ( $r=0.5$ ;  $p<0.001$ ). When patients with T2DM were excluded, levels of fasting plasma insulin, HOMA-IR and the prevalence of insulin-resistance, were significantly higher among those with severe fibrosis ( $p=0.004$ ,  $p=0.003$  and  $p=0.049$ , respectively) and the positive correlation between HOMA-IR and liver fibrosis remained significantly present ( $r=0.45$ ;  $p<0.001$ ).

**Conclusions:** Our data support that hyperinsulinism and insulin-resistance are frequently observed in HCV/HIV co-infected patients with severe liver fibrosis even in absence of overt T2DM. A high stage of liver fibrosis screening in HCV/HIV co-infected patients is another reason to optimize glycaemic control in this population.

## Secondary hyperparathyroidism in HIV-patients increases cardiovascular risk factors

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**Objectives:** Low levels of vitamin D may result in secondary hyperparathyroidism (SH). This has been linked to an increased of cardiovascular risk in general population. However, the spectrum of cardiovascular risk associated with SH in HIV-infected adults it is still uncertain. The aim of this study is to determine the potential association of secondary hyperparathyroidism with different markers of cardiovascular risk in HIV-infected adults.

**Methods:** Cross-sectional study. Clinical data related to obesity, blood pressure, glucose metabolism, lipid profile, toxics use and renal function were recorded. Hypovitaminosis D was defined by 25-hydroxy vitamin D level  $<30$  ng/mL. SH was defined by parathyroid hormone  $>65$  pg/mL in presence of hypovitaminosis D. Patients were divided into three groups according to status of vitamin D and the presence of SH: A) SH and hypovitaminosis D; B) hypovitaminosis D without SH and C) vitamin D sufficient.

**Results:** 104 HIV patients were included. Median vitamin D was  $30.6 \pm 13.6$  ng/mL. Prevalence of hypovitaminosis D and SH were 53.8% and 13.5% respectively. Quantitatively, all parameters related to cardiovascular risk, except fasting glycemia, were higher among patients of group A, but only levels of total cholesterol, LDL, and

triglycerides reached significant difference ( $p=0.002$ ; 0.004 and 0.01 respectively). Also, prevalence of obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) was higher in patients that developed SH (group A) when compared to group B and C (28.6% vs 19% vs 2% respectively;  $p=0.004$ ). In multivariate analysis, SH was not associated with any cardiovascular risk factor.

**Conclusions:** Though HIV-infected patients with SH due to hypovitaminosis D have worse cardiovascular risk profile, we can not conclude that SH is independently associated with major risk factors. Nevertheless, we think these patients require a tighter monitoring of lipid profile, blood pressure and renal function. Further studies will be useful to clarify the role of SH in determining unfavorable cardiovascular outcomes in HIV population.

## Visceral adiposity index is a better predictor for non-alcoholic liver fibrosis in HIV/HCV co-infected patients than body mass index

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**Objectives:** Although association between liver fibrosis and body mass index (BMI) is well known in general population it isn't in HIV/HCV patients. Different clinical conditions including lipodystrophy and malnutrition may influence in this relationship. The main aim of this study is to investigate the utility of visceral adiposity index (VAI) as a predictor of liver fibrosis in this population compared to body mass index.

**Methods:** We conducted a cross-sectional study in a cohort of HIV/HCV co-infected outpatients attended in our hospital. Demographic, clinical and anthropometric characteristics were collected. Liver stiffness was measured by transient elastography (Fibroscan™). Patients were divided into three groups according to VAI score tertiles.

**Results:** From a database of 61 co-infected patients, 53 male patients were eligible for final analysis. Mean age was  $46.9 \pm 5.4$  years old. Malnutrition was present in 37.7% of the cohort. Patients with the highest VAI score (third tertile) had higher liver fibrosis ( $p=0.003$ ), large waist circumference ( $p=0.003$ ), higher triglycerides serum levels ( $p<0.001$ ), higher LDL levels ( $p=0.006$ ) and lower HDL ( $p<0.001$ ). A positive correlation between VAI and liver fibrosis was found ( $r=0.392$ ;  $p=0.004$ ). This correlation was stronger than the observed with BMI ( $r=0.291$ ;  $p=0.035$ ). In multivariate analysis, VAI was an independent predictor for liver fibrosis (OR 1.7; CI 95%: 1.04-2.78;  $p=0.033$ ).

**Conclusion:** We propose the use of VAI as the best anthropometric predictor for non-alcoholic liver fibrosis in HIV/HCV co-infected patients.

## It is only subacute thyroiditis not malignancy or Mycobacterium tuberculosis

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**Introduction:** Subacute thyroiditis is the inflammation of the thyroid gland, resulting in the spontaneous remission. It is more common in women between 40-60 years of age. Even though the disease usually emerges 2-8 weeks after a viral infection, there has not been a clear factor. The clinical course of this disease low-grade fever, palpitations, irritability, fatigue, hoarseness, difficulty swallowing, pain in both lobes of the thyroid can be seen. With low radioactive iodine uptake along with high ESR (100 mm/h) and CRP. High T3, T4, thyroglobulin levels can be seen.

**Case report:** 43 years old female patient went to the ear, nose and throat clinic with hacking cough complaints 1.5 months ago and as a result of investigations antihistamines treatment began with a diagnosis of allergic rhinitis. Upon detection ESR 143 mm/h, CRP 124 mg/l she was redirected to the chest diseases clinic for further research. With suspicion of M. tuberculosis and malignancy some investigations took place. However, there were no clear respiratory pathologies. So that, empirical moxifloxacin 400 mg tablets 1x1 treatment was applied for 7 days. In follow-up examination, ESR, CRP values did not decrease, and coughing complaint continued. Patient was redirected to internal medicine clinic for more advanced research. Detailed medical history revealed that the patient lost 4.5 kg in the last 1.5 months and she had stated complaints of fatigue, productive cough and fever which increased at night. A growth had been noticed in the thyroid gland at the initial examination, and the patient had sensitivity in the area of thyroid gland in the current examination. In the light of the present findings, subacute thyroiditis was the possible diagnosis and the related tests were planned. ESR 106 mm/h, CRP 89.7 mg/l, TSH 0.110 UI/ml, free T3 2.59 pg/ml, free T4 1.08 ng/dL, thyroglobulin 41.5 ng/ml was detected. After thyroid ultrasound and thyroid scintigraphy, patient was diagnosed with subacute thyroiditis. The patient was prescribed NSAID. Complaints decreased at the 4th day of the treatment, and ESR, CRP and thyroid function tests were normal at the follow-up examination 1 month later.

**Discussion:** In the case of fever unknown origin, and high levels of in ESR and CRP, subacute thyroiditis should be among the preliminary diagnosis. It should be kept in mind that the most important thing during the diagnosis is that medical history and physical examination.

## Plasma urotensin II concentration in gestational diabetes

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**Objectives:** Urotensin II (UII) and urotensin II receptor (UTR) has been implicated in the pathophysiology of diabetes and metabolic syndrome by contributing to hyperglycemia, insulin resistance, and essential hypertension. In this study, we tried to evaluate and compare UII in gestational diabetes mellitus (GDM).

**Methods:** GDM was diagnosed at 24-28 weeks of gestation with 100 g 3-hour oral glucose tolerance test. The diagnostic criterion of the International Association of Diabetic Pregnancy

Study Group (IADPSG) of GDM was used. 36 pregnant women (21 GDM women consisted group 1 and 15 non-GDM women consisted group 2 subjects) enrolled in this study. The 3rd group consisted of age matched 22 non pregnant healthy subjects. Exclusion criteria for all groups were as follows: 1) Inability to give a written consent, 2) Age <18 years, 3) Presence of hypo or hyperthyroidism, renal dysfunction, hypertension, ischemic heart disease, or malignancy, 4) Presence of chronic infections or inflammatory status. Plasma UII levels were determined at the beginning of the study. After 12 weeks of delivery, second plasma UII was determined from group 1 and 2.

**Results:** Gestational UII levels of both GDM and non-GDM subjects were higher than non-pregnant healthy controls (p was 0.0001 for both). Both gestational and postpartum UII levels of GDM subjects were higher than non-GDM pregnant subjects but had not reached statistical significance (p $\geq$ 0.05). Plasma UII concentrations in non-GDM subjects significantly decreased after delivery but not in GDM subjects (p was 0.036 and  $\geq$ 0.05, respectively).

**Conclusions:** The finding of not decreased high gestational plasma UII concentrations in GDM patients after delivery (in compare to non-GDM subjects) shows that UII and its system may have a role in the pathogenesis of GDM. Further detailed studies are needed in this field.

## A case report: malignant bilateral adrenal masses found incidentally in a septic patient

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**Introduction:** Adrenocortical carcinoma is a very rare malignancy with an annual incidence of 1-2 per million population and poor prognosis. The importance of recognizing adrenal carcinoma as a potential origin of sepsis of unknown cause is underlined throughout the clinical case.

**Case report:** A 57 years old white female presented to the emergency room with a 2-month history of progressive weakness, shortness of breath, and a febrile temperature. She was admitted in a very severe condition. Initial testing revealed picture of severe sepsis, accompanied with rapid renal function deterioration. Multiple laboratory and instrumental investigations were done for the exploration of the diagnosis. Abdominal ultrasound and computed tomography (CT) showed bilateral adrenal masses (2.5x5.8 cm on the right side and 4.7x6.1 cm on the left side). In addition, CT scans revealed splenomegaly and splenic infarction. Patient's condition deteriorated very rapidly, despite extensive treatment, and she died within one week after admitting. Due to very severe course of disease, no additional hormonal testing was done to prove the character of adrenal masses. Based of clinical findings, the first clinical diagnosis was idiopathic sepsis with multiple organ dysfunction, progressive kidney injury, bone marrow suppression, splenic infarction, hepatosplenomegaly, right side retrobulbar neuritis, bilateral hypostatic pneumonia, massive bilateral adrenal masses. Postmortem examination was done, to clarify the diagnosis. Only histopathological testing revealed the real cause of death – bilateral adrenocortical

carcinoma with multiple microscopic metastatic thrombi in lungs, brain, liver, spleen, lymph nodes.

**Discussion:** With our case we wanted to stress the importance of recognizing adrenal carcinoma as a potential origin of sepsis of unknown origin. Screening of hormone excess for incidentally discovered bilateral adrenal masses would be helpful, but would not change the course of disease in our patient.

## **A case report: hyponatremia as the first presentation of empty sella syndrome with secondary adrenal insufficiency and primary hypothyroidism**

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**Introduction:** Hyponatremia is one of the most common electrolyte disorders seen in clinical practice. Although most cases are mild or relatively asymptomatic, it is important because it can substantially increase mortality. Hyponatremia as the presenting manifestation of empty sella syndrome is rare. Secondary adrenocortical deficiency could be related to changes in ADH secretion with resulting hyponatremia. Glucocorticoid substitution is the mainstay treatment in this setting. Frequent monitoring of sodium level is necessary to prevent neurologic deficits and myelinolysis.

**Case report:** A 77 years old white woman was admitted to the internal medicine ward for evaluation of complaints of headache, fatigue, progressing mental deterioration. Laboratory findings showed electrolyte disbalance (K 6.4 mmol/l [3.5-5.1], Na 119.1 mmol/l [136-145]), low renal function (creatinine 160 mcmol/l [44-80], GFR 28.8 ml/min) and mildly elevated inflammatory markers. Any concomitant drug use interfering with sodium levels was excluded. Serum osmolality was normal. Endocrine work-up showed mildly elevated TSH with lower fT4, serum cortisol was normal, but low levels of ACTH were detected. Due to suspected secondary adrenal insufficiency pituitary MRI was performed revealing possible empty sella. Diagnosis of empty sella syndrome with secondary adrenal insufficiency, severe electrolyte disbalance, primary hypothyroidism, acute deterioration of chronic kidney disease was made. The patient was treated with 5.9% NaCl, Ca gluconate and glucose infusions, levothyroxine. Intravenous and subsequent oral hydrocortisone was added after the established diagnosis of secondary adrenal insufficiency. Renal function and electrolyte levels were normalized during hospitalization, though low normal levels of sodium persisted. Mental status of the patient improved significantly.

**Discussion:** Severe hyponatremia due to hypopituitarism and adrenal insufficiency can be life-threatening and treatment with glucocorticoids is very effective once the diagnosis of the underlying disorder has been made. The diagnosis of hypopituitarism in hyponatraemic patients is often overlooked. Before correction of glucocorticoid deficiency in empty sella patients' sodium levels must be tested, as too rapid treatment could create serious neurological deficits.

## **Massive gastrointestinal bleeding associated with ectopic Cushing's syndrome**

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**Introduction:** Cushing's syndrome refers to a symptom complex resulting from excess glucocorticoid hormone production by the adrenal glands or from sustained administration of glucocorticoids. There are several reports about gastrointestinal complications in patients with Cushing's syndrome; however the ulcerogenic potential of glucocorticoids is controversial.

**Case report:** A 76 years female patient was treated in another hospital due to general weakness and hypokalemic metabolic alkalosis. 2 weeks later she was hospitalized again with massive gastrointestinal bleeding from a duodenal ulcer uncontrolled via endoscopic techniques; gastrectomy with Billroth 2 anastomosis was performed. Several days after surgery she was admitted to our department with electrolyte disturbances. The coexistence of hypokalemic metabolic alkalosis, uncontrolled diabetes and gastrointestinal bleeding raised our suspicion of Cushing's syndrome, despite absence of characteristic features on her physical examination. Additional investigation revealed an exceptionally high urinary and blood cortisol, unsuppressed blood cortisol after 1 mg overnight dexamethasone test and high baseline ACTH. Metopirone therapy was started without further laboratory investigation due to her life-threatening condition. No tumor was demonstrated on pituitary MRI imaging; chest CT revealed several small unsuspected lung nodules and bilateral adrenal hyperplasia. PET DOTATATE scan revealed a suspicious nodule with high uptake in the right middle lung lobe. CT-scan revision revealed previously unnoticed 2 cm lesion in RML concealed by heart silhouette. Right middle lung lobectomy with hilar lymph node dissection was performed and resulted in full clinical remission. Histologic examination revealed a low grade neuroendocrine with involvement of hilar lymph nodes.

**Discussion:** The ulcerogenic potential of corticosteroid excess remains controversial. The true incidence of hypercortisolism associated peptic ulcer disease is unknown. Hypercortisolism may cause peptic ulcer by decrease mucus formation, inhibition of prostaglandin synthesis and enhancement of gastric acid cell hyperplasia with increased acid secretion. Our case report supports the hypothesis that severe Cushing's syndrome due to ectopic ACTH secretion can present with peptic ulcer and GI bleeding.

## **Non-compliance of the diagnostic algorithm of hyperandrogenism as the cause of iatrogenia**

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**Objective:** To inquire about adherence to diagnostic protocol for hyperandrogenism by endocrinologists in clinical practice.

**Methods:** We have performed retrospective analysis (February – May 2015) of 8 case reports of women who had been presented with established diagnosis of hyperandrogenism. They were 28±7 years old. The following parameters were analyzed: clinical manifestations of hyperandrogenism (menstrual irregularities, hirsutism (Ferriman-Gallwey scale), alopecia, and acne), biochemical hyperandrogeny according to laboratory studies, adherence to diagnostic protocol for hyperandrogenism, prescribed drugs and complications.

**Results:** Hirsutism and alopecia were absent in all women. One woman had only acne and the other one had only oligomenorrhea. Thereby, there were no any clinical indications for further laboratory examination that were nevertheless performed. No one woman had biochemical hyperandrogeny. Moreover inadequate laboratory studies were performed in 3 women (free testosterone, DHEA-S, 17OH-progesterone were initially detected instead of total testosterone). There were total noncompliance of the diagnostic algorithm of hyperandrogenism and the diagnosis «hyperandrogenism» was unauthorized. However, glucocorticoid treatment was prescribed to all patients. 6 women took methylprednisolone in supraphysiological doses: 3 women – 6 mg during about 3 months, 3 women – 8 mg during about 11 months. 2 women took hydrocortisone in supraphysiological doses: 1 woman – 30mg during about 6 months, 1 woman – 40 mg during about 12 months. Iatrogenic hypercortisolism were observed in 2 women during glucocorticoid treatment. The abolition of glucocorticoid treatment was performed in all patients. Nevertheless, chronic adrenal insufficiency developed in one woman, which required lifelong replacement glucocorticoid treatment.

**Conclusions:** No one case report had indications for clinical and laboratory examination for hyperandrogenism. But non-compliance of the diagnostic algorithm of hyperandrogenism caused false diagnosis and unauthorized glucocorticoid treatment that led to iatrogenic hypercortisolism and chronic adrenal insufficiency.

## Metformin therapy can be delayed for vitamin B12?

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**Objectives:** Diabetes is an important complex disease with increasing prevalence, causes serious medical problems due to its chronic complications. While metformin which is used in the first treatment phase is widely accepted as an effective drug, it might lead to vitamin B12 deficiency in long-term treatment. Moreover it might contribute to neuropathic complications. In this study, we aim to evaluate the relationship between vitamin B12 deficiency and neuropathy in patients with type 2 diabetes.

**Methods:** Our study included 256 patients admitted to Malatya State Hospital Endocrinology Department between October 2013 and January 2015. Patients were divided into two groups: patients on diet (group 1, n=112), and patients on diet and only used metformin (group 2, n=144). Complete blood count, fasting

glucose, post-prandial glucose, lipid levels, HbA<sub>1c</sub>, and vitamin B12 levels of the patients were observed. They were questioned if they had complaints of neuropathy. SPSS package was used for the statistical analyses.

**Results:** There were no significant age, diabetes duration, and HbA<sub>1c</sub> level differences between the two groups. Individuals with vitamin B12 levels <150 pmol/L were considered as vitamin B12 deficient. 11 patients (9.1%) with vitamin B12 deficiency in group 1 had mild neuropathic complaints. 28 patients (19.4%) with vitamin B12 deficiency in group 2 had more severe neuropathic complaints.

**Conclusions:** We reported higher ratios of vitamin B12 deficiency in group 2 patients than the ones in group 1. We think that vitamin B12 deficiency can contribute to neuropathy development. Therefore, we suggest that vitamin B12 replacement should be performed prior to anemia development, considering this treatment might decrease the neuropathic complaints. This requires further prospective studies on the effects of vitamin B12 deficiency on neuropathy development.

## Relationship between biochemical markers of endothelial dysfunction, clinical and metabolic parameters in men with type 2 diabetes

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**Background:** Endothelial dysfunction is the starting mechanism of any vascular disease and its progression. The search of the most significant and early markers of endothelial dysfunction in patients with type 2 diabetes, which have a high risk of developing of cardiovascular disease is extremely important.

**Objective:** To examine the relationship between the endothelial dysfunction markers (VCAM-1, P-selectin, E-selectin), clinical and metabolic parameters in men with type 2 diabetes.

**Material and methods:** We examined 115 men (mean age 54,2±6,2 ys) with type 2 diabetes. As a biochemical markers of endothelial dysfunction were studied levels of VCAM-1, P-selectin and E-selectin. Doppler ultrasound by the method of D. Celermajer was used to assess the vascular reactivity of the brachial artery. To evaluate the severity of symptoms of diabetes mellitus and androgen deficiency were used the DSC and AMS questionnaires. Statistical analysis was performed using Spearman correlation.

**Results:** Analysis of the results showed a significant ( $p<0.05$ ) positive correlation of VCAM-1 and BMI ( $r=0,39$ ), triglycerides and low density lipoprotein ( $r=0,38$ ), D-dimer ( $r=0,35$ ), and E-selectin ( $r=0,26$ ) levels. The level of P-selectin had a positive association with the duration of diabetes ( $r=0,26$ ), the severity of diabetic symptoms on neurological sensitivity ( $r=0,36$ ) and pain ( $r=0,3$ ) scales, also the brachial artery diameter ( $r=0,33$ ) and the linear flow velocity ( $r=0,28$ ) in endothelium-dependent vasodilatation. The level of E-selectin was more closely associated with clinical parameters – BMI ( $r=0,35$ ) and the severity of diabetes

symptoms, according to a questionnaire DSC and symptoms of androgen deficiency, according to a AMS questionnaire ( $r=0,42$ ).

**Conclusions:** The study revealed a close relationship between VCAM-1 level and biochemical parameters, especially lipid metabolism. The level of P-selectin was more influenced on the neurological symptoms of diabetes, as well as parameters of endothelium dependent vasodilatation of blood vessels. E-selectin was correlated not only with the severity of the diabetic symptoms, but also the severity of androgen deficiency symptoms.

**Acknowledgement:** The study was supported by the Russian Science Foundation, № 14-25-00052.

## Genetic determinants of endothelial dysfunction in men with type 2 diabetes

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**Objectives:** It is well known that type 2 diabetes contributes to dysfunction of endothelium, leading to the development and progression of cardio-vascular diseases. However, the severity of vascular complications of diabetes depends on the duration and the compensation of diabetes, but also is influenced by numerous factors, including genetic. The aim of the study was to evaluate the effect of endothelial nitric oxide synthase (eNOS3) gene s.582 + 353\_379del polymorphism on endothelial function in men with type 2 diabetes.

**Material and methods:** We examined 88 men with type 2 diabetes aged 40-65 years. Patients were divided into 2 groups according to the presence of eNOS3 gene s.582 + 353\_379del polymorphism. The groups were matched for age, duration of diabetes, levels of arterial blood pressure, HbA<sub>1c</sub> and sex hormones. The arterial vasoreactivity was evaluated by Doppler ultrasound of the brachial artery.

**Results:** There were no significant differences in baseline diameter of the brachial artery and flow-mediated dilation between two groups. Cuts a figure the fact that the time until the endothelium-dependent vasodilatation of the brachial artery in patients with eNOS3 gene s.582 + 353\_379del polymorphism was significantly longer ( $p=0.05$ ) than in the second group ( $148,1\pm 41,4$  vs  $112,5\pm 37,9$  sec). This may be due to the delay in the rate of NO synthesis by nitric oxide synthase in patients with eNOS3 gene polymorphism. The studies revealed a significant ( $p=0.047$ ) increase in the linear flow velocity in the endothelium-dependent vasodilatation ( $171,6\pm 26,3$  vs  $152,7\pm 25,8$  cm/sec), and the severity of its response to hyperemia ( $108,3\pm 37,7$  vs  $88,5\pm 40,1\%$ ) ( $p=0.049$ ) in patients with eNOS3 gene polymorphism. The assessment of biochemical markers of endothelial dysfunction shows a significant increase of the VCAM-1, ICAM-1, and VEGF-1 levels in patients with eNOS3 gene polymorphism.

**Conclusion:** The presence of the eNOS3 gene S.582+353\_379del polymorphism delays endothelium-dependent vasodilatation of vessels in patients with type 2 diabetes, which may be one of the

early mechanisms for the formation of endothelial dysfunction in patients with type 2 diabetes.

**Acknowledgement:** The study was supported by the Russian Science Foundation, № 14-25-00052.

## Study of motor nerve conduction velocity in patients of thyroid dysfunction in central India

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**Objectives:** To assess motor nerve functions in thyroid dysfunction patients. To study effect of body mass index (BMI) in thyroid dysfunction patients.

**Methods:** The study will be conducted on thyroid dysfunction patients attending the OPD coming for treatment. Control group will be normal (healthy) subjects. Total 50 subjects will be taken in the study in the age group of 18-66 yrs. Out of 50 subjects 25 will be diagnosed thyroid dysfunction patient and 25 subjects will be healthy individual. Informed written consent will be taken from all the subjects. Nerve conduction study consists of motor nerve conduction and F wave study of median, ulnar, tibial, peroneal. Parameters such as distal motor latency, CMAP amplitude, conduction velocity for motor nerve and F wave minimum latency of motor nerve will be recorded and analyzed in clinical neurophysiology unit of Acharya Vinoba Bhawe Rural Teaching Hospital in central India. Electrophysiological parameters like compound muscle action potential, distal motor latency and conduction velocity were evaluated

**Results:** It was found that the latencies were significantly prolonged ( $p<0.05$ ) and conduction velocity and amplitude were significantly reduced in median and peroneal nerves in cases as compared to controls.

**Conclusions:** The study clearly depicts the peripheral neurological involvement in thyroid dysfunction. Hence electrophysiological studies can be useful in the diagnosis of subclinical polyneuropathy in thyroid disorder. Since this neuropathy is reversible, it can also be used to test the prognosis of patient on treatment.

## The role of inflammasome in macrovascular complications in type 2 diabetes patients

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**Objective:** We investigated common polymorphisms in inflammasome coding genes and the risk for macro and microvascular complications in type 2 diabetes mellitus (T2DM).

**Methods:** In total 181 clinically well characterized T2DM patients were genotyped for NLRP3 rs35829419 and CARD8 rs2043211. Risk for diabetic complications was assessed using logistic regression.

**Results:** Patients with median duration of T2DM 11 (6-17) years had relatively well controlled blood glucose and lipid levels and

blood pressure on the prescribed treatment regimen. Duration of T2DM and plasma cholesterol levels were the most important clinical risk factors for macrovascular complications ( $p=0.007$  and  $p=0.031$ ). NLRP3 rs35829419 was associated with increased risk for macrovascular complications ( $p=0.004$ ), with myocardial infarction in particular ( $p=0.052$ ). No association was observed between CARD8 polymorphism and any of T2DM complications.

**Conclusion:** Our preliminary data suggest the role of NLRP3 polymorphism in diabetic macrovascular complications, especially in myocardial infarction.

## Ethnic aspects of personalized medicine

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**Objective:** To identify the ethnic features of the genome, metabolome and several diseases course among indigenous ethnic group of Eastern Siberia-Buryats, in comparison with the Russian ethnic group.

**Methods:** Complex clinical biochemical examination of representatives of indigenous ethnos of Siberia (Buryat belonging to Mongoloid race) and Russians (as representatives of Caucasian race) in various age and gender groups carried out.

**Results:** Determined that the contents of some hormones, lipid metabolism and oxidative stress in indigenous peoples of Eastern Siberia differ from Russians (Caucasians). In adolescence their lipid metabolism is more stable in comparison with the older age period. It was revealed that the incidence and prevalence of diabetes mellitus type 1 (T1DM) in Buryat ethnic groups below Russian indicators. HLA-II profile bore differs significantly from Russian: frequency of predisposing to T1DM haplotypes in the Group bore below the frequency of protective is considerably higher, and bore the low frequency of late vascular complications. Higher frequency of occurrence of an insertion insertional deletion polymorphism of angiotensin I converting enzyme gene in Buryat ethnic group teenagers in comparison with the Russian one revealed. Intensity of processes of a lipids peroxidation at Buryat teenagers with essential arterial hypertension is much lower, than in Russians. It was revealed that course of such diseases as T1DM, essential arterial hypertension, chronic obstructive pulmonary disease, cardiovascular disease are more favorable for Buryats, and adverse-tuberculosis, endocrine infertility, complicated pregnancy, glaucoma, bones and joints diseases are more complicated.

**Conclusion:** Proposed to take into account the ethnic characteristics of genome, metabolome, microbiome, reproduction, epidemiology and pathogenesis of diseases to develop personalized approach for diagnosis, prevention and treatment of certain pathologies, as well as to use this information for the formulation of socio-economic and health forecasts to improve health-care system.

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## Gender aspects of obesity in patients with metabolic syndrome

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**Objective:** To examine gender features of obesity among young patients with metabolic syndrome (MS).

**Material and methods:** There were examined 189 patients (107 women and 82 men) with MS at the age of 18–44 years (mean age  $36,2\pm 0,3$  years). The control group – 65 healthy men and women (average age  $29,5\pm 0,5$  years). We've examined anthropometric parameters (weight, BMI, waist circumference (WC), lipid metabolism (total cholesterol (CT), HDL and low-density (HDL, LDL), triglycerides (TG), glucose metabolism (fasting glucose, an oral glucose tolerance test (OGTT)), hormonal measurements (levels of estradiol (E2), total testosterone (T) binding globulin sex hormone (SHBG), leptin, insulin, insulin resistance index definition and free androgen index (FAI)). There were developed individual treatment plans for patients with MS include drug and non-drug therapies. The duration of follow-up period was 3 years.

**Results:** The decreasing of weight among men ( $8,19\pm 0,02$  kg/year) exceeded the a similar indicator among women ( $7,7\pm 0,05$  kg/year). The annual dynamics WC among women ( $3,90\pm 0,11$  cm/year) was lower than that among men ( $4,63\pm 0,04$  cm/year). Hyperleptinemia common among 43.9% women and 25.6% men with MS. Leptin was normalized among 12.7% women and 17.0% men with MS. Leptin resistance among female patients was higher by 36.4% than that of men. The treatment of leptin/BMI decreased in men 2.1 times faster than that of women. The weight loss 1 kg was associated with a reduction FAI on 0.14% and leptin on 1.95 ng/ml. Weight loss of 9.4 kg among obese men helped to improve decrease FAI on 3.1% and leptin on 1.16 ng/ml. For patients with the metabolic syndrome characterized by increased triglycerides on 37.7% and decreased HDL-C on 33.5%. Among men with MS was total cholesterol level higher on 40%, LDL-cholesterol on 21.1%. Impaired glucose tolerance (IGT) was found among 55% of patients (50% women and 59.6% men). Weight loss was positively correlated with HOMA-IR (63% women and 79.2% men) ( $r=0,74$ ;  $r=0,69$ ,  $p < 0,01$ ).

**Conclusion:** Hyperandrogenism, relative hypoestrogenemy among women and relative decrease of testosterone among men are predictors of visceral obesity that determines the gender differences to the management of patients with obesity and metabolic syndrome.

## Rhabdomyolysis and multiple serous effusions due to hypothyroidism

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**Introduction:** Hypothyroidism can lead to many cardiovascular, pulmonary and neuromuscular symptoms. Hypothyroidism-

related serous effusions usually have been associated with pericardial fluid and less frequently with ascites, while pleural effusions are a rare complication. Moreover, hypothyroid myopathy, which manifests with myalgias, cramps, proximal muscle weakness and moderate elevation of muscle enzymes, is not uncommon. However, rhabdomyolysis due to hypothyroidism is rare, especially when other precipitating factors are absent, and only few cases have been reported. We describe a patient with rhabdomyolysis, pericardial and pleural effusions, and ascites due to primary hypothyroidism.

**Case report:** A 38 year old man was admitted to our hospital due to progressively deteriorating shortness of breath during the past month. He did not exercise and did not take any drugs. On clinical examination the patient was afebrile and had non pitting edema in upper and lower limbs. Blood studies revealed normocytic anemia, leucopenia, abnormal liver function tests and elevated serum LDH and creatinine kinase (CK). Urine analysis demonstrated myoglobinuria. The cardiac ultrasound showed normal ejection fraction and mild pericardial effusion, while computed tomography scan demonstrated bilateral pleural effusions and mild ascites. Additional testing was performed and confirmed the diagnosis of primary hypothyroidism. Thyroid hormone replacement therapy resulted in improvement of clinical symptoms, resolution of serous effusions and reduction in the serum CK level.

**Discussion:** Hypothyroid serous effusions are non inflammatory and have characteristics of both transudates and exudates. Increased capillary permeability, reduced lymph clearance and impairment of free water secretion seem to be related to their pathogenesis. Additionally, the pathogenetic mechanism of hypothyroid-induced rhabdomyolysis seems to involve decreased mitochondrial oxidation capacity with impaired glycogenolysis and an insulin resistant state. A reduction in beta-adrenergic receptors and decreased protein metabolism and muscle uptake of triglycerides may also contribute to impaired energy consumption. Rhabdomyolysis, even without predisposing factors, and serous effusions, especially pleural effusions, are rare complications of hypothyroidism. They may be presenting symptoms of the disease, preceding the more typical manifestations of hypothyroidism, thus misleading the clinician.

## Prevalence of metabolic complications and their association with disease control indicators in a cohort of diabetic patients

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**Objectives:** To evaluate prevalence of metabolic complications (MC) in patients with diabetes mellitus (DM), to find out association with age, sex, type of DM, disease duration, treatment, metabolic compensation level, diabetic foot indicators.

**Methods:** A retrospective cohort study was performed. Participants were randomly included from Internal medicine clinic of Riga Eastern Clinical University Hospital, Latvia. Interviewing, diabetic foot testing, observation and retrospective analysis of case files were performed for necessary data selection.

**Results:** 100 patients – 41 (41%) men and 59 (59%) women were included. Patients were divided into 3 age groups [group I ( $\leq 45$  years) – 18%, group II (46-59 years) – 29%, group III ( $\geq 60$  years) 53%] and into groups by DM type [type 1 DM – 19%, type 2 DM – 77%, other (secondary) – 4%], by DM duration [1st (0-5 years of DM) – 24%, 2nd (6-10 years) – 24%, 3rd (11-20 years) – 37%, 4th ( $> 20$  years) – 14%] and by type of therapy [patients with long-term insulin therapy (57%) and patients with peroral therapy, diet or recently prescribed insulin treatment (43%)]. Frequency of MC were identified – neuropathy (68%), retinopathy (57%), nephropathy (24%), microangiopathy (42%), macroangiopathy (17%). Prevalence of neuropathy was found statistically significant in 3 disease duration groups (2nd group 75%, 3rd group 78%, 4th group 100%;  $p < 0,001$ ) and in group of patients with long-term insulin therapy (86%;  $p < 0,001$ ). Neuropathy was associated with abnormal foot vibratory perception (83%;  $p < 0,039$ ) and impaired foot temperature sensation (66%;  $p < 0,038$ ). Prevalence of retinopathy was found significant in male gender (71%;  $p < 0,017$ ), in type 1 DM (85%;  $p < 0,026$ ), in the 4th duration group (100%,  $p < 0,004$ ), in patients with prolonged insulin therapy (70%;  $p < 0,001$ ). Microangiopathy was found associated with type 1 DM (74%;  $p < 0,007$ ), in the 4th duration group (93%;  $p < 0,001$ ), in patients with long-term insulin therapy (65%;  $p < 0,001$ ), with impaired peripheral sensation (86%;  $p < 0,008$ ) and vibratory perception (70%;  $p < 0,006$ ). Both, nephropathy (57%;  $p < 0,003$ ) and macroangiopathy (50%;  $p < 0,004$ ) had significant association in patients of the 4th group of patients.

**Conclusion:** MC in diabetic patients of our hospital had statistically significant stronger association with type 1 DM, longer duration of disease and long-term insulin therapy what matches the general population data.

## Prevalence of dermatological changes in diabetic patients and their association with age, sex, disease duration, treatment and compensation level

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**Objectives:** To determine and evaluate the most common skin disorders in patients with diabetes mellitus (DM), and to find out their association with age, sex, duration of disease, type of DM, treatment and metabolic compensation level in DM patients.

**Methods:** A retrospective cohort study was performed. Participants were randomly included from Internal medicine clinic of Riga Eastern Clinical University Hospital, Latvia. Patient interviewing, observation and retrospective analysis of case files were performed for necessary data selection.

**Results:** 100 patients were included in the study – 41 (41%) men and 59 (59%) women; the mean age was  $60,1 \pm 15$  years. Patients were divided into 3 age groups – group I ( $\leq 45$  years) – 18%, group II (46-59 years) – 29%, group III ( $\geq 60$  years) – 53%. All patients were also divided into groups by DM duration type and therapy – (0-5 years of DM) 24%, (6-10 years) 24%, (11-20 years) 37%, ( $> 20$  years) 14%; type 1 DM 19%, type 2 DM 77%, other (secondary) 4%; patients who had insulin therapy (57%)



and patients who had peroral therapy or only diet (43%). 6 most frequent skin problems were identified – skin atrophy (71%), skin dryness (66%), onychomycosis (54%), necrobiosis lipoidica associated with DM (45,3%), hyperkeratosis (45%), lichenification (39%). Prevalence of skin atrophy was found statistically significant in patients with insulin therapy – 80,7% ( $p < 0,01$ ). Prevalence of onychomycosis was found statistically significant in age group III – 64,2% ( $p < 0,05$ ). Prevalence of necrobiosis was found significant in men – 53,7% ( $p < 0,032$ ) and in patients with insulin therapy – 54,4% ( $p < 0,002$ ). Prevalence of hyperkeratosis was associated with insulin therapy – 54,4% ( $p < 0,03$ ). Prevalence of lichenification was found significant in age group II – 51,7% ( $p < 0,05$ ).

**Conclusions:** Most common cutaneous changes were skin atrophy, dryness, onychomycosis, necrobiosis lipoidica, hyperkeratosis, lichenification, they had strong associations with age, sex and insulin treatment. Other independent values were not statistically significant, but the reason may be relatively small amount of patients, insufficient data in some patients, recall bias. More extensive studies are required.

## Effect of vitamin D insufficiency on cognitive functions in patient with type 2 diabetes mellitus

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**Objectives:** Vitamin D insufficiency and deficiency is one of the most frequent and major health problems. After understanding the effects of vitamin D on the nervous system, debates about the effects on cognitive functions had arisen, which were later subject to many scientific studies. Long-term diabetes also leads to deterioration of cognitive functions. Studies demonstrate that vitamin D deficiency is common in patients with diabetes. This study aims to investigate the effects of vitamin D deficiency on the cognitive functions in diabetic patients.

**Methods:** Randomly selected 118 type 2 diabetes mellitus (T2DM) patients with vitamin D deficiency were included as subject group and 118 T2DM patients without vitamin D deficiency were included in the study as a control group. We evaluated the cognitive functions of the study groups with the Mini Mental Status Examination Test (MMSE). The test collected data about orientation, registration, attention, calculation, recall and language abilities of patients. We used the SPSS software to perform statistical analyses and accepted  $p$  values less than 0.05 as significant.

**Results:** The mean age of the study subjects was  $57.6 \pm 7.1$  years. Study and control groups were significantly different with respect to mean age of the patients they included ( $56.7 \pm 7.1$  vs  $58.5 \pm 7.1$ , respectively;  $p = 0.021$ ,  $t$ -test). 153 (64.8%) of the patients were female and 67 (35.2%) were male. The female-to-male ratio among the whole study group was 1:0.54. 169 (71.6%) patients had diabetes for less than 10 years and 67 (28.4%) had diabetes for more than 10 years. Of these, 189 (80.1%) were using oral antidiabetic drugs, 17 (7.2%) were using insulin therapy, and 30 (12.7%) were using a combination therapy. The diabetic group

had a significantly lower vitamin D level than the control group ( $17.2 \pm 6.5$  vs  $39.9 \pm 11.9$ ;  $p = 0.00$ ,  $t$ -test). There were no significant correlations between vitamin D levels and cognitive functions of participating diabetic patients.

**Conclusions:** This study does not demonstrate any relations between vitamin D levels and cognitive functions of diabetic patients. There is a need for more detailed and structured studies demonstrating also active vitamin D levels in a more homogenous diabetic group.

## The broken seller

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**Introduction:** Through the presentation of a clinical case, explain the handled of a daily persistent headache with limitation on daily activities.

**Case report:** Male, 75 years old, was admitted to the hospital due to daily persistent bitemporal headache with no response to analgesia. His medical history talked about hypertension, pulmonary embolism in treatment with anticoagulant for 9 months, 2 years ago. His daily treatment was: simvastatin, clopidogrel and lorazepam. Physical exploration was normal, not showing any neurological symptoms. Before the beginning of the study some differential diagnosis should be taken into account: brain tumor, headache due to spontaneous cerebrospinal fluid leak, idiopathic intracranial hypertension (pseudotumor cerebri), infectious disease, sphenoid sinusitis, leptomeningeal metastasis, subarachnoid hemorrhage, cerebral venous sinus thrombosis, giant cell arteritis, dissection of carotid or vertebral artery due to the symptoms (no neurological deficit), the age of the patient like giant cell arthritis, cerebral venous sinus thrombosis or dissection of carotid or vertebral artery. To study this pathology disease some test must be done: complete analyze with hormones levels, serology, imaging test (brain TC and RM; abdominal ultrasounds) and ophthalmology evaluation. Results of blood tests: sodium 128 mEq/dL, TSH 0.14  $\mu$ UI/mL, T4 0.63 ng/dL, FSH 3.0 mUI/mL, LH 1.1 mUI/mL, prolactine 6.27 ng/mL, testosterone 38.8 ng/dL, basal cortisol 1.2  $\mu$ g/dL. Brain TC and MRA: mass in pituitary gland compatible with macroadenoma, being MRA brain normal. Rest of the tests was normal. The result shown hypopituitarism but owing to the sudden and severe headache and the hormonal deficiency the patient was diagnosticated of a subacute pituitary apoplexy.

**Discussion:** The hypopituitarism is an endocrinology disease which may be asymptomatic or present with symptoms related to a mass lesion or hormone deficiency, however patient could suffer from nonspecific symptoms, such as fatigue. Hypopituitarism most of the time is caused by sellar mass like adenoma; sometimes this adenoma can bleeding and cause apoplexy pituitary. In its most dramatic presentation, apoplexy causes sudden headache, diplopia owing to pressure on the oculomotor nerves, and hypopituitarism; sometimes symptoms manifests in a subacute way. The patients may improve after surgical decompression of the pituitary. Hence, problems may also improve spontaneously,

as blood is resorbed, over a course of weeks to months after the hemorrhage. Anyway, it is necessary to treat the deficiency caused by the adenoma hemorrhage using hormonal substitution.

## Hashimoto's encephalopathy in a young male in a after total thyroidectomy status – case report

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**Introduction:** Hashimoto's encephalopathy has been used to describe a syndrome of cerebral symptoms in patients with serologic evidence of autoimmune thyroid disease. It's a rare condition with an unknown etiopathogenic mechanism. It's thought to be an autoimmune vasculitis or other inflammatory process with deposition of immune complexes that can lead to cerebral microvascular disruption.

**Case report:** The authors describe a case of a 32 years old man who was admitted to the emergency room with impaired consciousness and seizures. 5 years ago he had been submitted to a total thyroidectomy due to Graves' disease. He had no previous epilepsy background or other neurological conditions. He was on 0.175 mg of levothyroxine per day. On examination he was afebrile, normotensive, normoglycemic, first and second heart sounds normal, no murmurs, 63 heart beats per minute. Exophthalmia was present. He had no muscle strength or sensation changes. He had no meningitis signs and cutaneous plantar reflex in flexion bilaterally. Analytically the patient showed up hypothyroidism (thyroid stimulating hormone 15.56  $\mu$ UI/ml, thyroxin 0.59 ng/dL) with thyroglobulin autoantibodies and anti-peroxidase positive (5.02 UI/ml and 14.89 UI/ml respectively). Anti-TSH receptor antibody was negative. Further autoimmune investigation was negative. The cerebral spinal fluid was normal. Sedimentation velocity and C reactive protein were negative. Head computed tomography and magnetic resonance imaging showed sequelae cortical-subcortical atrophic injuries. The electroencephalogram showed no paroxysmic activity. The patient started treatment with 60 mg of prednisolone per day with prompt clinical response.

**Discussion:** In the absence of other medical conditions that explained the clinical patient status we admitted the diagnosis of Hashimoto's encephalopathy.

## Isolated hypoaldosteronism: a cause for hyponatremia

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**Introduction:** There are few reports of isolated hypoaldosteronism as a cause of hyponatremia with normal levels of potassium. This could be related to the release of antidiuretic hormone by reflex mechanism in the baroreceptor of the carotid sinus. Treatment with fludrocortisone is effective, with normalization of serum sodium levels.

**Case report:** 85 year old female presented to the emergency room after episode of upper limbs involuntary movements, followed by fixed upward gaze, generalized hypotension and an abundant food vomiting. After this episode appears less reactive. She has history of dementia, neoplasm of the vulva, acute pancreatitis, type 2 diabetes, hypertension, and dyslipidemia. Usually medicated with: estazolam 2 mg bid, pravastatin 20 mg bid, metformin 700 mg bid, isosorbide mononitrate 20 mg bid, acetylsalicylic acid bid, ginkgo biloba 20 mg bid, fluoxetine 20 mg bid, enalapril 5 mg  $\frac{1}{2}$  bid, and omeprazole 20 mg bid. On physical examination she was disoriented, the pupils were equal, round, and reactive; the global muscular force was reduced, without lateralization, and with flexor plantar reflex; afebrile, with blood pressure 137/55 mmHg, SpO<sub>2</sub> 97%, and heart rate of 75 bpm. Laboratory tests: hemoglobin 12.7 g/dL, MCV 95.1, platelets 237x10<sup>9</sup>/L, leukocytes 15.6 x10<sup>9</sup>/L, PT +0.5", INR 1.08, prothrombinemia 88%, aPTT -4.0", urea nitrogen 15 mg/dL, creatinine 0.74 mg/dL, Na 122 mmol/L, K 4.4 mmol/L, Cl 95 mmol/L, Ca 8.9 mmol/L, osmolality 261 mOsm, CRP 0.49 mg/L. Cerebral CT: "microcirculatory leukoencephalopathy (Fazekas 3) and sequelae of vascular ischemic lesions". EEG without specific changes. The patient presented new generalized tonic-clonic seizure on the 6th day of hospitalization, coinciding with worsening hyponatremia. The hyponatremia was found to be present since 2012. There was no improvement after fluid administration. Further studies: TSH 1.7, T4 1.4, ACTH 17 pg/ml, cortisol 26 ug/dL (morning); 16 u/dL (afternoon), active renin 9.3 uU/ml (7-76), aldosterone 34.0 pg/ml (40 – 310), index aldosterone/renin activity 4.62 (<25). Urine 24h: sodium 65 mmol (40-220), potassium 48 mmol (25-125). Follow-up: our patient has isolated hypoaldosteronism, and since hyponatremia may lower the seizure threshold in patients with vascular epilepsy, we decided to start fludrocortisone 0.1 mg bid. The patient remains in outpatient follow-up, maintaining normal serum sodium levels and presenting a significant improvement in overall condition.

## Prevalence of microvascular complications and their relation with metabolic control and cardiovascular risk factors in type 2 diabetes mellitus

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**Objectives:** To determine the prevalence of microvascular complications in type 2 diabetes mellitus (T2DM) in patients admitted in an internal medicine ward in Portugal and its correlation with metabolic control and cardiovascular (CV) risk factors.

**Methods:** Review of clinical processes (SCLínico™, Alert™, Plataforma de Dados de Saúde™, EResults™) for a retrospective study in an internal medicine ward, between January 1st 2014 and February 28th 2015. Good glycemic control was defined as HbA<sub>1c</sub> <7,0%. Statistical analysis was performed using IBM SPSS Statistic™ software; p values of <0,05 were considered statistically significant.

**Results:** Total of 347 subjects (217 female and 130 male, mean age  $77 \pm 9,5$  years). There was a high prevalence of cardiovascular risk factors, 87% (n=302) had arterial hypertension, 68% (n=236) had dyslipidemia and 7,5% (n=26) were or had been smokers. The average value of HbA<sub>1c</sub> was of  $7,8 \pm 1,8\%$ . End organ disease was present in 279 (80,4%) subjects. Microvascular complications were present in 72,6% and macrovascular in 48,7%; 39,5% (n=137) had simultaneously both micro and macrovascular complications. Among the total subjects, 139 had been diagnosed with retinopathy, 182 with nephropathy, 67 with peripheral neuropathy and 63 with peripheral vascular disease (PVD). Good glycemic control was associated with less prevalence of retinopathy (29,5% versus 70,5%,  $p < 0,05$ ). Both arterial hypertension and dyslipidemia were associated to retinopathy and nephropathy ( $p < 0,05$ ).

**Conclusions:** There is a high prevalence of microvascular complications in T2DM. The relation between prevalence of micro and macrovascular complications in this study matches the expected within the disease. As expected, retinopathy and nephropathy were the most common complications of diabetes in our study. Arterial hypertension and dyslipidemia were both very prevalent. Good glycemic control was associated with less prevalence of retinopathy. A good glycemic control and an aggressive treatment of CV comorbidities are crucial in order to prevent microvascular complications of T2DM.

## Type 2 diabetes mellitus, dyslipidemia and cardiovascular risk factors – a retrospective study

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**Objectives:** To characterize the lipid profile in type 2 diabetes mellitus (T2DM) patients and its correlation with pharmacological therapeutics and cardiovascular (CV) risk factors.

**Methods:** Review of clinical processes (SCLínico™, Alert™, Plataforma de Dados de Saúde™, EResults™) for a retrospective study in an internal medicine ward, between January 1st 2014 and February 28th 2015. Statins were clustered according to its intensity in low, moderate and high. Good lipid control was defined as LDL cholesterol  $\leq 70$  mg/dL. Statistical analysis was performed using IBM SPSS Statistic™ software; p values of  $< 0,05$  were considered statistically significant.

**Results:** Total of 295 subjects (181 female and 114 male, mean age  $76,6 \pm 9,4$  years). 182 (61,7%) subjects were under hypolipidemic treatment. Simvastatin 20 mg was the most used statin. Total cholesterol average level was 142,5 mg/dL (93,9%  $\leq 200$  mg/dL; 84,4%  $\leq 180$  mg/dL; triglycerides average level was 124,6 mg/dL (74,9%  $\leq 150$  mg/dL); LDL-cholesterol average level was 76,8 mg/dL (83,1%  $\leq 100$  mg/dL; 46,8%  $\leq 70$  mg/dL). The majority of patients (88,5%) was on moderate intensity statins. Arterial hypertension was present in 86,8% of the patients; dyslipidemia in 71,2% and smoking habits in 9,2%. Acute myocardial infarction (AMI) was present in 18% (n=53) and cerebrovascular accident (CVA) in 39,3% (n=116).

Most subjects (n=187; 63,4%) had 2 CV risk factors. On patients with 3 risk factors, LDL average was 81,6 mg/dL (66,09-97,03; IC 95%). Among these, only 81,2% were under treatment with statins and only 7,7% with high intensity statins. Even though both AMI (56,6% versus 43,4%) and CVA (51,7% versus 48,3%) were more common among patients with LDL levels  $> 70$  mg/dL, these results were not statistically significant. There was a statistically significant negative association between treatment with statins and AMI ( $p < 0,05$ ).

**Conclusions:** There is a high prevalence of CV risk factors in patients with T2DM. Contrary to expectation, the majority of patients with multiple CV risk factors was not medicated with high intensity statins. The statistically significant negative association between treatment with statins and AMI, unrelated to LDL levels, enlightens the atherogenic nature of the LDL molecule regardless of its levels being on an adequate range. It is necessary to reinforce the importance of treating diabetic patients with CV risk factors with statins, in order to decrease the occurrence of major CV events.

## An unusual case: bilateral pheochromocytoma with pituitary adenoma

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**Introduction:** Pheochromocytomas are neuroendocrine tumors of the medulla of the adrenal glands which up to 25% may be familial. In adults, approximately 10% are bilateral, probably with one of MEN syndromes.

**Case report:** We like to present here 32 years old man had been operated for bilateral total adrenalectomy due to pheochromocytoma two years ago. He had all clinical, laboratory and radiological evidence for pheochromocytoma, also had a pituitary tumor 10x9 mm in diameter which couldn't determined functioning and no evidence and MEN-2 syndromes. His skin has changed and pigmented while he underwent hydrocortisone therapy after adrenalectomy. Lab tests revealed very high level of ACTH 258 pg/ml. IGF-1 was 329 ng/ml, GH levels were 7,12 ng/ml, 0,53 and 0,36 after OGTT respectively. MRI showed progressed 15x12 mm mass in pituitary. He underwent pituitary operation with the diagnosis of Nelson's syndrome. Interestingly pathology showed us pituitary adenoma expressed GH with diffuse GH positive and ACTH, TSH, LH, FSH, PRL negative in the immunochemistry panel, although pre-operatively tests did not reveal acromegaly. ACTH levels decreased 220 and 24.2 levels postoperatively at 7th day and 3rd month respectively. Although ACTH level has been found 1000 pg/ml at 9th month visit, MRI and MIBG (I-123) were found normal during the follow-up period. Dosage of hydrocortisone therapy was arranged again.

**Discussion:** In this case, we thought this pheochromocytoma could be unusual combination with pituitary adenoma which might have been subclinical acromegaly. Nelson syndrome can be explaining corticotrophin hyperplasia after surgery. We should probably perform further investigation on molecular genetic analyses for MEN syndromes while following the patient.

## Effect of anemia on the levels of HbA<sub>1c</sub>

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**Objective:** HbA<sub>1c</sub> or glycated hemoglobin is one of the most used methods for diagnosis and treatment monitoring in patients with diabetes mellitus (DM). It is formed in a non-enzymatic glycation pathway by hemoglobin's (Hb) exposure to plasma glucose. As the average amount of plasma glucose increases, the fraction of HbA<sub>1c</sub> increases in a predictable way. This serves as a marker for average blood glucose levels over the previous 3 months prior to the measurement, as this is the half-life of red blood cells. Several studies report that conditions affecting erythrocyte turnover also affect HbA<sub>1c</sub> concentrations, namely hemoglobinopathies, iron deficiency anemia and chronic disease anemia. The authors want to raise awareness to the effect of anemia on the levels of HbA<sub>1c</sub>.

**Methods:** We present a descriptive study of the patients admitted to an internal medicine ward in the year 2014 with HbA<sub>1c</sub> screening, according to their levels of Hb: Group I: Hb ≤8,5 g/dL associated with severe anemia; and Group II, with Hb ≥12,5 g/dL (values within the normal range according to the laboratory). Patients were evaluated according to gender, age, HbA<sub>1c</sub> and, in Group I, the cause of the anemia.

**Results:** Of the 1315 admitted patients, 502 patients had HbA<sub>1c</sub> screening. There were 147 patients included in the study: 29 in Group I (19,7%) and 118 in Group II (80,3%). Of these, 81 (55,1%) were male (10 in Group I [34,4%] and 47 in Group II [39,8%]); with a mean age of 69,9 years (Group I:73,9 years; Group II: 69,0 years). The mean level of HbA<sub>1c</sub> was 6,9% (Group I: 6,4% [from 14-4,8%] and Group II: 7,2% [from 11,2-4,9%]). In Group I, the mean level of Hb was 7,6 g/dL and the etiology of the anemia was: chronic disease – 16 patients (mean HbA<sub>1c</sub> 6,4%); acute blood loss – 12 (mean HbA<sub>1c</sub> 6,7%) and megaloblastic anemia – 1 patient (HbA<sub>1c</sub> 5,2%).

**Conclusions:** This work is accordant to others that studied the differences in HbA<sub>1c</sub> levels in diabetic patients with and without anemia. The mean HbA<sub>1c</sub> is significantly lower in patients with anemia (6,4% vs. 7,2%). No significant differences were found regarding age or cause of the anemia, although there were far more male patients in Group II than Group I (60,2% vs. 34,5%). Physicians need to be cautious when applying HbA<sub>1c</sub> reference ranges to patients with anemia, as glycemic control may be underestimated.

## Implications of hypothyroidism on diabetes mellitus and heart failure

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**Introduction:** Hypothyroidism (HT) and diabetes mellitus (DM) are two of the most common endocrine disorders and appear

to be closely linked, as 11% of patients with DM also have HT. This association is stronger in women above the age of 60 and in type 1 DM. HT is characterized by reduced metabolism, impaired gastrointestinal glucose absorption, decreased gluconeogenesis and peripheral tissue glucose disposal, contributing to insulin resistance. HT also leads to hypertension, decreased heart function and hypercholesterolemia, increasing cardiovascular risk. In diabetic patients with HT, an aggressive treatment is warranted. Several studies also reveal a suppressive effect of metformin on TSH secretion in hypothyroid patients, which can further hamper their laboratory assessment. We want to raise awareness to the association between HT and DM, through a clinical report.

**Case report:** A 58 year old female patient, with history of >15 years of primary hypothyroidism and type 2 DM, treated with oral levothyroxine (1400 mcg/week), metformin 1 g tid, detemir insulin 42 U/day and short acting insulin according to glucose levels. Both conditions were inadequately controlled due to poor treatment compliance (patient's range value: TSH 30,2->100 mUI/L; FT4 0,3-1,3 ng/dL; HbA<sub>1c</sub> 8,9-14,3%). She also has several comorbidities, namely ischemic and hypertensive cardiomyopathy, hypertriglyceridemia, hepatic steatosis and vascular leukoencephalopathy. After numerous hospital admissions for congestive heart failure, several interventions were made, including therapeutic patient education and initiation of intramuscular levothyroxine (500 mcg/week) due to malabsorption of oral levothyroxine. She was able to improve the glycemic and lipid control, thyroid function (TSH 4,96 mUI/L; FT4 0,82 ng/dL; HbA<sub>1c</sub> 7%) and reduce the number of hospital admissions for symptomatic heart failure.

**Discussion:** A complex pattern of interactions can be observed in patients with HT and DM, as thyroid hormones have acknowledged effects on glucose and lipid metabolism and on insulin secretion and insulin sensitivity. Understanding of these interactions is necessary to optimize these patients' treatment. In this particular report, the difficulty in treating HT had strong repercussions on glycemic control and heart function. Facing the high prevalence of HT, screening of thyroid function in diabetic patients should be emphasized.

## Autoimmune thyroiditis and Epstein-Barr virus infection: cause or coincidence

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**Introduction:** Although the involvement of environmental factors in the pathogenesis of autoimmune diseases is seen as consensual, the description and documentation of this combination is relatively rare. With regard to infection by Epstein Barr virus (EBV) and subacute or chronic lymphocytic thyroiditis (CLT), there are only two cases reported in the literature, one of a 3 years old girl and another of a young woman. Its role in the natural history of thyroid disease remains unclear.

**Case report:** 53 years old female with an asymmetric additive polyarthritis, asthenia and anterior neck pain, starting one week after a flu-like syndrome 2 weeks long. The relevant clinical and laboratory data reported initially were a mild thyroid

enlargement without palpable nodules and pitting edema of both wrists and ankles bilaterally, slightly elevated erythrocyte sedimentation rate (70 mm/h) and C-reactive protein (2.5 mg/dl). Serological tests were compatible with a late phase of primary infection or reactivation of an EBV infection (IgG and IgM viral capsid antigen 4 times and 2 times the upper limit of normal (ULN) respectively and EBV nuclear antigen >600 U/ml), DNA-EBV negative. The evaluation of the thyroid gland revealed subclinical hypothyroidism (TSH 7.3 uIU/ml, free T4 1.0 uIU/mL), elevated antiperoxidase (6xULN) and negative antithyroglobulin and anti-TSH receptor antibodies. The thyroid ultrasound showed an enlarged isthmus (7.8 mm), and diffusely heterogeneous texture, with ill-defined hypoechoic areas without individualized nodules. Scintigram showed increased uptake of thyroid radiopharmaceutical compatible with a CLT. After initial therapy with deflazacort inflammatory parameters normalized and the patient went asymptomatic. However, both TSH and serological values for EBV remained persistently elevated.

**Discussion:** Various mechanisms have been proposed to clarify the influence of EBV infection in the development of autoimmune thyroid diseases, and some studies have already proven the presence of viral genes in disease affected tissues and organs. Since both autoimmune thyroiditis and chronic EBV infection are risk factors for the development of thyroid lymphoma, identifying both conditions in the same patient may place on a higher frequency of ultrasound observation and monitoring of thyroid so it can be identified in a timelier manner.

## Neurocognitive and CNS abnormalities in humans with defective thyroid receptor alpha

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**Objectives:** The severe neurodevelopmental phenotype of untreated congenital hypothyroidism exemplifies the critical role of thyroid hormones (TH) in CNS development, acting via thyroid hormone receptor  $\alpha 1$  (TR $\alpha 1$ ) on cortical neurogenesis, cerebellar development and oligodendrocyte differentiation. We have identified the first humans with defective TR $\alpha 1$  and investigated neurocognitive phenotype and CNS abnormalities in this disorder.

**Methods:** 4 affected individuals (P1: female 8yrs; P2: female 13 yrs; P3, father of P2 53yrs; P4, female 43 yrs) were studied. Neurological investigation, cognitive testing and brain magnetic resonance imaging and spectroscopy (MRI/S) were undertaken.

**Results:** All subjects exhibited developmental delay; P4 also has severe learning disability and epilepsy. Neurological abnormalities common to all cases include gross and fine motor incoordination, with ataxic gait, dysdiadochokinesis and slow speech, associated with reduced cerebellar volume on MRI. IQ is variably reduced (P1 84, P2 90, P3 85, P4 52) and adult cases exhibit marked microcephaly; reduced N-acetylaspartate (NAA) levels (expressed as NAA/creatinine ratio) measured by magnetic resonance spectroscopy (frontal white matter: P3 1.77,

P4 1.54, controls 2.2 $\pm$ 0.2); thalamic: P3 2.05, P4 1.9, controls 2.09-2.25) suggests neuronal loss or dysfunction. Diffusion tensor imaging (P1, P2) indicates reduced axonal density/myelination and tract organization; impaired verbal long-term memory (P1) correlates with significant reduction (20%) in hippocampal volume. Known neural target genes (hairless, KLF-9) in patient derived mononuclear cells are TH refractory.

**Conclusions:** Observed neurocognitive deficits (motor incoordination, reduced IQ, impaired long-term memory) and structural abnormalities (microcephaly, reduced cerebellar and hippocampal volume, diminished white matter density) accord with known developmental actions of thyroid hormone and substantiate the critical CNS role of TR $\alpha 1$ . Studies of neural cell types generated from their inducible pluripotent stem cells may elucidate TH-dependent brain pathways.

## Hyponatremia in patients admitted into internal medicine hospitalization wards from the emergency ward

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**Objectives:** Hyponatremia (HN) is the most common hydroelectrolytic disorder, which complexity usually results in underdiagnosis and undertreatment. The aim is to describe the etiology and the management of patients with HN that are admitted into de internal medicine hospitalization ward (IM) of a third-level hospital from its emergency ward (EW).

**Methods:** Revision of patient data records of adults admitted into IM from EW within January 2015, whose serum sodium values were found to be  $\leq 133$  mmol/l, regardless of the reason of the visit.

**Results:** Among the 207 patients with HN in the EW, 61 (29.5%) were admitted into IM, 6.5% due to HN. 62% were women with a mean age of 82 $\pm$ 11 years [52-98]. 31% came from nursing homes, and a median of 7 drugs per patient. Medical history: heart failure 31%, renal failure 15%, neoplasia 12% and 1 case of inappropriate antidiuretic hormone secretion (IADHS). 59% took HN-inducing drugs, 30% loop diuretics and 26% thiazides. Most common reason of the visit was dyspnea (26%). 59% had normal, 28% increased and 13% decreased extracellular volume. 72% HN  $\leq 30$  mmol/l, the mean first sodium value was 130.1 (median 132.0 mmol/l). 82.4% the exact chronology of HN could not be elucidated. Urinary ion analysis was performed in 33%, thyroid function tests in 75% and cortisol in 13%. HN was among the diagnostics at discharge in only 33%. Causes: heart failure 21%, unknown 20%, thiazides 18%, gastrointestinal losses 11%, furosemide 10%, hyperglycemia 7%, IADHS 5%, renal failure 5%, multifactorial 3%. 44% received normal 0.9% saline, 37% with diuretics and 19% with fluid restriction. Hypertonic fluid was used in 3 cases and tolvaptan only once. 82% HN were corrected during their hospital stay; mean days to correction of HN were 3.3 (27% within the first day, 22% within the second day and 18% five days or more). 18% were discharged with uncorrected sodium values. Mean hospitalization was 9 $\pm$ 7 days (median 7).

There were no cases of osmotic demyelination syndrome and no deaths due to HN.

**Conclusions:** HN is a common disorder, usually underdiagnosed, with a higher rate of prevalence in elderly patients under polypharmacy and comorbidity, corrected in the 82% patients admitted into IM from EW. Most of them mild, HN occurs in the context of heart failure or diuretic treatment, and even 20% of unknown cause. An important proportion of patients were not diagnosed. Simple and available tests, such as serum osmolality and urine ion analysis, were not performed; leaving some IADHS cases undiagnosed by criteria.

## **Familial hypercholesterolemia: treatment by low density lipoprotein aphaeresis: Lebanese experience**

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**Objectives:** In Lebanon, familial hypercholesterolemia (FHC) shows an incidence about 25 times higher than in Europe, homozygous familial hypercholesterolemia has an estimated prevalence between 20 to 30 cases per one million inhabitants (Lebanese population: 4.7 million). This high prevalence is due to intermarriage between family members (e.g. cousins) in isolated villages. There are currently 45 FHC patients regularly treated to achieve better quality of life by reducing co-morbidity and mortality from cardiovascular events.

**Methods:** More than 9,500 sessions were performed until July 2011 for adults and children. 45 patients are regularly treated twice a month. <10 y.o. – no patient (4 awaiting), 7 (16%) are between 10-18 y.o., 29 (64%) – between 19-35 y.o., 8 (18%) – between 36-60 y.o., 1 (2%) is >60 y.o. The sex distribution is: 19 male and 26 female. 41 (91%) patients are homozygous (with low density lipoprotein (LDL)-cholesterol level >600 mg/dL at date of arrival to the center). 4 (9%) patients are severe heterozygous. All of the patients have severe hypercholesterolemia with LDL-C levels ranging from 420 to appx. 900 mg/dL despite conservative treatment (diet, resin, ezetimib, statins, Mena Q7 & Q10 and omega 3). All of them have multiple xanthomas and ~ 2/3 of the patients have a lipid corneal arch. 9 patients lost family members due to coronary heart disease (CHD). LDL apheresis was approved by the Food and Drug Administration in 1996 for use in patients who despite diet and maximum tolerated drug therapy have: LDL-C >300 mg/dL in the absence of coronary heart disease and >200 mg/dL when CHD is present. The procedure is usually performed in regional centers. A patient registry has been established to monitor prospectively clinical outcome and adverse effects.

**Results:** Acute LDL-C reductions in all 7 infants patients and 15/29 adults for a total of ~1540/2532 sessions averaged 64-65%. 1) No deaths during session. 2) Overall physical improvement in the patients. 3) Disappearance of the angina and dyspnea. 4) Net regression of xanthomas and xanthelasma. 5) Reduction of coronary events. 6) Better exercise tolerance. 7) Better quality of life. 8) All of the patients are improving and accepted the concept of a chronic apheresis treatment without any psychological

problems and without fistula operations. 9) No serious adverse effects were observed. 10) LDL-cholesterol reduction averaged 64-65% (compared with 58% LDL-reduction in 2008). 11) The long term reduction of LDL-cholesterol was reduce the cardiovascular events and reduces the mortality-morbidity of the patients. 12) Using Direct Adsorption of Lipoproteins (Dali) system is a well tolerated, safe, effective and a simple way of reducing LDL-C in patients not responding adequately to drug therapy. 13) LDL apheresis gives good long-term results both in adults, infants and in children.

**Conclusion:** LDL apheresis reduces cardiovascular events in hypercholesterolemic patients and may be an effective treatment for other vascular diseases including cholesterol embolic disease, focal segmental glomerular sclerosis, sudden hearing loss, and age-related macular degeneration.

## **Increased risk in patients with arterial hypertension associated with type 2 diabetes mellitus versus patients with arterial hypertension only**

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**Objectives:** Type 2 diabetes is a cardiovascular risk factor. The coexistence of arterial hypertension (AH) in diabetic patients greatly enhances their likelihood of developing CVD. Other important risk factors for CVD in these patients include the following: obesity, atherosclerosis, dyslipidemia, microalbuminuria, inflammation, retinopathy, and "diabetic cardiomyopathy". We aimed to assess the impact of type 2 diabetes mellitus associated with high blood pressure over these cardiovascular risk factors.

**Methods:** We performed a transversal study, lasting 12 months, in which 100 patients with essential AH, and type 2 diabetes, with medium age  $60.7 \pm 9.3$  years were evaluated in comparison with 100 patients with only AH. We evaluate these patients for: BMI; waist circumference; IMT by carotid ultrasonography; microalbuminuria in spot morning urine; fundus oculi, LVMI for left ventricular hypertrophy by echocardiography. Serum PCR and lipid concentrations were measured.

**Results:** The diabetic hypertensive subjects significantly had higher BMI ( $p=0.01$ ) and waist circumference statistically significant ( $p=0.005$ ). Patients with AH and diabetes had a significant greater left ventricular mass index (66% vs 51%;  $p=0.04$ ). Mean value for IMT was  $1.1 \pm 0.3$  mm for diabetic patients and  $0.93 \pm 0.2$  mm for the other group ( $p<0.001$ ) and its prevalence was high in diabetics (75% vs 64%,  $p=0.1$ ). Prevalence of microalbuminuria was significantly high in diabetics (44% vs 14%,  $p<0.001$ ). PCR as marker of inflammation was prevalently high in people with diabetes and AH (32% vs 16%,  $p=0.013$ ). Also, prevalence of retinopathy was significantly high in people with diabetes and AH compare to other group (27% vs 12%,  $p=0.012$ ). There was strong relation between LVMI, microalbuminuria, IMT and PCR. Waist circumference had correlation with IMT and microalbuminuria.

**Conclusions:** DM is an independent risk factor for the increased LV mass and impaired diastolic function regardless of association

with AH or not. Central obesity is associated with an increase risk for cardio metabolic diseases such as atherosclerosis and diabetic nephropathy. Atherosclerosis is characterized by chronic inflammation affecting the arterial intima. Thus, individuals with type 2 diabetes and AH had increased risk for CVD.

### **Methylglyoxal-induced glycation changes hepatic lipid content in high-fat diet-fed rats, analyzed by lipidomic and magnetic resonance imaging approaches**

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**Objectives:** Fatty liver disease is a cause and a consequence of type 2 diabetes. Hepatic lipid metabolism (HLM) may be altered in obese patients, possibly causing insulin resistance. More, inhibition of insulin signaling affects HLM, causing a feedback that lead to hepatic steatosis, common in such patients. In this work, we intended to assess the role of glycation in the HLM of high-fat diet-fed rats, using lipidomic approaches and magnetic resonance spectroscopy, which identify hepatic lipid species, including triacylglycerols (TG), diacylglycerols (DAG) and fatty acids (FA).

**Methods:** Wistar rats were maintained during 4 months with methylglyoxal (MG) supplementation (MG group), a high-fat diet rich in TG (HFD group) or both (HFDMG group) and compared with controls feeding a standard diet (n=6/ group). Mass spectrometry and gas chromatography were used to determine liver composition in FA. <sup>1</sup>H nuclear magnetic resonance (NMR) spectroscopy (9 Tesla) of liver tissues in vivo was used to non-invasively determine TG and DAG. Levels of mediators of insulin receptor pathway were determined by western blotting.

**Results:** HFD group showed increased body weight in relation to controls, but this effect was partially inhibited by MG supplementation (HFDMG group). Moreover, HFDMG group showed increased plasma free FA levels, hyperinsulinemia and insulin resistance. Lipidomic techniques showed increased fat mass in the liver of HFD and HFDMG rats. HFD rats, but not HFDMG, showed increased total levels of the 18:1 FA. These data were consistent with NMR spectroscopy, where the HFD and HFDMG groups showed increased hepatic lipid levels. Only HFDMG rats showed decreased fraction of unsaturated lipids and increased fraction of saturated lipids; this difference was obtained due to a decrease in monounsaturated FA. More, HFDMG group showed lower percentage of esterified glycerol carbons, suggesting an increased concentration of DAG and lower concentration of TG. In accordance, this group showed higher FA/glycerol ratio, suggesting increased liver free FA levels. Western Blotting analyses showed decreased activation of Akt in all treated groups, especially in HFD and HFDMG groups, as well as decreased activation of the insulin receptor in HFDMG group.

**Conclusion:** Our data suggest that glycation changes lipid metabolism in a context of hyperlipidemia, possibly contributing to hepatic lipotoxicity and to accelerated progression of insulin resistance.

### **The effect of L-thyroxine treatment on mean platelet volume in patients with hypothyroidism**

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**Objectives:** Elevated mean platelet volume (MPV) is an independent risk factor for cardiovascular diseases. Hypothyroidism is often related with protrombotic condition and increased platelet activity. The aim of this study is to compare the mean platelet volume (MPV) in hypothyroidic patients before and after the levothyroxine treatment with healthy subjects.

**Methods:** 63 hypothyroidic and 34 healthy subjects were included in this single center prospective study. Patients with malignancy, thyroid surgery, over 65 years old, pregnant, coronary artery disease (CAD), chronic inflammatory disease, diabetes mellitus (DM), hypertension, and using antiaggregant and anticoagulants were excluded. Demographic data including age, gender, weight, body mass index (BMI), and blood pressure were recorded. In all patients and healthy subjects; serum free triiodothyronine (fT3), free thyroxine (fT4), thyroid-stimulating hormone (TSH), anti-thyroid peroxidase antibody (TPOab) levels were measured. Complete blood count (CBC), mean platelet volume (MPV) were analyzed (blood samples anticoagulated with EDTA). In hypothyroidic group, the thyroid hormone replacement was administered, and serum TSH concentrations were repeated within 6 and 8 weeks period. The levothyroxin dose was increased until the patient's TSH concentration reached normal reference ranges. MPV was compared between hypothyroidic group (before and after levothyroxin treatment) and control group.

**Results:** MPV was significantly increased in patients with hypothyroidism (8,3±1,5 fl) than control group (7,5±1 fl). When hypothyroidic group maintained euthyroid after levothyroxin treatment, a significant reduction was detected in MPV (p=0.031). However, in post-treatment group MPV were not significantly different from control group.

**Conclusions:** Based on our results, we suggest that hypothyroidism is associated with high MPV levels. Thyroid hormone replacement causing a decrease in MPV levels may be protective against cardiovascular diseases.

### **The importance of calcitonin measurement in thyroid nodules: a case of medullary thyroid cancer with benign fine needle aspiration biopsy but elevated serum calcitonin**

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**Introduction:** The prevalence of thyroid nodules detected by imaging methods is around 20-76%. When thyroid nodules are detected, echogenicity, presence of calcification, size of nodule and Doppler blood-flow patterns should be evaluated thoroughly with regards to malignancy potential and, if necessary, thyroid fine needle aspiration biopsy (FNAB) should be performed as well.

Additionally, if a nodule is detected in a patient for the first time, calcitonin level should be checked in order to confirm or rule out the medullary thyroid cancer (MTC). MTC is a rare cancer constituting 4 % of thyroid tumors and originates from calcitonin-secreting parafollicular C cells. About 75% of MTCs are sporadic while the remaining 25% of MTCs are hereditary. RET proto-oncogene is responsible for the genetic transition of the disease. Apart from calcitonin, there are no other blood parameters used for screening thyroid malignancies. Herein, we present a case of MTC with an initial FNAB reporting erroneously a benign lesion, which revealed to be malign as identified by a second biopsy obtained following the finding of an increased serum calcitonin concentration.

**Case report:** A 49 years old female patient was referred to endocrinology clinic due to an incidental thyroid nodule identified through an ultrasound (US). Thyroid US revealed a solitary hypoechoic nodule, measuring 4x2 cm in the right inferior lobe extending into the retrosternal region. Her thyroid function tests were normal. FNAB of the nodule was reported to be of benign cytology. Since this was her first examination, calcitonin levels were studied and revealed to be 28000 pg/ml (reference: 0-5 pg/ml). Repeat calcitonin, as well as CEA level confirmed these results and therefore FNAB was repeated and this time confirmed the prediagnosis of malignancy. RET gene mutation analysis was positive. Screening for hyperparathyroidism and pheochromocytoma showed no related abnormality. Given the fact that her calcitonin level was above 500, the patient was also screened for metastasis and computerized tomography revealed metastases within the mediastinum and lumbar spine. The patient was diagnosed with stage 4 MTC and total thyroidectomy followed by radiation therapy was scheduled.

**Discussion:** Herein, we aimed to emphasize the importance and necessity of the assessment of calcitonin levels, regardless of the size of the thyroid nodules or FNAB results, in patients with a high risk of developing MTC.

## The association between insulin resistance and magnesium among obese and non-obese hypertensive cases

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**Objectives:** Magnesium is a trace element, which has been proven to have a role in hypertension, endothelial dysfunction, insulin resistance, inflammation and atherosclerosis. In our study, we investigated whether obesity worsens hypertension-associated insulin resistance and whether magnesium plays a role in insulin resistance.

**Methods:** 40 essential hypertensive patients (16 male/24 female) and 20 healthy controls (10 male/10 female) were included in this study. Patients were divided into two groups according to their body mass index (BMI) (more or less than 25 kg/m<sup>2</sup>). Patients group was consisted of 20 hypertensive and obese patients and 20 hypertensive and non-obese patients. Insulin resistance (HOMA-IR), magnesium levels (mEq/L), fasting blood glucose (mg/dL) and BMI (kg/m<sup>2</sup>) of subjects were recorded and evaluated.

**Results:** There was no statistical significance in insulin resistance between control subjects and obese and non-obese patients (2.10±0.82, 2.42±1.51, 3.35±2.88, respectively; p > 0.05). But blood glucose levels were significantly higher in obese hypertensive patients than control subjects (92.2±9 versus 84.6±8.9; p=0.018). According to data obesity has an impact on blood glucose levels, but not on insulin resistance, in hypertensive patients (but none of them has diabetes). There was no statistical difference in urine and blood magnesium levels between obese and non-obese hypertensive patients (74.1±29.3 versus 79.7±23.7 and 2.07±0.36 versus 2.14±0.28; p=0.859 and p=0.950, respectively), and both groups have higher blood magnesium levels (p=0.0001) and lower urine magnesium levels than control subjects (p=0.0001).

**Conclusions:** Determining mechanisms of insulin resistance will present new approaches in diagnosis and treatments of both hypertensive and/or metabolic syndrome patients. Our study has shown that magnesium may have a role in pathogenesis of hypertension but it has not any effect on insulin resistance. Further studies are needed in this field.

## Pituitary apoplexy – a case report

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**Introduction:** Pituitary apoplexy is a relatively rare condition, with most series indicating an incidence between 2% and 7%. It is caused by infarction and/or hemorrhage of the pituitary gland, normally in association with a pituitary adenoma.

**Case report:** A 79 years old man was admitted to hospital with a new-onset headache, bitemporal and severe, associated to photophobia and episodes of vomiting. The patient denied visual disturbances, jaw claudication and other focal neurological symptoms. The patient was fully conscious, afebrile and hemodynamically stable. Fundus showed a well-defined optical disk and visible bilateral venous pulse. His erythrocyte sedimentation rate was high (84 mm/h) and serum sodium level was low (133 mmol/L). Normal brain CT scan. Given the clinical suspicion of giant cell arteritis, despite the need for cerebral venous thrombosis exclusion, the patient started prednisolone 40 mg per day, acetylsalicylic acid 100 mg per day and artery temporal biopsy was scheduled. MRI showed a slightly increased of the size of the pituitary gland and pituitary function tests indicated an ACTH, LH, prolactin and testosterone low. MRI directed to sella turcica showed an increase of the gland which was done at the expense of the adenohipophysis, with alterations compatible to pituitary apoplexy, but optic chiasmus was preserved. Temporal artery biopsy didn't find lesions compatible with giant cell arteritis. The patient stopped prednisolone and started hydrocortisone, with careful control of fluid and electrolyte balance and conservative nonsurgical management.

**Discussion:** Pituitary apoplexy is a rare, medical emergency. The precise mechanism that leads to pituitary apoplexy is poorly understood. The differential diagnosis is wide and the diagnosis of pituitary apoplexy should be considered in all patients presenting with acute severe headache with or without ophthalmic signs. MRI is the diagnostic imaging modality of choice.



## Non-insulinoma pancreatogenous hypoglycemia syndrome: a rare cause of hyperinsulinemic hypoglycemia

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**Introduction:** Spontaneous hypoglycemia in a non-diabetic patient is rare. It associates with increased morbimortality and a prompt evaluation is warranted when it is documented. The diagnosis is challenging and recommendations for its management are mainly based on clinical experience.

**Case report:** A 72 years old woman with a history of hearing loss was assisted in the emergency room after she was found unconscious in the early morning. Hypoglycemia was documented (39 mg/dL in a glucometer) and she recovered consciousness after glycemia normalization with i.v. hypertonic glucose administration. She had no history of alcohol or hypoglycemic drugs consumption. Physical examination was normal. Adrenal insufficiency and growth hormone deficiency were excluded. The 72-hour fast test was negative. Chest radiograph and abdominal ultrasound were normal. She was discharged to our outpatient clinic for further study. 10 days later, she presented again with hypoglycemic coma. Venous plasma glucose was 16mg/dL, with inappropriate high levels of insulin (38,3 microU/mL) and C-peptide (10,7 ng/mL), confirming endogenous hyperinsulinism. Anti-insulin antibodies were negative. The abdominal computed tomography (CT) showed a 10 mm hypercaptant area in the anterior portion of the pancreatic head suggestive of insulinoma. The patient underwent laparoscopic surgery but intraoperative inspection and ultrasonography detected no pancreatic lesions. The histologic analysis of a pancreatic sample was normal. A selective intraarterial calcium stimulation test was then performed. It was diffusely positive (>2 fold increase in hepatic vein insulin concentration after stimulation of superior mesenteric, gastroduodenal and splenic arteries), suggesting the diagnosis of non-insulinoma pancreatogenous hypoglycemia syndrome (NIPHS). The patient was treated initially with a low free carbohydrate diet and diazoxide 50 mg tid. Prednisolone 10 mg bid, verapamil 40 mg tid and acarbose 25mg tid were progressively added. Hypoglycemia recurred. She is currently on octreotide 30 mg/month.

**Discussion:** NIPHS is a rare cause of hypoglycemia, usually associated with diffuse pancreatic hyperproduction of insulin. Treatment options are based on case reports and largely unsuccessful.

## Primary aldosteronism secondary to adenoma of Conn

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**Introduction:** Primary hyperaldosteronism is an important cause of hypertension. Its real prevalence unknown, possible it's responsible for 5 to 15% of cases of hypertension. It characterized

by inappropriate production of aldosterone and should be considered in patients with hypertension and hypokalemia because their potential reversibility.

**Case report:** A 47 years old women, referred to department of Internal Medicine for hypertension for the last 6 years, treated with 3 antihypertensive drugs. The patient had no complaints. The most noteworthy aspect of the physical examination is blood pressure of 164/87 mmHg. Physical examination was unremarkable. Blood samples showed hypokalemia (2.9 mEq/L), high ratio aldosterone/renin. Abdominal computed tomography revealed a lesion measuring about 2.3x1.1 cm in the right suprarenal gland. Echocardiography revealed mild left ventricular hypertrophy. Saline test suppression was positive. She underwent right adrenalectomy under general anesthesia and the exophytic mass was resected. Patient tolerated the procedure well and made a good post operative recovery. Histopathology was consistent with adrenal adenoma. Her blood pressure became normal and her anti-hypertensive medications were gradually tapered. Potassium post-operative was normal.

**Discussion:** Primary hyperaldosteronism represents one of the few treatable causes of hypertension. High degree of suspicion and a systematic approach will achieve the diagnosis. The surgery in most cases allows the resolution of hypertension.

## Assessment of the relationship between function, autoimmunity and sonographic features of thyroid and neutrophil lymphocyte ratio in patients with Hashimoto thyroiditis

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**Objective:** The aim of this study is to evaluate the relations between neutrophil/lymphocyte ratio (NLR) (which is a sign of sub-clinical inflammation in patients with Hashimoto thyroid) and thyroid functions, autoimmunity and sonographical properties.

**Material and methods:** The study included 40 patients with HT diagnosis and 25 healthy voluntary. The neutrophil, lymphocyte, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid stimulant hormone (TSH), free-T4, free-T3, anti-thyroglobulin (Tg) and anti-thyroid peroxidase antibody (TPO) values were measured. NLR was calculated with neutrophil and lymphocyte values. Thyroid ultrasound was applied in order to evaluate the thyroid parenchyma heterogeneity, and thyroid dimensions were measured.

**Results:** The age averages of patient and control groups were similar. Significant difference was detected between groups in terms of TSH, anti TPO and anti Tg levels ( $p=0.04$ ,  $p<0.001$  and  $p<0.001$ , respectively). While CRP level was  $0.44\pm 0.31$  in the patient group, it was  $0.26\pm 0.1$  in control group and the difference was assumed to be significant. ( $p=0.003$ ). No significant difference between groups was detected in terms of ESR and NLR. Significant difference was detected between groups in terms of parenchyma heterogeneity, border irregularity, and pseudo-nodule existence. ( $p<0.001$ ,  $p=0.003$  and  $p=0.01$ ). Significant positive correlation was detected between NLR and CRP ( $r=0.31$ ,  $p=0.04$ ).

**Conclusions:** In this study where we research the importance of NLR for detecting inflammation in patients with hypothyroidism (HT), while a relation between HT and CRP was detected, no significant relation with NLR was detected. However the existence of positive correlation between CRP and NLR shows us that more prospective studies about this issue with more patients are required.

### **Utilization of continuous glucose sensors (“Professional CGM”) improves glycemic control in diabetic patients who use insulin pumps**

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**Objectives:** Although insulin delivery with pumps gives programmable insulin administration in basal and bolus fashion, thus mimicking physiological demands, optimal control still depends on measurement of blood glucose levels. A 3-day professional continuous glucose monitoring (CGM) with interstitial fluid glucose sensing can provide data which can be downloaded and retrospectively reviewed, and used for therapeutic purposes. We report our experience in an Academic Diabetes Unit with office use of minimally invasive CGM to improve glycemic control in patients treated with insulin pump therapy.

**Methods:** We reviewed all patients with diabetes on pump therapy who used the professional CGM at the Diabetes Unit over a 2.5-year period. The data was analyzed with respect to age, gender, type of diabetes, and effect on glucose control. 71 patients wore the 3-day Medtronic CGMS iPro (Medtronic Minimed, USA) and therapy changes were made based on retrospective review of downloaded data tracings.

**Results:** The mean age was 45 years with a range of 24-72, 33 had type 1 and 38 type 2 diabetes. CGM information was used to adjust basal and/or short-acting bolus insulin doses, confirm or uncover hypoglycemic episodes, change insulin-to-carbohydrate ratio and supplemental factor, and modify pump settings. The glycosylated hemoglobin (HbA<sub>1c</sub>) prior to CGM use was 7.5% while a 6-month after CGM the HbA<sub>1c</sub> fell to 6.8% (p=0.04). Severe hypoglycemic episodes were reduced from 3.1 per patient per year to 2.2.

**Conclusions:** The personal CGM can be a valuable tool that gives detailed information in assessing glucose trends in patients using continuous insulin delivery via pumps. In a setting where expertise is available, it can be used to adjust and fine-tune intensive insulin therapy, and as feedback for diabetes self-care behavior modification.

### **Early glycemic derangements in pre-diabetes, metabolic syndrome and polycystic ovarian syndrome: a case series**

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**Objective:** To describe a case series of symptomatic postprandial reactive hypoglycemia (PRH) as a component of glucose intolerance and the metabolic syndrome.

**Methods:** We undertook a detailed analysis of 8 patients who were referred for endocrine consultation because of hypoglycemic symptoms, self-reported hypoglycemia, or a long-standing label of ‘hypoglycemia’ from their primary physician. All were young females ranging in age from 26 to 40 years of age. History and clinical findings were indicative of either mild to moderate hypoglycemia by self-monitored blood glucose (between 50 to 70 mg/dL) or symptoms compatible with hypoglycemia, occurring in the post-prandial period – between 2 to 5 hours after a meal. Only one patient had a documented glucose less than 50 mg/dL, and none reported any episodes of severe hypoglycemia.

**Results:** A general pattern of attributing nonspecific symptoms to hypoglycemia was observed, with most patients exhibiting a low threshold for ‘treatment’ (blood glucose <90 mg/dL). 7 patients had either impaired fasting glucose or impaired glucose tolerance; 2 were diagnosed with type 2 diabetes; and 7 fulfilled the criteria for the diagnosis of the metabolic syndrome. Hypertension and dyslipidemia were present in 5 and 7 patients, respectively. 2 patients had a history of gestational diabetes mellitus (GDM), and one patient had a family history of GDM (mother). 6 patients had clinical features of the polycystic ovarian syndrome (PCOS).

**Conclusions:** Both postprandial hyperglycemia and hypoglycemia are the earliest metabolic defects in the pathway to glucose intolerance, type 2 diabetes, the metabolic syndrome, and PCOS. They are independent risk factors for cardiovascular disease. Insulin resistance and hyperinsulinemia may be at the basis of this constellation of pathophysiologic findings.

### **Ectopic intrathyroidic parathyroid adenoma causing hypercalcemia: localization and treatment**

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**Case report:** A 62 years old female was found to have hypercalcemia on routine evaluation. She complained of fatigue and constipation but denied abdominal pain or a history of fractures. Medical history was significant for hypertension, diabetes, hypothyroidism, CHF, COPD, and sleep apnea. In addition to prescription medications, she was taking vitamin D supplements, but no calcium or multivitamin tablets. On questioning, she reported two episodes of kidney stones 8 years ago for which she underwent lithotripsy. Her vital signs were normal. There was no neck mass, abdominal tenderness, or peripheral edema on physical examination. Labs showed increased calcium level of 11.1 mg/dL and elevated parathyroid hormone (PTH) of 105.7 pg/ml. A bone density (DEXA) revealed osteoporosis at the hip, with a T-score of -2.7. The patient was deemed a candidate for surgical treatment of primary hyperparathyroidism, and referred to ENT surgery. Neck/chest imaging localization with a sestamibi scan showed findings consistent with possible parathyroid lesion in the left anterior/upper mediastinal retrosternal region at the level of the mid aortic arch, confirmed by a 1.1x1.0x0.8 cm nodule in the upper anterior mediastinum left of midline. At surgery, the suspected adenoma couldn’t be reached via an initial attempt with a collar/neck incision. Therefore, a mediastinal exploration

was undertaken. No parathyroid tissue could be identified after 3 hours of dissection time and the procedure was changed to an open approach. Finally, a thymectomy was performed and the parathyroid adenoma was identified on frozen section within the thymus. The intraoperative PTH level declined to 15.9 pg/ml, thus indicating successful removal of the hyperparathyroid focus. The final pathology report confirmed the intrathymic parathyroid adenoma weighing 930 mg, surrounded by involuted thymic tissue.

**Discussion:** This case illustrates a rare, ectopic location of a hyperfunctioning parathyroid adenoma causing hypercalcemia and longstanding complications of hyperparathyroidism, including bone disease, osteoporosis, and nephrolithiasis. A concerted effort at preoperative localization pointed to a mediastinal source; however, even a protracted surgical intervention eventually necessitated complete thymectomy to identify the culprit tumor accompanied by a reassuring drop in intraoperative PTH. The ectopic location of intrathymic mediastinal adenoma is a rare cause of primary hyperparathyroidism which should be kept in mind by primary care physicians, endocrinologists, radiologists, and endocrine surgeons.

### A rare cause of febrile illness

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**Introduction:** The etiological diagnosis of a febrile illness (FI) is not established in 15-50% of cases. Subacute thyroiditis (TS) is a rare cause of FI. It is more common in women and its diagnosis is clinical. 96% have cervical pain, fever; asthenia and anorexia are also common. 50% of patients have hyperthyroidism, which reverses in 2-8 weeks.

**Case report:** Female, 51 years old, Caucasian, admitted in an Internal Medicine ward for a 3 weeks history of fever with chills that yielded to paracetamol, dry cough and a 4 kg loss. She denied contact with domestic animals, recent travel, contact with cattle or stagnant water, and consumption of unpasteurized products. On physical exam: T 37.5°C, sinus tachycardia, without meningeal signs or skin abnormalities. There were no adenomegaly and cardiopulmonary auscultation and abdomen observation were normal. Laboratory results: normal hemogram, C-reactive protein 7 mg/dL, erythrocyte sedimentation rate 120 mm/h. Renal function, ionogram, liver injury markers and chest X-ray in the normal range. During hospitalization the patient described one month history of intense anterior cervical pain. On physical examination: pain on palpation in the region of the isthmus of thyroid, without palpable nodules. FI Investigation: blood cultures, viral serology and autoimmunity negative. Chest, abdomen and pelvis computed tomography (CT) and echocardiography were normal. Thyroid function tests: hyperthyroidism (TSH <0,01 mU/L, FT4 2,47 ng/dL). Thyroid scintigraphy: subacute thyroiditis. Anti-TPO, TG and TRAb antibodies were negative. TS was admitted on hyperthyroid phase, and was initiated therapy with ibuprofen and propranolol with good response. The patient was discharged after 8 days and was euthyroid 2 weeks after discharge.

**Discussion:** This case report was typical of TS, but was not initially valorized. Anamnesis is crucial for the right diagnosis of a FI.

### Plasma and urinary metal levels in metabolic syndrome

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**Objective:** We evaluated metals zinc (Zn), copper (Cu) and magnesium (Mg) levels in plasma and 24-hour urine and the relationships between these metals and metabolic syndrome (MS).

**Material and methods:** 30 patients with MS that diagnosed according to NCEP ATP III diagnostic criteria and 20 healthy controls were studied. Zn, Cu and Mg levels in fasting plasma and 24-hour urine were evaluated in all patients.

**Results:** 42 of patients were females (84%) and 8 of patients were males (16%). Plasma Zn level were significantly lower in MS when compared with control group (respectively plasma Zn 96.3±23.2 mg/dl and 115.3±25.2 mg/dl, p=0.012). Zn excretion in 24-hour urine in MS group were significantly higher than control group (respectively urinary Zn 1.32±0.87 µg/dl and 0.73±0.46 µg/dl, p=0.016). When the results were corrected according to patients age, the differences between MS group and control group were still significant (p=0.007). Hypozincemia and hyperzincuria were not significantly correlated with metabolic syndrome's components (p>0.05). There was no significantly difference between MS group and control group as regards Mg and Cu.

**Conclusions:** Zn plays role in insulin sensitivity and activity. Zn levels and insulin sensitivity correlation in diabetic patients were reported. Lower plasma levels and higher urinary excretion of Zn in patients with MS may play role in insulin resistance in these patients. Orally Zn treatment may prevent for insulin resistance in MS but there is need for several studies to show the effectiveness of this treatment.

### Is there vitamin D deficiency in a sunny country?

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**Objectives:** There is an increasing interest in Vitamin D functions and its benefits. Despite augmented levels with sun exposure, new cases of deficiency have been reported in sunny regions where optimal levels are expected. The aim of this study was to analyze 25-hydroxvitamin D levels in patients in a medicine ward.

**Methods:** This was a 6 month prospective and observational study, conducted in a medicine ward, where 25-hydroxvitamin D levels were analyzed and described as insufficiency (25-75 nmol/L) and deficiency (<25 nmol/L).

**Results:** A total of 42 adults were included, with a median age of 79,4 years and the majority was female (n=27). All patients had vitamin D levels below 75 nmol/L (n=42; 100%) and 9 had deficiency (21,4%) with 4 of them with undetectable levels (<20 nmol/L). The average vitamin D level was 37,7 nmol/L. Only 4 patients (9,5%) were previously on vitamin D supplementation.

**Conclusions:** In a Portuguese medical ward, all the patients tested had at least vitamin D insufficiency. These results emphasize the importance of vitamin D measurements and supplementation even in a sunny Mediterranean region.

## Diastolic function of left ventricle at patients with diabetes 2 types with the accompanying arterial hypertension

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**Objective:** To estimate the dependence of diastolic dysfunction at patients with Type 2 diabetes mellitus (DM) on compensation of carbohydrate exchange and existence of the arterial hypertension (AH).

**Material and methods:** 55 patients with type 2 DM (middle age  $47.2 \pm 4.0$ ) were examined. The average duration of DM was  $7.0 \pm 1.2$  years. To all patients the level HbA<sub>1c</sub> and echocardiography was carried out. Systolic dysfunction of the left ventricle (LV) was diagnosed at the level of ejection fraction (EF) less than 50%. Existence of diastolic dysfunction was defined according to standards, of the working group of the European Society of Cardiology.

**Results:** Among the examined patients 37 (67.2%) had arterial hypertension and 47 patients (85.4%) had elevated levels of HbA<sub>1c</sub> ( $7.8 \pm 1.5$  %), that indicates on decompensated DM. Among the patients with increased HbA<sub>1c</sub> level 32 patients (61.8%) had arterial hypertension. Systolic dysfunction in all of the examined patients was not diagnosed (EF  $59.9 \pm 5.0$ %). Diastolic dysfunction was observed at 29 (52.7%) patients with DM. The impaired diastolic function was most often observed at patients with type 2DM and the accompanying AH (56.7%) in comparison with patients without hypertension and also patients with decompensated DM (55.3 %). Heavier violation of diastolic function was connected with AH as its existence at the decompensated patients in comparison with the same group without hypertension led to duplication of pseudo-normal type of diastolic dysfunction (29,4% and 14,2%). It confirms that decompensation of DM in patients with hypertension leads to remodeling of LV (21.8%) affected by the expense of concentric (14,2%) and eccentric (14,2%) types of LV hypertrophy.

**Conclusions:** The impaired diastolic function meets almost at a half of patients with Type 2 DM. Arterial hypertension, especially at patients with elevated HbA<sub>1c</sub>, leads to increasing of LV dysfunction due to reduction of diastolic tensile properties of the camera and to more frequent onset of pseudonormal type of LV filling.

## The neutrophil-to-lymphocyte ratio is higher in type 2 diabetic patients with cerebrovascular disease

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**Objectives:** Cerebrovascular disease (CVD) is a frequent event among diabetic patients, and the neutrophil-to-lymphocyte ratio

(NLR) has recently emerged among inflammatory parameters as a potential indicator of vascular complications and poorer outcome in patients with diabetes. This study aimed to evaluate the association of CVD and NLR in type 2 diabetic patients, during last decade.

**Methods:** We select type 2 diabetic patients from our outpatient clinic from 2005 to 2014 with 20901 visits in this decade. Patients with type 1 and secondary diabetes were excluded. The main outcomes of diabetic management were selected. We calculated the mean values for each patient for BMI, blood pressure, lipid profile, renal function, systemic inflammatory markers (as CRP, monocyte %, white blood cell count). Comorbidities and drug treatments were also recorded. Documented CVD was defined as at least one hospital admission for a CV event. Descriptive statistical methods were applied. Results are presented as median and STD error. T-test and Pearson's correlations were used for continuous variables and the chi-square for categorical ones.

**Results:** Were included 2551 consecutive patients, with a median of follow up period of  $6 \pm 1.6$  years with a median of  $6 \pm 1$  visits and per a patient. They were  $66.3 \pm 18$  years old at the first observation and 980 were men. We found (n=257) patients with CVD who had a significant higher NLR than the others (2.3 vs 1.9;  $p=0.002$ ). These patients with CVD had also statistically significant associations with other inflammatory markers as monocytes % ( $p=0.008$ ), white blood cell count ( $p=0.001$ ), CRP ( $p=0.042$ ), diastolic blood pressure ( $p<0.001$ ), creatinine ( $p<0.001$ ), uric acid ( $p<0.001$ ), albuminuria ( $p<0.001$ ), HDL ( $p<0.002$ ), and total cholesterol ( $p<0.015$ ). The median age ( $70.0$  vs  $64.7$ ) was also significantly different ( $p<0.001$ ).

**Conclusions:** NLR is increased among diabetic patients with CVD. This study presents the results achieved in a hospital diabetic clinic in Portugal to control CV risk factors in diabetic patients. Age, average levels of inflammatory markers, blood pressure and lipid profile during a decade were also higher in our patients with CVD, but other study design would be required to evaluate the underlying pathophysiological mechanisms behind our findings.

## The fatty liver index: exploring hepatic steatosis in type 2 diabetic patients

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**Objectives:** Fatty liver (FL) is a frequent disease in obesity and in patients with cardiometabolic risk. We used data from the outpatient clinic of our department using a simple algorithm for the prediction of FL in the general population.

**Methods:** 127 type 2 diabetic consecutive patients with or without suspected liver disease were studied in the diabetic clinic. FL index was calculated and potential predictors of FL [gender, age, ethanol intake, alanine transaminase, aspartate transaminase, gamma-glutamyl transferase (GGT), body mass index (BMI), waist circumference, glucose, triglycerides, and cholesterol]. Blood pressure and comorbidities were also

recorded. We explored the distribution of the FL according to the presence of diabetes and the presence of comorbidities. As published elsewhere "fatty liver index" (FLI) <30 was considered negative and a FLI ≥60 was considered positive for fatty liver. Patients with ethanol consumption, type 1 and secondary diabetes were excluded.

**Results:** The median age of the patients was 55.5 years old; diabetes duration 8.8 years and 12.7% were male. As the algorithm is based on BMI, waist circumference, triglycerides and GGT and as expected these variables correlated strongly with FLI. The same is true for HDL-C, CRP, waist/height ratio ( $p < 0.01$ ). Despite the small number of cases ( $n=6$ ), patients with past cerebrovascular events had a significant higher FLI than the others (92.3 vs 70.3),  $p > 0.001$ .

**Conclusions:** FLI is simple to obtain and may help physicians select subjects for liver ultrasonography and intensified lifestyle counseling, and researchers to select patients for epidemiologic studies. Other cross-sectional study suggests that subjects with FLI >60 are at higher risk of atherosclerotic lesions, and our finding goes in the same direction, associating fatty liver and the presence of cerebrovascular disease.

## The results of the treatment and follow up in patients with diabetic foot ulcer receiving treatment with wound care products

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**Objectives:** In recently, a number of new methods, applications, devices, and equipment have been introduced into use for wound care. Herein, we present our results with a total of 90 patients with diabetic foot ulcers (DFUs) who received treatment with such novel treatment modalities.

**Methods:** A total of 90 patients treated and followed-up at DFU outpatient unit between December 2012 and March 2014 were included in this study. Patients with osteomyelitis or hemodynamic instability were excluded.

**Results:** The mean age was  $61.8 \pm 10.2$  years, and the duration of diabetes was  $\leq 5$  years in 25%, and  $\geq 6$  years in 75% of the cases. Nearly 40% of the cases had a previous history of wound in the feet. Of the study subjects, 42.2% reported that the foot ulcer developed within a period of 3 weeks, while 57.8% noted that the ulcer developed within a period of 4 weeks or longer. No clear explanation could be made by 26% of the patients for the mechanism(s), through which the ulcer developed. However, 25% reported that the most common cause for the development of the wound was burns. According to PEDIS classification (perfusion, extent/size, depth/tissue loss infection and sensation) 20%, 45.6%, and 34.4% of the DFUs were stage 1, 2 or 3 lesions, respectively. The tissue perfusion was stage 2 or 3 in 55% of the patients, and 92% reported sensory loss. While 64.5% of the patients received with a single supportive wound care product in addition to the standard wound care, 35.5% received treatment with such products on more than one occasion during the course of their wound care. The products that have been used most commonly were, in the decreasing

order of frequency, collagen containing wound powder (38.9%), wound dressing products with antimicrobial silver (22.6%), autolytic debridement dressings containing sodium alginate and hyaff (18.9%), products with growth factors (13.1%), and pets providing hyaluronic acid (6.5%). Of the patients 42% were admitted for treatment and received IV antibiotics. Surgical debridement was performed in 85%, hyperbaric oxygen was given in 23%, and 4.4% received revascularization. The average duration of treatment was 10 weeks. In 85.6% of the cases the wound was healed at the completion of treatment, 10% required amputation, and 4.4% discontinued the treatment prematurely. At the end of the 12 months of follow-up, 66 patients could be contacted. At that time, the wound healing rate declined to 68%, 10.6% have persistent wound lesion, 7.6% had new lesion at another site, while 13.6% died due to major cardiovascular events. In only patients with DFU duration between 0 and 3 weeks, the rate of persistence of wound healing was significantly higher ( $p < 0.001$ ) than the occurrence of other conditions (persistence of the wound, wound development at another site, death).

**Conclusions:** A total of 90 patients with DFU received treatment with supportive wound care products. In 66 patients, success rate exceeding 65% could be obtained. A shorter DFU was associated with improved morbidity and mortality.

## A case with diabetic ketoacidosis and salicylate intoxication

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**Introduction:** Salicylate intoxication (SI) is mostly seen with acetylsalicylic acid (ASA). The doses over 100 mg/dl causes severe poisoning. Salicylates lead to respiratory alkalosis (RA) by stimulating the respiratory center. They increase the excretion of bicarbonates, sodium and potassium from the kidneys which provokes dehydration and metabolic acidosis (MA) with wide anion gap. We present the association of diabetic ketoacidosis (DKA) and SI as a result of taking ASA overdose as suicidal behavior of a case with type 1 diabetes mellitus (T1DM).

**Case report:** A 24 year-old woman with a known history of T1DM for 9 years was admitted to the ER with complaints of nausea, vomiting and abdominal pain. On admission: GCS was recorded as 13; in addition to exhibiting Kussmaul breathing. She had dehydration, hypotension and tachycardia. Laboratory tests revealed increased blood glucose level to 376 mg/dl, hypokalemia, hyperchloremia and ketonuria. In the arterial blood gas, MA and RA were detected (pH 7.17, PCO<sub>2</sub> 23 mmHg, HCO<sub>3</sub> 8.1 mmol/l, BE -14.2 mmol/l and lactate 7 mmol/l). The relatives of the patient stated that she took 25-30 tablets of 325 mg ASA with enteric coating. Blood ASA level was requested to be measured and 1-2 g/kg activated charcoal was given to the patient. Upon recording the blood ASA level as 48.8 mg/dl (normally: 15-30 mg/dl), the patient was taken to the intensive care unit (ICU). Over the next 24 hours she was treated with a normal maintenance fluid rate (0.45% saline, 5% dextrose) and IV insulin (0.1 U/kg/h). However, the glycemia regulation

of the patient could hardly be controlled due to hypoglycemia attacks she experienced over and over again. The MA and RA conditions of the patient, who has urine pH of 5.5 and ketonuria, were remained almost the same (pH 7.29, PCO<sub>2</sub> 28 mmHg, HCO<sub>3</sub> 13 mmol/l, BE -12 mmol/l and lactate: 4 mmol/l), thus 240 mEq/24h HCO<sub>3</sub> was given to the patient for urine alkalization. Additionally, IV K<sup>+</sup> infusion therapy was continued. The laboratory values were improved. Salicylate level of the patient decreased to 8 mg/dl during the monitoring. She was transferred from ICU to the ward. After regulating her blood sugar, the patient was discharged from the hospital.

**Discussion:** DKA and SI are two urgent internal medicine cases which are very similar in clinical and biochemical properties. The management of the case should be handled according to the findings from the laboratory and integrated treatments for both cases.

## Mean platelet volume changes before and after the HbA<sub>1c</sub> improvement on a large study population

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**Objectives:** Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia associated with both microvascular and macrovascular complications. Mean platelet volume (MPV) is a marker of platelet activity which plays a major role in the development of vascular complications of DM. Although there are many studies about the comparison of MPV between diabetics and non-diabetic controls, there are few studies with small study populations comparing the MPV levels before and after the treatment. The aim of this study is to compare the MPV levels before and after the decrease of HbA<sub>1c</sub> levels on a large diabetic population.

**Methods:** This was a retrospective study conducted on type 2 diabetic patients from the outpatient clinic for one year between 2014 and 2015. Among 10038 participations of diabetic patients 595 patients recruited to the study. The main inclusion criteria of recruitment were, to be examined in outpatient clinics at least two times a year with full laboratory parameters as HbA<sub>1c</sub> with whole blood count and having a decrease of HbA<sub>1c</sub> at least 0,5% during these treatment period.

**Results:** When we compared the basal and post-treatment values, a significant decrease of MPV and HbA<sub>1c</sub> levels were revealed (HbA<sub>1c</sub>: 9.41±1.98 vs 7.43±1.29, p<0.001; MPV: 9.11±1.42 vs 8.17±1.04, p<0.001). There was also a positive correlation between the mean changes of MPV and HbA<sub>1c</sub> levels after the treatment ( $\Delta$ MPV: 0.93±0.96 vs  $\Delta$ HbA<sub>1c</sub>: 1.96±1.43; p=0.005, r=0.115). The participants also were divided into two groups according to their basal HbA<sub>1c</sub> levels (group A: HbA<sub>1c</sub> ≤6.5 and group B: HbA<sub>1c</sub> >6.5). We compared each group before and after the improvement of glucose levels. It was obviously seen that further decrease of HbA<sub>1c</sub>, in group A still provide a significant decrease of MPV levels. (Group A: MPV basal vs post treatment: 8.73±1.40 vs 7.86±0.91, p<0.001 and Group B: MPV basal vs

post treatment: 9.12±1.42 vs 8.18±1.04, p<0.001). There were also significant differences of MPV among OAD and insulin using patients before and after glycemc improvement (p<0.001 for both groups).

**Conclusions:** Our study revealed that improved glycemc control reduces platelet activity and even further decrease of HbA<sub>1c</sub> below 6.5% may still provide a decrease of platelet activity. Regardless of treatment modalities both insulin and oral antidiabetic agents can provide a decrease of MPV values together with glycemc control.

## Dysautonomia in autoimmune thyroiditis – case report

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**Introduction:** Thyroid disorders are common endocrine conditions in clinical practice. Thyrotoxicosis falls into three etiologic categories: abnormal stimulation of the thyroid gland, gland autonomy and gland inflammation with unregulated thyroid hormone release. Cardiovascular changes may be attributed to hyperthyroidism: morphologic cardiac changes, exercise intolerance, arrhythmias and sympathovagal imbalance. Postural orthostatic tachycardia syndrome (POTS) is one of the most common presentations of orthostatic intolerance. Symptoms consist of persistent orthostatic tachycardia, heart rate increase at least 30 beats/min, lasting at least 10 minutes of standing or head-up tilt in the absence of orthostatic hypotension. POTS manifests with symptoms of cerebral hypoperfusion and excessive sympathoexcitation. Management of POTS includes avoidance of precipitating factors, volume expansion, exercise training, pharmacotherapy and behavioral-cognitive therapy.

**Case report:** A 32 years old woman with Brooke-Fordyce disease was admitted to the hospital because of a syncopal event. Such episodes began 8 years ago and she was followed by her general practitioner. She had no palpitations, orthopnea or paroxysmal nocturnal dyspnea. She had no domiciliary medication. On examination, afebrile, blood pressure 110/70 mmHg, pulse 110 beats/min, regular, respiratory rate 16 breaths/min, and 100% oxygen saturation (ambient air). Heart sounds were normal with no murmur. Blood levels of electrolytes were normal, as well as other test results. The electrocardiogram showed sinus tachycardia, and the chest radiograph was normal. The patient was discharged for internal medicine consultation for future research. Analytically, the patient showed up euthyroid status with thyroglobulin autoantibodies and anti-peroxidase positive (25.6 and 145 respectively); anti-TSH receptor antibody negative. Thyroid scintigraphy with technetium showed an increased index, multinodular goiter and autoimmune thyroiditis in hyperfunctional phase. The ambulatory blood pressure monitoring -without global hypertensive profile. On Holter – sinus rhythm throughout all recording. Tilt test showed postural orthostatic tachycardia syndrome. The patient was treated with 50 mg propylol three times a day and bisoprolol 2,5 mg per day.

**Discussion:** Autoimmune thyroiditis patients have a smaller vagal reserve and a worst vagal modulation after a sympathetic stimulus. These kinds of patient have a functional cardiovascular sympathovagal imbalance.

## Pancreas glucagonoma: case report

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**Introduction:** Glucagonoma is a neuroendocrine tumor from the pancreatic  $\alpha$ -cells, which present 8-13% of all neuroendocrine tumors (NET). This is a functional tumor with malignant growth in 50% of cases, characterized by common clinical symptoms – glucagonoma syndrome, which includes necrolytic erythema migrans with the secondary bullous dermatitis, glucose intolerance and diabetes, weight loss, anemia, thrombophilia, digestive disorders and mental disturbances. Diagnosis could be confirmed by the determination of glucagon level in blood plasma.

**Case report:** Female of 56 years old suffered from type 2 diabetes since 1996. 4 years ago the patient presented with pancreatic tumor at stage 4. She underwent 6 courses of chemotherapy. Over the next 5 years neoplastic proliferation did not revealed. Patient condition on admission to hospital was moderate. Patient is undernourished. The skin is pale with signs of hyperpigmentation and desquamation. Skin on femor and forearm has red-cinnamon erythematous rash with the superficial necrolytic patch. The tongue is dry and raspberry color. The abdomen is soft and moderately painful on palpation. In the upper-left abdomen quadrant there is a palpable restrictedly movable painless compact formation with the torous surface 10x15 cm in size. Complete blood count: Hb 93 g/L, RBC 3,3x10<sup>12</sup>/L, ESR 45 mm/h. Blood biochemistry: glucose 10,7 mmol/L, other blood values were normal. Glucose profile: 6,7-8,0-4,8 mmol/L. CA 15-3 19,6 U/ml, AFP 3,83 ng/ml, CA 125 8,93 U/ml. CT and MRI findings: in the upper left abdomen there is a homogeneous mass consisted of diffusively thickened stomach, duodenum and jejunum walls, pushing aside lien and pancreas. Pancreas is forced greatly forward; the tail and body of pancreas are increased in size. Pancreas architectonics has heterogeneous pattern. Wirsung duct is uniformly dilated at the level of pancreas body. Multiple enlarged lymphatic nodes form conglomerates in porta hepatic, jejunal loops and near aorta. So, the patient underwent laparotomy, and the subtotal cytoreductive tumor resection was performed. Histopathological examination: tumor in fibrous capsule composed of monomorphic hyperchromatic cells forming alveoli and solid fields. Mitoses are rare; cytoplasm is scanty and low basophilic, hyalinosis of stroma. Reaction with SMA in tumor is negative. Reaction with insulin is negative. Reaction with glucagon, chromogranin A, synaptophysin, S-100, NSE – is positive in tumor cells: neuroendocrine carcinoma, malignant glucagonoma. The patient received sandostatin 150  $\mu$ g tid. Patient's condition has improved. Skin rash did not relapse. Appetite has improved and vomiting stopped. Body weight gains amount of 8 kg. Over the 7 years after the surgery continued tumor growth was diagnosed. Antineoplastic systemic drugs (5-fluorouracil, platins) did not provide a long-term effect. Post mortem examination revealed poorly differentiated endocrine pancreas carcinoma with multiple distant metastases.

**Discussion:** Glucagonoma has a slow growth; median survival is about 15 years. Cytoreductive surgical treatment and the use

of somatostatin analogues allow to maintain patient quality of life for a long period of time.

## Hypomagnesaemia and glycemic control in diabetes – the reality in a Portuguese hospital

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**Objectives:** Diabetes mellitus (DM) is a chronic disease in expansion worldwide with a significant impact in health quality and life expectancy and consequently in health systems. Portugal is amongst the European countries with the highest prevalence of DM with approximately 13% of adult population being affected and an estimate of 44% undiagnosed patients, representing a strong impact in the health of Portuguese population. It is therefore important to analyze the multiples aspects that can contribute to a better assessment of the disease and improve patient's outcome. It has been shown that magnesium has a key role in the glycemic metabolism and insulin homeostasis, and several studies have demonstrated an inverse relation between hyperglycemia and the serum level of magnesium, which could be used as a prognostic factor in diabetic patients. In this study the authors analyzed the prevalence of hypomagnesaemia in the diabetic patients admitted at Hospital Vila Franca de Xira, and its relation with glycemic control.

**Methods:** A transversal observation study was performed by measuring glycated hemoglobin (HbA<sub>1c</sub>) and serum magnesium (MgS) levels in ward admitted patients on the 16th of April 2015. Statistical analysis was conducted using SPSS 20®.

**Results:** HbA<sub>1c</sub> and MgS where measured in 92 patients, of which 34 were diabetic and therefore included in this study. The majority of patients was admitted in medical wards, aged between 70 and 89 years old, with no gender predomination. The mean HbA<sub>1c</sub> was 7 $\pm$ 2.04% and 24% of patients had poor glycemic control (HbA<sub>c</sub>  $\geq$ 7.5%). The mean MgS level was 1.9 $\pm$ 0.43 mg/dL and 33% of the analyzed individuals had hypomagnesaemia. 24% of patients with hypomagnesaemia had inadequate metabolic control.

**Conclusions:** In this study the incidence of hypomagnesaemia in patients with DM was coincident with the numbers in current literature. However a statistically significant relation between hypomagnesaemia and glycemic control was not verified, possibly limited by the sample size, but it may also indicate a more complex relation between these factors than the one described so far, and it is important to continue to investigate.

## Incidence and clinical presentation of gastroenteropancreatic neuroendocrine tumors in Northern Spain

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**Objectives:** The main objective was to estimate the incidence of the gastroenteropancreatic neuroendocrine tumors (GEP-

NETs) during a 5 years period. The secondary objective was to describe the clinical presentation of GEP-NETs in clinical practice.

**Methods:** We developed a retrospective epidemiological study in a hospital in Northern Spain (Hospital de Cabueñes, Gijón) between January 2009 and December 2013. Patients were collected from an electronic database. All patients with immunohistological confirmation of GEP-NET were included.

**Results:** We identified 39 patients with GEP-NETs, 22 (56%) men and 17 (44%) women, mean age 63 years (SD 11, range 28-78). The incidence was gradually increased over time, from 5/100.000/year in 2009 to 12/100.000/year 2013, with an average of 7.8/100.000/year. The small intestine was the primary tumor site (26%), mainly terminal ileum, followed by pancreas (21%). Other locations were gut (13%), colon (13%), rectum (10%) and appendix (10%). In 7% of cases the primary tumor site was unknown. Only in 3 patients (8%) the tumor was functioning. Surgery was the procedure with the highest yield of tumor detection (54%) followed by FNAC (38%). Incidental autopsy diagnosis occurred in 3 cases (8%). The histological grade (WHO classification 2010) was G1: 48.3%, G2: 20.7% and G3: 31.1%. At diagnosis, 33% of patients had distant metastases, 92% of which were in the liver. Tumor was symptomatic in 54% of patients and the most common symptoms were abdominal pain (62%) and diarrhea (29%). Intestinal obstruction was seen in 4 patients (19%). Chromogranin A was done in 72% of patients (mean value 1274 ng/ml) and 5-hydroxyindole acetic acid in 23%. Octreoscan was performed in 33% of patients and 62% of them were positive. About 64% patients underwent surgery (most of them with curative intent), 15% received somatostatin analogues, 18% chemotherapy and 13% combined treatment. At the last follow-up, 41% of patients were free of disease, 10% were in progression, 2% were stable and 38% have died.

**Conclusions:** GEP-NETs are an emerging entity with a wide clinical behavior. The number of detected GEP-NETs increased about 2-fold between 2009 and 2013 reaching an incidence of 12/100.000 inhabitants/year. In most cases are non-functioning forms originated in the small intestine and pancreas. The diagnosis in advanced stages is common.

## Intraabdominal fat deposition and development of comorbidity in metabolic syndrome

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**Objective:** To investigate the influence of intraabdominal fat deposition on comorbidity development in metabolic syndrome (MS).

**Material and methods:** 200 patients with MS were investigated: 106 women and 94 men, average age  $61,9 \pm 1,2$  years. Examination of patients includes antropometric, laboratory and instrumental investigations. Intraabdominal fat thickness (IAFT) was measured during ultrasound investigation of abdominal cavity. Statistical analyses were carried out using Statistica 6.0.

**Results:** IAFT was  $55,5 \pm 2$  mm (from 21 to 110 mm). IAFT correlates with male gender regardless of carbohydrate

metabolism disorders ( $r=0,23$ ;  $p=0,0013$ ), presence of diabetes mellitus type 2 ( $r=0,19$ ;  $p=0,007$ ) and generally with carbohydrate metabolism disorders ( $r=0,2$ ;  $p=0,006$ ), body mass index ( $r=0,39$ ;  $p=0,000001$ ), waist circumference ( $r=0,56$ ;  $p=0,000001$ ), uric acid level ( $r=0,56$ ;  $p=0,0008$ ), HDL level ( $r=-0,17$ ;  $p=0,02$ ) and fasting glucose level ( $r=0,25$ ;  $p=0,0006$ ). IAFT demonstrates correlations with the oblique-vertical liver size ( $r=0,22$ ;  $p=0,002$ ), transverse size of the gallbladder ( $r=0,3$ ;  $p=0,0002$ ), gallbladder wall thickness ( $r=0,25$ ;  $p=0,002$ ), pancreas head size ( $r=0,34$ ;  $p=0,000013$ ). IAFT correlates with end-diastolic and end-systolic sizes of left ventricle ( $r=0,26$ ;  $p=0,0007$  and  $r=0,25$ ;  $p=0,001$  respectively), thickness of left ventricle posterior wall ( $r=0,22$ ;  $p=0,004$ ). Respiratory problem in MS also depends on IAFT: negative correlation with SpO2 level ( $r=-0,56$ ;  $p=0,0006$ ); VC ( $r=-0,47$ ;  $p=0,004$ ), FVC ( $r=-0,49$ ;  $p=0,002$ ), FEV1 ( $r=-0,49$ ;  $p=0,001$ ), FEF25% ( $r=-0,35$ ;  $p=0,03$ ), FEF50% ( $r=-0,35$ ;  $p=0,003$ ), FEF75% ( $r=-0,54$ ;  $p=0,0004$ ), even in the absence of pulmonary diseases. In addition IAFT was associated with aspartate aminotransferase and alanine aminotransferase levels in men ( $r=0,28$ ;  $p=0,01$  and  $r=0,23$ ;  $p=0,04$  respectively); in women IAFT correlation with spirometric parameters stronger than in men.

**Conclusions:** Prominent IAFT was associated with development of carbohydrate metabolism disorders, hyperuricemia, liver and pancreatic steatosis, chronic cholecystitis, left ventricle dilatation, restrictive and obstructive respiratory disorders. Early diagnostics of all types of comorbidity is required in MS.

## Cushing's syndrome due to ectopic ACTH production by a mediastinal paraganglioma

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**Introduction:** Cushing's syndrome due to ectopic ACTH production by a mediastinal paraganglioma. Ectopic secretion of ACTH is an infrequent cause of Cushing's syndrome. Ectopic Cushing's syndrome is usually caused by small cell carcinomas of the lung, carcinoid tumors, pancreatic islet cell tumors, medullary thyroid carcinomas and rarely paragangliomas. Mediastinal paragangliomas are rare, highly vascularized tumors arising from chromaffin tissue located in the para-aortic ganglia. Tumors tend to invade bordering structures and may also form metastasis. Up to 50% of patients are asymptomatic and diagnosis is incidental. Ectopic ACTH production is an uncommon manifestation of this uncommon disease. Complete surgical resection remains the standard of care due to malignant potential of the tumor and poor response to chemotherapy or radiation.

**Case report:** A 48 years old woman with previous history of hard to control diabetes mellitus type 2. She was admitted in the Internal Medicine service with clinical features of Cushing's syndrome, serious hypokalemia, hypertension and metabolic alkalosis. Octreoscan revealed a mediastinal tumor with somatostatin's receptors. Endocrinological investigation confirmed the diagnosis of ectopic ACTH production. Thoracic tomography scan image showed a 25 mm anterior mediastinal mass, and two cavitory lesions: a 13 mm lesion in the left superior lobe and another



9 mm lesion in the right medial lobe. Percutaneous needle aspiration from the left pulmonary lesion was performed, informed as a granulomatous negative in the Mantoux test, but positive Citomegalovirus and Aspergillus serologies those were studied and treated. Resection of the mediastinal tumor and the left pulmonary lesion normalized ACTH and cortisol secretion. The tumor was found to be a paraganglioma through microscopic analysis and immunohistochemical staining methods defined a neuroendocrine benign tumor. In the lung tissue was observed cytoplasmic inclusions of Citomegalovirus and hipas compatible with Aspergillus spp. This patient is waiting for genetic testing SDH and Oncogen-ret which has been requested. On follow-up 6 months later the patient showed nearly complete clinical recovery without mediastinal or pulmonary imageological findings.

**Discussion:** Ectopic ACTH production is an uncommon heterogeneous condition not often caused by paragangliomas those are rare too, being diagnosed incidentally as a differential diagnosis of a middle mediastinal mass.

### Ultrasonography-guided fine-needle aspiration biopsies of thyroid nodules: single center experience

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**Objectives:** Thyroid nodules (TN), the incidence of which is quite high, constitute a diagnostic challenge. Thyroid fine-needle aspiration biopsy (TFNAB) which is performed depending on the results of the other diagnostic methods is the most reliable method for the diagnosis of TN. In this study, we aimed to investigate the efficiency of ultrasound-guided TFNAB (US-TFNAB) in our clinic.

**Methods:** 701 patients with TN were included in the study during 2000-2011. US-TFNAB was performed at interventional radiology department. Initially, thyroid US was performed. The biggest diameter was determined measuring 3 dimensions of nodule. If multiple nodules were found, TFNAB was performed from the biggest one.

**Results:** The result of US-TFNAB was insufficient in 11.7% of patients. US-TFNAB was reported as benign in 79.3% of patients, suspected malignant (SM) in 4%, malignant in 3.9% and suspected follicular neoplasm (SFN) in 1.1%. When SFN and SM cases were included into malignant group, the malignancy ratio based on US-TFNAB was 9% (n=63). 146 cases were operated (20.8%), 19 (2.7%) – didn't accept the surgery. According to histopathology results of operated patients, 66 patient were malignant (9.4%) and 80 – benign (11.4%). 28.7% of 66 malignant cases were papillary microcarcinoma, 46.9% were papillary carcinoma, 15.2% were papillary Ca follicular variant, 3% were follicular carcinoma, 3% were Hurthle cell carcinoma and 3% were medullary carcinoma. No significant gender difference was determined for benign or malignant histopathology results ( $p > 0.05$ ). When US-TFNAB cytology results and surgical histopathology results were examined, of 9 patients with insufficient US-TFNAB result,

the histopathology result was benign in 6 (66.6%) and malignant in 3 (33.3%). Of 8 cases who classified into SFN, histopathology result was benign in 7 (87.5%) and malignant in 1 (12.5%). There were 23 malignant and 5 benign cases in a group consisted of patients with SM (suspected malignancy + suspected papillary carcinoma) according to histopathology. When all groups were separately analyzed, histopathology result was malignant in 11 of 15 cases whose cytology result was SM (73.3%). Also, histopathology result was malignant in 12 of 13 cases with suspected papillary carcinoma according to cytology (92.3%). Of them, 8 patients were reported as papillary carcinoma, 3 were papillary microcarcinoma and 1 was papillary Ca follicular variant. The US-TFNAB and surgical histopathology results were consistent in 26 cases for malignancy (100%). 75 cases reported as benign in US-TFNAB cytology results were operated and surgical histopathology result was benign in 62 cases (82.6%) and malignant in 13 cases (17.4%). When all cases with SFN, suspected Huth-cell neoplasm, SM and suspected papillary carcinoma were included into malignancy group, the sensitivity was 79.4%, specificity was 83.8%, overall accuracy rate was 81.8%, positive predictive value was 80.6% and negative predictive value was 82.7%.

**Conclusion:** A clinical assessment performed an experienced clinician, US-guided TFNAB performed by an experienced radiologist and pathologic evaluation by a cytologist is a team work which will achieve success to identification of malignant TN in patients with TN.

### Comparative evaluation of assessment methods of dry skin of the feet in diabetic patients and correlation with peripheral neuropathy

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**Objectives:** Dryness of the skin of the feet (FDS) is common in patients with type 2 diabetes mellitus (DM) and has been associated with diabetic neuropathy (DN) and increased risk for foot ulceration. The indicator plaster Neuropad is an objective test for the assessment of FDS. However, no study so far has examined the performance of clinical methods in comparison with Neuropad testing for the diagnosis of FDS. In this study we examined the performance of the available clinical methods in comparison with Neuropad testing for the diagnosis of FDS.

**Methods:** 98 patients with DM (males n=60; females n=38; mean age  $58.8 \pm 11$  years) participated in the study. FDS was assessed by the indicator plaster Neuropad (standard method) and the clinical scoring systems of the European Group on Efficacy Measurement of Cosmetics including overall dry skin score (ODS; score range 0-4) and specific symptom sum score (SRRC, Scaling-Roughness-Redness and Cracks; score range 0-16). Neuropad test was applied under the first metatarsal head and the complete colour change was assessed after 10 min of application; results were evaluated as normal (complete colour change) or abnormal (no or partial colour change). In addition, patients were examined for peripheral

DN using the neuropathy symptom score (NSS), neuropathy disability score (NDS), vibration perception threshold (VPT) and monofilament testing (MT).

**Results:** FDS was diagnosed in 44.6% of the subjects using Neuropad testing. An optimal ODS value of 1.5 provided a sensitivity of 66% and a specificity of 57% for the diagnosis of FDS. An optimal SRRC value of 3.5 provided a sensitivity of 33% and a specificity of 68% for the diagnosis of FDS. The combination of the ODS and the SRRC scores using the same optimal cut-off values did not improve performance for the diagnosis of FDS (sensitivity 33%, specificity 68%). ODS and SRRC were associated to age ( $r=0.25$ ,  $p=0.05$  and  $r=0.24$ , respectively,  $p=0.05$ ), NSS ( $r=0.26$ ,  $p=0.04$  and  $r=0.25$ ,  $p=0.05$ ), NDS ( $r=0.28$ ,  $p=0.03$  and  $r=0.37$ ,  $p=0.007$ ), VPT ( $r=0.34$ ,  $p=0.008$  and  $r=0.48$ ,  $p<0.001$ ) and MT ( $r=-0.38$ ,  $p=0.003$  and  $r=-0.49$ , respectively,  $p<0.001$ ).

**Conclusions:** The clinical methods used for the diagnosis of FDS have low performance for the diagnosis of this manifestation at the feet of subjects with DM. Because FDS has been associated with foot ulceration, it is not safe to use clinical criteria, while more objective methods should be used for the diagnosis of this disturbance in subjects with DM.

### Gender and age differences in the prevalence of obesity among adults in Central Kazakhstan: cross-sectional study

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**Objective:** The aim of this study to assess the prevalence of obesity and its features in urban and rural adult population living in Karaganda region, central Kazakhstan.

**Methods:** A cross (cross-sectional) study including 3320 adults aged 18 years and over among urban (Saran, Balkhash,  $n=1868$ ) and rural population (Osakarovsky District, Zhanarkinsky district,  $n=1452$ ) of Karaganda region from the general population 1,364 million. Age Me of all respondents in the study was 46.5 (18-65) years. Me of men age was 47 years, women – 46 years. Body weight was determined with electronic scales, height – using stadiometer; body mass index (BMI) was calculated by dividing body weight (kg) on the square of height ( $m^2$ ). BMI was assessed according to the World Health Organization classification 1997. Obesity was diagnosed based on  $BMI \geq 30$   $kg/m^2$ . Statistical analysis was performed using IBM SPSS Statistics 20 software package. Prevalence of obesity was assessed using a 95% confidence interval. Assessment of significance of differences in the groups were tested using Pearson's chi-squared tests.

**Results:** Prevalence of obesity in general population was 27.7% (95%CI: 27-29.4). Prevalence of obesity increased with age in both men and women ( $p$  for both linear trend  $<0.001$ ). While the prevalence of obesity among men in the age groups 18-39, 40-59, 60 and older was 13.5%, respectively, 23.8%, 43.0%, the corresponding proportion for women was 29.9%, 35.1%, 46.6%. BMI analysis in different age groups without gender regard revealed significant increase of obese people number, increasing with age especially in the elder group ( $\chi^2=339,035$ ,

$\kappa=20$ ,  $p<0.001$ ). Differences in the prevalence of obesity reached statistically significant values in all groups ( $p<0.001$ ).

**Conclusions:** Gender and age differences in the prevalence of obesity among adults of Central Kazakhstan, living in the Karaganda region, revealed high prevalence of obesity among both urban and rural residents, with a predominance of women, especially in elder age group. Significant increase of obese people also was found in connection with age.

### Overweight and obesity in a rural area of Portugal

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**Objectives:** Overweight and obesity are leading public health concerns in the worldwide that are preventable conditions in the majority of cases. Overweight and obesity are associated with a number of serious and costly chronic medical conditions, including type 2 diabetes, cardiovascular diseases, hypertension and certain cancers. The economic impact of overweight and obesity on the health care system is staggering. The objectives of this study were to determine the prevalence of overweight and obesity in a provincial adult population of the east of Portugal (North Alentejo).

**Methods:** This survey was a cross sectional study in which a random sample of adults ( $n=883$ , age  $>18$ ) were selected. For each individual a questionnaire was completed, in which height, weight, waist circumference and demographic characteristics were recorded. The overweight and obesity were defined by BMI 25-29.9 and  $>30$   $kg/m^2$ , respectively. The obesity classes were defined: class 1, class 2 and class 3 if the BMI are between 30-34.9, 35-35.9 and  $>40$   $kg/m^2$ , respectively. The abdominal obesity was defined for women and men by waist circumference  $>88$  cm and  $>102$  cm, respectively.

**Results:** The prevalence of obesity and overweight were 19% (class 1: 14.9%, class 2: 3.2% and class 3: 0.9%) and 40.9%, respectively. In addition 34.3% of women and 46.4% of men were overweight; 21.3% of women and 17.2% of men were obese with the following distribution: for men 14.9% had obesity class 1, 1.9% – class 2 and 0.4% – class 3. In women 15.1% had obesity class 1, 4.7% – class 2 and 1.5% – class 3. The waist circumference was  $>88$  cm in 38.7% of women and  $>102$  cm in 20.5% of men.

**Conclusions:** In the North Alentejo (Portugal), overweight and obesity levels are a very important health problem. It is necessary to analyze in further depth the factors involved in the genesis of obesity and to institutionalize community health programs for its prevention, monitoring and treatment.

### Serum salusin- $\alpha$ as an atherosclerotic risk marker in hypothyroidism

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**Objectives:** Salusins (salusin  $\alpha$ , salusin  $\beta$ ) are multifunctional endogenous vasoactive peptides shown in human and rat tissues. Serum salusin  $\alpha$  level is known to be decreased in coronary artery disease and hypertension and lack of salusin  $\alpha$ , enhancing coronary atherosclerosis. Hypothyroidism is a chronic inflammatory disease that has a high risk of developing cardiovascular disease with accelerated atherosclerosis and hypertension. In this study, we aimed to search the relationship of overt hypothyroidism and subclinical hypothyroidism with salusin  $\alpha$  and other inflammatory markers, also the effect of L-thyroxine treatment on these findings.

**Methods:** 32 patients (31 female, 1 male) with overt hypothyroidism taking L-thyroxine treatment, 18 patients (all female) with subclinical hypothyroidism without treatment and 25 healthy patients (21 female, 4 male) as control group were included in the study. Serum salusin  $\alpha$ , TNF  $\alpha$ , sCRP, glucose, insulin and lipid levels were tested for all 3 groups and results were evaluated with SPSS statistical analysis method.

**Results:** The mean age for overt hypothyroidism group was  $40,3 \pm 12,2$  years, subclinical hypothyroidism  $38,4 \pm 9,2$  years, control group  $37,3 \pm 9,9$  years. HDL, sCRP, salusin mean values were different in all 3 groups and difference was statistically significant ( $p=0,018$ ,  $p<0,001$  and  $p=0,003$ ). HDL level was statistically significant higher in control group compared to treatment group ( $p=0,018$ ). sCRP level was higher and salusin level was lower in both treatment and non-treatment hypothyroidism groups compared to control group ( $p<0,001$ ,  $p=0,002$ ,  $p=0,003$  and  $p=0,016$  in order). When treatment and non-treatment hypothyroidism groups were compared, there was no statistically significant difference for salusin  $\alpha$  but, HDL level was statistically significant high and insulin level statistically significant low in treatment group ( $p<0,001$  and  $p=0,017$ ).

**Conclusion:** Salusin  $\alpha$  which is shown to be protective for coronary artery disease and hypertension, is found to be significantly low in hypothyroidism, thus it is a marker that increases the cardiovascular disease risk in this specific patient group.

## Consciousness level and awareness of the disease among diabetes patients

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**Objectives:** Diabetes mellitus is a growing health problem with its increasing prevalence and complications. Prevention of this problem is only possible with enhancement of knowledge and awareness of the disease. In this study, we aimed to point out the awareness and conception of the disease by diabetic patients. **Methods:** 87 type 2 diabetes mellitus patients, 30 years old and older, who had been tested for their blood glucose and HbA<sub>1c</sub> levels in the previous 3 months from internal medicine outpatient clinic were included in the study. Questions including socio-demographic description were asked and a 5-step questionnaire was applied to patients about diabetes. The answers were classified and evaluated according to right answer percentages.

**Results:** The questions and answers to the questionnaire were

as follows: 1) What is diabetes: 26% – lack of insulin/a disorder about obesity, 74% – wrong/no answer; 2) Because of which organ's failure, does diabetes develop: 23% – pancreas, 15% – kidney, 7% – liver, 44% – doesn't know, 11% – other organs; 3) What is the optimum value of fasting and satiety blood glucose: 47% – right or acceptable answer, 53% -wrong answer/ does not know; 4) What happens if diabetes is not cured right or effectively: 52% – eye or kidney disorder, 46% – irrelevant answer, 2% – does not know; 5) What is insulin: 52% -medicine/hormone, 47% – injection, 1% – does not know. Most of the patients had low educational levels, 5 years and longer diabetes duration and accompanying diseases. 79% of patients were on oral anti-diabetics, 8% on insulin regimen and 13% on oral anti-diabetic + insulin treatment. HbA<sub>1c</sub> levels were  $\leq 6.9$  in 32% of the patients, 6.9-8.5 in 44% and  $\geq 8.5$  in 24%. Although they generally had HbA<sub>1c</sub> levels above ideal levels, very small percentage of the patients were on insulin therapy and they mostly used oral anti-diabetics despite their diabetes was not regulated. When the answers of the questionnaire were evaluated, it was found out that the knowledge and awareness of the disease was not sufficient. Thus, patients mostly had complications and accompanying diseases.

**Conclusions:** Patient education aims to deal with diseases, to keep the disease under control, to make things like following diet, physical exercise, medical therapy and controls regularly, a life style and develop the feeling of responsibility. Right precision of the disease and sufficient knowledge is essential for the management of diabetes.

## Ultrasonography as a new method of invisible lipohypertrophy diagnostics

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**Objective:** To compare the frequency of insulin induced lipohypertrophy (LH) in diabetic patients revealed by ultrasonography of subcutaneous fat with those founded by palpatory method.

**Material and methods:** This study was done on 215 diabetic patients (142 females and 73 males, mean age was 46 years) who had been under the treatment with insulin a mean 10 years. Observation and palpation techniques, as well as ultrasonography of subcutaneous fat were used in assessing LH in these diabetics. Evaluation of subcutaneous fat was made in typical injection sites: paraumbilical and buttocks regions, lateral surfaces of hips and shoulders. All patients injected insulin in physiological (basis-bolus) regimen.

**Results:** On the basis of palpation LH were revealed in 66 patients (30,7%), while pathologic areas of subcutaneous fat didn't discover in 149 subjects (69,3%). Further ultrasonography of injection sites was performed to all patients. LH were revealed in 186 patients (86,5%), including those 66 subjects with palpatory changes. Pathologic areas of subcutaneous fat the most often were occurred in paraumbilical regions – 131 patients (61%). Also LH was found simultaneously in two sites: paraumbilical regions

and lateral surface of hips – 32 subjects (15%); paraumbilical regions and lateral surface of shoulders – 24 patients (11%).

**Conclusions:** LH were modified due to good quality modern insulin and expansion their concentration. As a result, pathologic areas of subcutaneous fat were revealed in 30,7% patients by palpation, while LH were found in 86,5% subjects by ultrasonography. Ultrasonography of subcutaneous fat could be used to diagnose LH in diabetic patients in clinical daily practice.

## Current features of clinical presentations and diagnostics of pheochromocytoma

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**Objective:** To study current features of clinic manifestation, results of instrumental methods and factors which influence on treatment efficiency of patients with confirmed diagnosis of pheochromocytoma (Ph).

**Methods:** We performed a retrospective analysis of case reports of 9 patients with histologically confirmed diagnosis of Ph (1 man 56 years old; 8 women who were  $37,6 \pm 15,5$  years old). Next parameters were evaluated: presence of arterial hypertension (AH), specific features of Ph (sympathetic attack); indications for screening of Ph, the time from the appearance of indications for screening till the laboratory confirmed diagnosis, characteristics of CT (native density, size, contrast washout, specific features (cystic, heterogeneous structure with areas of necrosis and hemorrhage)), features of preoperative preparation, presence of intraoperative complications, efficiency of the surgery. Used descriptive statistics were percentage, mean M, standard deviation SD and 95% confidence interval CI.

**Results:** AH was presented in 6 patients (67%), among whom 4 patients had specific features which indicated symptomatic AH. These 4 patients had the classic triad of Ph (44%). Indications for screening of Ph in 4 patients were specific features of Ph (time from screening indication appearance till laboratory confirmed diagnosis was  $41 \pm 14$  months (95% CI 18; 63), in other 5 – adrenal incidentaloma (AI) (time from the detection of AI until the laboratory confirmed diagnosis was  $13 \pm 9$  days (95% CI 2; 24). CT characteristics were the next: native density –  $49,9 \pm 12,8$  HU (95% CI 40; 59,7), lesion size –  $5,4 \pm 1,8$ cm (95% CI 4; 6,7), contrast washout exceeded the threshold value (50%). Only 2 patients had so called specific CT features. All patients received preoperative alpha-blockers for at least 2 weeks, with the achievement of the target values of blood pressure. There were no any specific intraoperative complications in all cases. After surgery metanephrine and normetanephrine were within reference range.

**Conclusions:** 1/3 of patients with Ph had not clinical manifestations. Specific CT features presented in a smaller percentage. The success of surgery entirely depends on adequate preoperative prescription of alpha-blockers. The prolonged time of establishing diagnosis of Ph (in the presence of specific features) probably indicates a low awareness of doctors about Ph, which requires measures to raise awareness about this potentially fatal disease.

## Glucose control in the transition from the internal medicine department to the community: successes, failures and insights

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**Background:** Diabetes poses a considerable morbidity burden on healthcare systems. Glucose levels have been shown to be increased by 32-38% in patients hospitalized in internal medicine wards. High glucose levels during hospitalization increase morbidity and mortality risks. In this setting, glucose control in the hospitalized patient is a therapeutic challenge due to the short duration, fluctuations in glucose levels, and dietary and lifestyle changes accompanying the hospitalization. These observations have highlighted the difficulties and necessity of improving diabetes care during hospitalization. Long-acting insulin, combined as needed with correction values of short-acting insulin, is recognized as preferred treatment for hospitalized diabetic patients with uncontrolled blood glucose. However, the question remains as to whether treatment regimens established during hospitalization are implemented in the community by patients and primary physicians.

**Objectives:** 1) To examine implementation of hospital discharge recommendations for treating diabetes by primary physicians. 2) To examine patient compliance to the recommendations. 3) To examine changes in HbA<sub>1c</sub> levels 3-6 months after hospital discharge.

**Methods:** A retrospective review of patients records who were treated for hyperglycemia and were discharged during the months January to June 2013 from our internal medicine department. Data of medications prescribed by primary physicians and purchases by patients were accessed from the computerized system (OFEC) that is at the interface of hospital and community medical information.

**Results:** We analyzed discharged records of 207 diabetic patients; 53% male, mean age  $72 \pm 13.2$  years and mean HbA<sub>1c</sub> at admission  $8.12 \pm 2\%$ . At discharge, 49% were recommended to use insulin (97% basal, 63% short-acting), 50% metformin, 17% sulfonylurea and 13% DPP4 inhibitors. The degree of total implementation by the primary physician of the discharge recommendations was 52%; the degree of total compliance by the patient of the implemented recommendations was 65%. The transition from hospitalization to the community led to decreased use of short-acting insulin, DPP4 inhibitors, and sulfonylureas. For patients with HbA<sub>1c</sub> above 9% at admission, HbA<sub>1c</sub> was improved by a mean of 1.58% ( $p < 0.001$ ) at 6 months; for those with HbA<sub>1c</sub> of 7-9%, there was no change; and for those with HbA<sub>1c</sub> <7%, the level worsened by a mean of 0.33% ( $p < 0.05$ ).

**Conclusions:** The substantially improved glucose control at 6 months after discharge, for patients with admission HbA<sub>1c</sub> >9%, suggests focusing treatment on this population. The observation of reduced use of short acting insulin and sulfonylurea in combination with basal insulin in the transition from hospitalization to the community help us to establish discharge protocol for diabetic patients and improve transition to the community.

## Analysis of factors contributing to morbidity rate of diabetes mellitus type 2 in the Republic of Mordovia

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**Objectives:** Diabetes mellitus of type 2 (T2DM) is a chronic, non-infectious disease, associated with an intensive rise in the morbidity rate and often, with its latent course. According to the World Health Organization prognosis diabetes mellitus is among the three top diseases that most frequently lead to disability and death, with almost half of fatal outcomes among the people under the age of 70. The aim was to study the dynamics of the epidemiological indices of T2DM in the Republic of Mordovia (RM).

**Material and methods:** Analysis of the data on T2DM within the period 2009-2014 obtained from the Medical Centre of Information and Analysis of the Ministry of Health Care of RM.

**Results:** Prevalence of T2DM among the population of RM within the studied 5 yrs. increased from 19.6 to 25.8 per 1000 (31,6%). In the city of Saransk a similar rise in the morbidity rate was noted, from 24.8 to 32.9 per 1000 (32,7%). The annual rise in T2DM morbidity rate comprised between 3.6 and 7.8% in RM and 4.9-7.9% in Saransk. The highest morbidity rate was recorded in 2013, which may be accounted for the implementation of new regulations in the follow-up surveillance over the population. In 2013 144851 inhabitants went through the 1-st stage of surveillance (100% of those liable to this monitoring), with 136235 (96%) who went through all the stages. T2DM was revealed in 473 (0,35% of the patients who underwent a complete surveillance). The most common risk factors for the revealed condition were: imbalanced nutrition, low physical activity, excess body mass, dyslipidemia, arterial hypertension, fasting hyperglycemia and impaired glucose tolerance. Over 40% of the individuals had 2 or more risk factors. In 2014 the number of people who went through the first stage of follow-up surveillance comprised 155632 (over 100%), of which 141287 (90,8%) underwent a complete surveillance. T2DM was revealed in 1527 (4,8%). However, a rise in the morbidity rate was somewhat lower (3,6% in RM and 5,1% in Saransk).

**Conclusion:** It is likely, that this decrease occurred due to improved education on prophylaxis among the individuals with risk factors for T2DM.

## A rare case of papillary thyroid carcinoma with isolated lymph node metastasis and undetectable primary tumor

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**Introduction:** The incidence of thyroid malignancy is gradually increasing, being most of which papillary thyroid carcinoma

(PTC). The most common clinical presentation of PTC is palpable thyroid nodules and rarely lymph nodes in the neck area. Primary focus is almost always detected in the thyroid gland after the involvement of lymph nodes. We present here a case of cervical lymph node metastasis with undetected primary tumor in the thyroid gland.

**Case report:** A 54 years old male patient applied to the outpatient clinic due to a painless palpable lump in the neck area. His thyroid status was euthyroid. Physical exam revealed a nodule in the left side of the thyroid. Ultrasonography showed that a 34x54 mm nodule in the left lobe of the thyroid. The fine needle aspiration biopsy was reported as benign cytology. Then, left thyroid lobectomy was performed. During the operation, a suspicious coherent lymph node was also excised along with the main nodule. Although there was no malignancy in operation specimen, metastatic PTC was detected in the lymph node (<2 mm). Complementary lobectomy was performed after 3 months because of PTC metastasis. In the second operation, primary carcinoma focus was not observed, either. In postoperative radioactive iodine (RAI) screening, no ectopic tumor focus was detected. RAI treatment was planned for the patient who was regarded as at high-risk group due to lymph node metastasis.

**Discussion:** Lymph node metastasis of thyroid cancer around the neck area is important in terms of clinical complaints. However, it may be seen an isolated lymph node involvement without any findings of primary tumor focus in the thyroid and this can be originated from ectopic thyroid focuses which are too small to be detected.

## A case of Graves' disease, resistant to anti-thyroid medicines

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**Introduction:** Graves' disease (GD) is characterized by hyperthyroidism, goiter, orbitopathy, and dermopathy. The goals of treatment are to alleviate the symptoms and reduce the secretion of thyroid hormones. Available treatment options are anti-thyroid medications, radioactive iodine therapy and surgery. Here, we would like to present a rare case of Graves' disease resistant to anti-thyroid treatment.

**Case report:** A 22 years old male patient presenting with excess sweating, palpitation and weight loss was diagnosed with GD and started methimazole (MM) and propranolol. MM was stopped 2 months later due to intractable nausea and skin rash. Upon stopping MM, complaints have lessened. Later, propylthiouracil (PTU) was given. In a 2-year follow-up period, euthyroidism could not be achieved despite anti-thyroid medicines. When the patient applied to our clinic, he had still symptoms of thyrotoxicosis (TSH: 0.001 mIU/ml, reference: 0.35-4.94, fT3: 7.31 pg/ml, reference: 1.71-3.71, fT4: 2.35 ng/dL, reference: 0.70-1.48). Thyroid USG showed an increased vascularity without any nodularity. The dose of PTU was increased up to 1000 mg/day, propranolol 320 mg/day. 6 weeks later, serum levels of thyroid hormones were still high, and transaminases were increased greater than three-fold of upper limits of normal, and clinically thyrotoxicosis went on. Consequently, we regarded this condition a case of intractable

thyrotoxicosis, stopped antithyroid drugs, and prepared the patient for surgery. Lugol's solution (3 times 10 drops a day) and dexamethasone (4 times 0.5 mg a day) was started. After 10 days with this treatment regimen, serum levels of thyroid hormones but not TSH were decreased to normal ranges (fT3: 4.24 pg/ml, fT4: 1.08 ng/dL, TSH: 0.001mIU/ml), and total thyroidectomy was performed. No perioperative complication was observed, and the patient was placed on replacement dose of levothyroxine.

**Discussion:** Though only one patient, our case shows a typical antithyroid drug resistance of GD and preparation of the case for operation with non-classic antithyroid agents. Despite the advances in the treatment modalities, sometimes therapy of GD poses a challenging condition. In these conditions, euthyroidism should be achieved by using some nonclassic antithyroid agents such as inorganic iodine solutions; corticosteroid, cholestyramine, and plasmapheresis, etc. After obtaining euthyroidism, the patient should have a definitive therapy with surgery or radioiodine.

## Long term therapeutic consequences in patients with autoimmune hepatitis

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**Objectives:** Autoimmune hepatitis (AIH) is a chronic inflammation of the liver, the cause of which is unknown. The long-term outcome of patients with AIH has not been well-defined. The aim of this study was to clarify the long-term outcomes and determinants of outcome in patients with AIH.

**Methods:** In this cohort, a total of 150 AIH patients were enrolled in the study. Patients were followed up for an average of 60 months. Clinical, biochemical, pathological and imaging data were gathered from all the patients at both the beginning and the end of the follow-up with 3 checkpoints between these time periods. Results are expressed as mean  $\pm$  SD.  $P < 0.05$  was statistically significant.

**Results:** 150 patients, 113 female, 37 male, mean age  $42.4 \pm 14.6$  years, participated in the study. The most common symptoms were icterus (88.7%), fatigue (84.7%), pruritus (80%) and loss of appetite (36.6%) at diagnosis. 73 patients (48.7%) reached remission; 34 patients (22.7%) relapsed, 32 patients (21.3%) had incomplete response and 11 patients (7.3%) had treatment failure. Predictors for disease progression were age at presentation of 20-40 years and number of relapses ( $p < 0.05$ ). The prognosis of patients experiencing 2 or more relapses was significantly poorer than that of patients with remission or a single relapse both in univariate ( $p < 0.001$ ) and multivariate ( $p < 0.001$ ) analyses.

**Conclusion:** Repeated relapses of disease are significantly associated with a poorer long term consequences in patients with autoimmune hepatitis.

## Non-invasive serum fibrosis markers: A study in chronic hepatitis

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**Objectives:** Chronic hepatitis is specified as inflammatory disease of the liver lasting for more than six months. Role of noninvasive fibrosis markers as prognostication factors of the presence or absence of significant fibrosis on liver biopsy of patients with chronic hepatitis is the aim of this study.

**Methods:** 221 patients with chronic hepatitis involved in the study between 2011 and 2013. Routine biochemical indices and serum fibrosis markers such as aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR), AST to platelet

ratio index (APRI) and Fibrosis 4 score (FIB-4) were evaluated, and the histological grade and stage of the liver biopsy specimens were scored according to the Ishak scoring system. Diagnostic accuracies of these markers for prediction of significant fibrosis were assessed by receiver operating characteristic (ROC) curve analysis.

**Results:** Contemporaneous laboratory indices for imputing AAR, APRI, and FIB-4 were identified with liver biopsies. From all, 135 males (61.1%) and 86 females (38.9%), with mean age of  $39.6 \pm 14.4$  years old were studied. Significant correlation between stages of fibrosis and FIB-4, APRI and AAR were detected, with a correlation coefficient higher than that of other markers in the patients with Hepatitis B ( $r = 0.46$ ), C ( $r = 0.58$ ) and autoimmune hepatitis ( $r = 0.28$ ). FIB-4 (AUROC = 0.84) and APRI (AUROC = 0.78) were superior to AAR at distinguishing severe fibrosis from mild-to-moderate fibrosis and gave the highest diagnostic accuracy.

**Conclusion:** Application of these markers was good at distinguishing significant fibrosis and decreased the need for staging liver biopsy specimens among patients with chronic hepatitis.

## Upper-gastrointestinal bleeding in the emergency department: frequency and outcomes of different endoscopy diagnosis

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**Objectives:** To describe the frequency and different clinical outcomes of various upper endoscopy (UE) diagnosis encountered in the setting of acute upper-gastrointestinal bleeding (UGB).

**Methods:** A cross-sectional study was performed in our hospital including all patients with the diagnosis of acute UGB that underwent UE over the year of 2014. Frequency of each endoscopy diagnosis was evaluated, comparing several outcomes among each group.

**Results:** 531 endoscopies were analyzed, of which 6 were excluded, regarding patients that underwent repeated endoscopies in the same day. In the endoscopies included, 27.4% ( $n = 144$ ) had peptic ulcer (PU), 21% ( $n = 110$ ) did not have any lesion, 16% ( $n = 84$ ) had either esophagitis or gastroduodenitis (EGD), 16% had esophagogastric varices (EGV), 5.3% ( $n = 28$ ) had a neoplastic (NEO) lesion, 2.7% ( $n = 14$ ) had a Mallory-Weiss (MW) lesion and 11.6% had other type of lesions. Only 13.2% ( $n = 19$ ) in the PU group were taking proton pump inhibitors (PPIs), compared to 46.3% ( $n = 38$ ) in the EGV group and 33.3% ( $n = 28$ ) in the EGD group. Hemodynamic instability rates were higher in the EGV and PU groups (34.5% each,  $n = 29$  and 49, respectively). The mean

hemoglobin value was 7.5 g/dL for those who had a NEO lesion, and nearly 8.8 g/dL in PU and EGV, compared to 9.2 g/dL in normal endoscopies. The NEO group had higher rates of severe grade lesion detected with a total of 35.7% (n=10). EGV, PU and EGD had lower rates, accounting for 28.6% (n=24), 13.9% (n=20) and 13.1% (n=11), respectively. NEO lesion also required more blood transfusions (71.4%, n=20), followed by EGV (58.3%, n=49), PU (51.4%, n=74) and EGD (41.7%, n=35). Rebleeding rates within each group were 8.6% (n=7) for EGV, 8% (n=2) for NEO lesion and 7.3% (n=10) for PU. Mortality rates were 17.8% (n=5) for NEO lesion, 4.9% (n=7) for PU and 3.6% (n=3) for EGV. Nonetheless the absolute rebleeding and death cases were higher in the PU group.

**Conclusions:** The NEO group was associated with the worst outcomes, namely hemoglobin values, severe grade lesion and mortality. EGV and PU had a more serious acute presentation, with higher rates of hemodynamic instability. PU, being the most common lesion detected, had a low rate of PPI's use. Early UE is essential in diagnosing severe lesions, leading to a more effective approach of emergent situations.

### **Prolonged-release torasemide on edema and ascites in patients with cirrhosis**

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**Objectives:** The aim of this study was to evaluate the efficacy of prolonged-release torasemide (torasemide-PR) in patients with liver cirrhosis.

**Methods:** In study were enrolled 42 patients with liver cirrhosis complicated by ascites and edema. Mean (SD) age of the patients was 57.4 (11.5) years. They were randomized into 2 groups. Main group received torasemide-PR (n=20), and control group – furosemide (n=22). All patients received spironolactone. Drugs were dosed according to the recommendations of EASL. The duration of the study was on the average of 3 weeks. Efficacy was evaluated by the dynamics of daily diuresis, body weight, blood pressure (BP), level of electrolytes and creatinine, dynamics of daily natriuresis.

**Results:** There showed a decrease of edematous syndrome on the background of diuretic therapy in both groups. No significant difference were found in the dynamics of body weight between groups: in group of torasemide-PR body weight decreased by 8±4 kg, and in group of furosemide – 5,8±3,8 kg (p=0,06). However in group of torasemide-PR diuresis increased average by 865±660 ml, and in group of furosemide – 400±300 ml (p=0,018). In group of torasemide-PR showed significant difference of daily urinary sodium excretion 93±63 mmol/day, compared with control group – 51±20 mmol/day (p=0,012). Statistically significant differences in the level of potassium, sodium, creatinine, and blood pressure in two groups were not received.

**Conclusions:** The usage of torasemide-PR in patients with decompensated liver cirrhosis and edematous-ascitic syndrome

appears to be effective along with furosemide. Torasemide-PR provides significantly greater diuretic effect and greater daily urinary sodium excretion.

### **Microbiocenosis condition of a small and large intestine at the patients with a primary immunodeficiency**

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**Objectives:** The infections of bronchopulmonary system are the leading clinical manifestations of primary immunodeficiency by their humoral type; in a number of cases the diseases connected with autoimmune inflammation are brought to the forefront. The defect of antibody production leads to the structure and microbiota disturbance of the gastrointestinal tract. There are almost no researches reflecting the features of immune system and microbic structure of intestine response at the different clinical variants of primary agammaglobulinemia (PA). Intestine microbiota condition and the immune status study at the patients with autoimmune and infectious phenotypes of the primary immunodeficiency by their humoral type.

**Methods:** The intestine microbiota condition was estimated by the excrement bacteriological inoculation (EBI), the respiratory hydrogen test (RHT) with lactulose (GastrcH – Gastrolyzer, Bedford, UK), by the maintenance definition of the short chain fat acids and anaerobic index (AI) in excrements using gas-liquid chromatography (GLC), and by a method of flow cytofluorometry was phenotyped. 11 patients were examined, 4 – with autoimmune phenotype (AP), 7 – with an infectious phenotype (IP) the PA.

**Results:** It was revealed more significant increase of opportunistic pathogenic water producing microflora at the patients with AP: 143.8±53.4 ppt, at the patients with IP – 131.8±46.5 ppt. During bacteriological research more significant decrease in quantity of bifido- and lacto bacterium was established at the patients with IP on the average group –  $2.1 \times 10^+1$  Ig. During GLC in the group with autoimmune variant AI was lowered in the area of distinctly negative values (at patients with IP it was lowered to the direction of weakly negative ones). Significant distinctions were noted in subpopulation structure of T-lymphocytes, and at the AP case the increase of cytotoxic cells number was not accompanied by the reduction lymphocytes:  $1.2 \pm 0.1$ , unlike the patients with infectious manifestations ( $0.6 \pm 0.1$ ). The differences in functional cell potential of congenital immunity were shown by TLR4 expression strengthening at the patients with AP (63±8%) in comparison with the norm (20±4%) and the patients with IP (21±3%).

**Conclusions:** The changes revealed intestinal microbiota profile and Toll receptors may influence the prognosis of the disease. The structure of the intestinal microbiota changes in patients with primary immunodeficiency dictates the development of personalized treatment.



## Upper gastrointestinal bleeding as the primary presentation of neoplastic disease in the emergency room

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**Objective:** Describe the most typical presentations, endoscopic findings, histological types and outcomes of patients admitted in the emergency room (ER) with upper gastrointestinal bleeding (UGB) whose final diagnosis was neoplastic disease.

**Methods:** Cross-sectional descriptive study which included patients admitted at the ER with a diagnosis of acute UGB that underwent upper endoscopy (UE) whose final diagnosis was neoplastic disease, during the year of 2014.

**Results:** The study included 531 patients of whom 5.3% (n=28) showed UGB as the first expression of neoplastic disease. Predominance in males (59.9%) and the mean age of 73.5 years. Most common clinical presentation was melena (35.7%) followed by hematemesis (25%) and the combination of both (18%). The average amount of hemoglobin was 7,5 g/dL, opposed to the ones who had no endoscopic lesion (9,2 g/dL). Of these, 71.4% (n=20) required transfusion support. The mean Rockall score before UE was 3.2. UE showed no bleeding stigmata in 46.4% of patients (n=13), 32.2% (n=9) presented blood in the gastrointestinal tract (GT) and only 21.4% (n=6) had adherent clots (n=3) or a visible bleeding vessel (n=3). Initially 21.4% (n=6) required endoscopic treatment for hemorrhagic control and 10.7% (n=3) underwent surgical treatment. A second UE was performed in 35.7% of patients (n=10), mainly by doubts in hemostasis. Until the 30 day, 17.9% of the patients experienced rebleeding episode and the mortality was 17.8% (n=5). It was found that 62.5% of these had blood in GT and a lower hemoglobin average (6.8 g/dL). Histological data demonstrated that 57.1% had adenocarcinoma (n=16), 10.7% poorly cohesive carcinoma cells (n=3), metastatic disease in the same proportion (n=3), followed by 7.1% of squamous cell carcinoma and 3.6% for type B lymphoma (n=1). Helicobacter pylori was demonstrated in only one sample, corresponding to the type B lymphoma.

**Conclusions:** In accordance with the literature, 5.3% of cancer patients had UGB as the first sign of the disease and adenocarcinoma was the most predominant histological type. Worst outcomes were associated with lower hemoglobin levels and the presence of blood in the gastrointestinal tract observed in the UE. The early performance of UE proved to be an important diagnostic and therapeutic resource for the management of these patients.

## Hepatic amoebiasis superimposed on autoimmune hepatitis – a diagnostic challenge

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**Introduction:** Autoimmune hepatitis poses a diagnostic challenge not only for being infrequent but also for causing symptoms only late in the course of the disease. Amoebiasis may affect different organs, the liver being a frequent site of infection. Hepatic disease due to amoeba may be severe if not properly detected and treated.

**Case report:** We present the case of a 21-year-old male who had lived in South America in the previous year. He was asymptomatic until about 6 months before when he began to lose weight (10 kg) and one month prior to hospital admission developed abdominal pain, jaundice, choloria and acholia associated with prostration. Laboratory results showed Hb 13.9 g/dL, leukocytes 5.2 x10<sup>9</sup>/L, neutrophils 55.8%, lymphocytes 36.4%, platelets 128 x10<sup>9</sup>/L, INR 2.1, albumin 0.03 g/L, total bilirubin 54.4 µmol/L, direct bilirubin 44.2 µmol/L, AST 1201 IU/L, ALT 1297 IU/L, AP 288 IU/L, GGT 164 IU/L, LDH 849 IU/L. Serologic tests for A, B and C hepatitis and HIV were negative. Serologic amoeba test was positive. Antinuclear antibodies were positive with a speckled pattern nucleus, positive mitosis and cytoplasm, title was 1/640; anti-smooth muscle was dubious and anti-mitochondria, anti-kidney and liver microsomes, anti-gastric parietal cell, anti-LKM 1, anti-LC1, anti-SLA/LP, anti-M2, anti-M2-3E, anti-Sp100, anti-PML, anti-gp210, and anti-Ro52 were negative. Abdominal ultra-sound: hepatomegaly with a starry sky appearance. Liver biopsy: chronic hepatitis, necro-inflammatory grade 8 and fibrosis stage 4 (Modified Hepatic Activity Index) in favor of an autoimmune etiology. During hospitalization, the patient needed several plasma and platelet units. He underwent treatment for Amoebiasis with good tolerance. The patient's hepatic function gradually recovered under corticosteroid therapy, which was continued in ambulatory follow-up associated with azathioprine.

**Discussion:** Hepatic amoebiasis was probably responsible for the clinical manifestation of hepatitis, leading to the diagnosis of an autoimmune disease that would otherwise be diagnosed only when severe hepatic damage was caused. Treating amoebiasis was imperative prior to treating the autoimmune hepatitis since immunomodulation could worsen the infectious disease. The authors would like to highlight the possibility of finding more than one diagnosis responsible for a presenting illness even in a young adult. Epidemiologic context led to the search for a second etiologic cause, with important prognostic impact.

## Magnesium deficiency and minimal hepatic encephalopathy among patients with compensated liver cirrhosis

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**Objectives:** Magnesium is an essential intracellular cation. Most of it is intracellular; therefore, correlation between its serum level and total body content is poor. Magnesium deficiency is a common finding and its prevalence among cirrhotic patients is even higher than among the general population. Minimal

hepatic encephalopathy (MHE) is a subclinical phase of hepatic encephalopathy in which there are no overt symptoms. Cognitive exams can reveal minimal changes in coordination, attention and visual motor function, whereas language and verbal intelligence are usually relatively spared.

**Methods:** In order to examine the correlation between intracellular and serum magnesium levels and MHE, outpatients with a diagnosis of compensated liver cirrhosis were recruited to this randomized, double-blinded study. The patients were divided into an interventional arm that was treated with magnesium oxide and a control (placebo) arm. Serum and intracellular magnesium levels were measured. Cognitive function was assessed by a specialized occupational internist.

**Results:** 29 patients met the inclusion criteria. While hypomagnesaemia was found in only 10%, 33.3% had low levels of intracellular magnesium. The levels of the initial laboratory parameters and cognitive performance were positively correlated. We also observed a trend toward improved hepatocellular enzyme levels in the treatment group.

**Conclusions:** Magnesium deficiency is common among patients with compensated liver cirrhosis. We found an association between magnesium deficiency and impairment in several cognitive function tests that might indicate involvement of magnesium in the pathophysiology of MHE.

## Mean platelet volume and FIB4 index correlation in patients with ultrasonographic grade 0-3 hepatosteatosis

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**Objectives:** Non-alcoholic fatty liver disease (NAFLD) is a clinicopathological condition that comprises a wide spectrum of liver damage. Patients with pure steatosis follow a relatively benign course, whereas patients with histological necro-inflammatory changes and/or fibrosis may progress to end-stage liver disease. Although a liver biopsy is the best diagnostic tool for confirming NAFLD, it is not routinely performed due to possible complications. We designed this study to evaluate mean platelet volume (MPV) and FIB4 Index Correlation as a fibrosis marker in patients with NAFLD retrospectively.

**Material and methods:** 249 patients with hepatic ultrasonography (USG) results were enrolled retrospectively into the study. NAFLD was defined by USG detection of hepatic steatosis (Grade 0-3) in the absence of other known liver diseases. ALT, AST, platelet count (PC) and MPV were obtained from a computerized database. Also FIB4 index was assessed.

**Results:** A total of 249 subjects (141 women and 108 men) were included in the study. We have divided the patients into 4 groups according to the USG findings. Hepatosteatosis (HS) Grade 0 as Group A, HS Grade 1 as Group B; HS Grade 2 as Group C; HS Grade 3 as Group D. MPV values are 8,6±1.5 in Group A; 8,6±1.4 in Group B; 8,9±1.6 in Group C, 9,0±2.2 in Group D. Although the mean MPV levels increases as the steatosis progresses in Groups, no significant result was obtained. MPV was only

negatively correlated with PC. FIB4 values were 1.31±0,8 in Group A; 1,18±0,6 in Group B; 1.03±0,5 in Group C and 1,1±0,4 in Group D. No significant result was obtained between groups in FIB4. We have found no significant correlation between FIB4 scores and MPV values.

**Conclusions:** Advanced fibrosis was found to be a significant predictor of mortality, mainly from cardiovascular causes, independent of other known factors. Also these patients are at risk for developing fibrosis may progress to end-stage liver disease. So determining the fibrosis in USG proven NAFLD patients using non invasive scores may be helpful in improvement in morbidity and mortality of these patients and also protecting them biopsy related complications. We used computer based retrospective data and the study population especially FIB4 score over 3,25 were only 6 patients that can affect the statistical analysis. Also biopsy proven fibrosis was unavailable. Considering MPV as an additional inflammation marker may play a role in predicting the fibrosis with larger scale studies.

## Evaluation of the functional state of the liver in patients with chronic acalculous cholecystitis

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**Background:** Chronic cholecystitis is a systemic disease of hepatobiliary tract. Research data concerning involvement of the liver in the pathological process in chronic acalculous cholecystitis are few and contradictory; there are no findings of a comprehensive study of functional disorders of the hepatobiliary system.

**Objective:** To evaluate the functional state of the liver in patients with chronic acalculous cholecystitis.

**Material and methods:** The study involved 42 patients with chronic acalculous cholecystitis (32 women and 10 men) aged 45.7±2.1 years. The comparison group consisted of 33 healthy people, and was comparable in sex and age. All patients underwent clinical studies, the study of the functional state of the liver based on the results of biochemical blood tests; fibrogastroduodenoscopy (EGD), ultrasound examination of the abdominal organs (US), dynamic hepatobiliary scintigraphy. Statistical processing was performed using the application package Microsoft Office Excel 2009.

**Results:** Laboratory signs of cholestasis, including indicators of the level of alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and cholesterol (TC) were detected in 23 (55%) patients. The value of ALP in the observation group exceeded the value in the comparison group by 35% and amounted to 104.8±11.6 U/L and 68.9±3.6 U/L ( $p < 0.05$ ) respectively; the level of GGT was 9% higher in the observation group than in the comparison group and equaled to 36±4.9 U/L and 32.9±1.3 U/L ( $p > 0.05$ ) respectively; cholesterol level was 10% higher in patients of the observation group than in patients of the comparison group and amounted to 5.2±0.23 mmol/L and 4.68±0.17 mmol/L ( $p < 0.001$ ) respectively. The changes of transaminase activity characteristic of cytotoxic syndrome occurred in 13 (31%) patients. In the observation group the level of alanine aminotransferase (ALT) was 24.4±1.3 U/L,

whereas in the comparison group it was  $17.9 \pm 0.98$  U/L ( $p < 0.001$ ). Activity index of aspartate aminotransferase (AST) was equal to  $25.7 \pm 1.83$  U/L in the observation group and to  $19.5 \pm 0.76$  U/L in the comparison group ( $p < 0.05$ ). Ultrasound examination revealed deformation of the gallbladder in 21 (50%) patients, diffuse changes in the pancreas in 25 (59%) patients and diffuse changes in the liver in 10 (24%) patients. During the EGD endoscopic signs of gastritis were revealed in all patients (100%), endoscopic signs of duodenitis were revealed in 19 (45%) patients, duodenogastric reflux was noted in 17 (40%) patients. The function of the hepatobiliary system was studied by dynamic hepatobiliary scintigraphy in 12 patients. Diffusely uneven distribution of the radiopharmaceutical was recorded in 100% cases, impairment of absorptive function was detected in 8 (67%) patients, and gallbladder dyskinesia was recorded in 10 (83%) patients.

**Conclusions:** The majority of patients with chronic cholecystitis showed signs characteristic of cytotoxicity syndrome and cholestasis that were revealed by laboratory studies. The patients with chronic cholecystitis were found to have the impairment of liver function associated with the deformation of the gallbladder and the changes in its motor function. The obtained findings indicate the need for medical correction of the functional state of the liver.

## Idiopathic recurrent acute pancreatitis, or maybe not so idiopathic

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**Introduction:** Recurrent acute pancreatitis (RAP) is defined as more than two episodes of acute pancreatitis (AP) without evidence of underlying chronic pancreatitis. It usually occurs in the idiopathic AP, representing 20-25% of all cases. In some studies, sphincter of Oddi dysfunction (SOD) has been reported to be the cause of idiopathic RAP (IRAP) in up to one-third of cases.

**Case report:** We describe a case of a 70 years old man, with clinical history of hypertension, type 2 diabetes non-insulin-treated, obesity and obesity-hypoventilation syndrome, hyperuricemia and depressive syndrome, medicated with perindopril 8 mg, irbesartan 300 mg, furosemide 40 mg, allopurinol 100 mg, simvastatin 20 mg, ranitidine 150 mg and fluoxetine 20 mg. The patient had multiple hospitalizations (total 8 episodes) caused by acute alithiasic pancreatitis since 2013, complicated with pancreatic inflammation and necrosis, peri-pancreatic collections, always with resolution, remaining only a small region of fibrosis. He underwent laparoscopic cholecystectomy because of the presence of biliary sludge on abdominal ultrasound, but the recurrences continued. Analytically, the patient had light hypertriglyceridemia ( $< 200$  mg/dL) and normal serum calcium levels. Autoimmune investigation, IgG subclasses and virological, bacteriological and parasitological research were all negative. Also the suspension of all drugs was ineffective to prevent recurrences. In the hospitalizations, he was submitted to several abdominal ultrasound, abdominal tomography, endoscopic retrograde cholangiopancreatography with sphincterotomy (ERCP with ETE), magnetic resonance

cholangiopancreatography, endoscopic ultrasound and pancreatic angiography, which were all unable to clarify other etiology of RAP. Finally, after multidisciplinary meeting, it was decided to carry out ERCP with new ETE and placement of pancreatic prosthesis on suspicion of sphincter of Oddi or pancreatic duct dysfunction. At follow-up one month after the procedure, the patient remained asymptomatic, denying the usual slight abdominal pain he always felt even when he was not having an acute episode of AP.

**Discussion:** SOD should be suspected in patients with IRAP after all other causes have been excluded. Treatment for SOD includes biliary and/or pancreatic sphincterotomy, with or without stenting, which might lead to relief in  $> 50\%$  patients. Regular follow-up of this patients is necessary because the risk of developing chronic pancreatitis.

## The danger of diagnostic “labels” – a gastroenterological case

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**Introduction:** Primary cytomegalovirus (CMV) infection occurs either in early childhood or adulthood. It is highly prevalent – up to 100% of the adult population may have serological evidence of past CMV infection. Reactivation usually occurs in impaired cellular immunity states such as cancer or immune deficiency syndrome. Organs usually involved are the lungs, central nervous system and gastrointestinal tract. The authors present a case of CMV colitis in a patient with mild immunosuppression, whose true condition went undetected for years due to perpetuation of a different diagnosis.

**Case report:** 69 years old woman, Caucasian, with known primary combined IgA and IgG deficiency (under intravenous immunoglobulin treatment), nonspecific interstitial pneumonia and chronic *Giardia lamblia* infection (diagnosed 4 years prior, with persistent diarrhea since). The patient was admitted to the emergency department due to rapid worsening of her chronic diarrhea for 6 weeks, along with a 10% body weight loss. On observation: pale and severely dehydrated; no other relevant findings. Blood testing: hypoalbuminemia (2.4 g/dL) and hypokalemia (2.65 mmol/L), search for *Clostridium difficile* toxin negative. Based on her medical history, she was admitted to the internal medicine ward with the diagnosis of aggravated giardiasis. She maintained multiple daily defecations under optimized diet. Despite the established diagnosis, the cause of diarrhea was studied over: negative *Giardia* antigen, anti-gliadine and anti-transglutaminase antibodies, HLA-DQ2 and anti-*Saccharomyces cerevisiae* antibody; negative Epstein-Barr serologies, negative CMV IgM and positive IgG, negative fecal parasite search, coproculture and autoimmunity markers, tuberculin skin test and serial hemocultures; vasoactive intestinal peptide, serotonin and parathyroid hormone values within normal range. Normal abdominal computed tomography. Upper endoscopy: Brunner gland hyperplasia. Duodenal biopsy: chronic duodenitis and villous atrophy. Normal colonoscopy. Colon biopsy: CMV colitis with marked inflammatory process. Capsule endoscopy: extensive

CMV enteritis with mucosal ulceration. The final diagnosis was established as CMV enterocolitis. Slow but near-complete symptom remission observed after 4 weeks of ganciclovir treatment.

**Discussion:** Physicians must never conform to patients' diagnostic "labels"; these assumptions must always be questioned and properly studied before being accepted, as the insistence on a wrong diagnosis is often prejudicial.

## Colorectal cancer incidence and incidence rates in Iran: a systematic review and meta-analysis

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**Objectives:** Colorectal cancer (CRC) is a major cause of morbidity and mortality throughout the world. It is the third most common cancer worldwide and the fourth most common cause of death. There are few reports about incidence rates of CRC in Iran, but they indicate significant increasing trend over just last decade. The increasing pattern of CRC incidence in Iran, and close relationship with the geographical location, are the underlying reason for this study.

**Methods:** We included in this systematic review and meta-analysis, studies reporting different measures of incidence, age-standardized incidence rates (ASR) and crude incidence rates (CR). All ASRs and CRs per 100,000 person-years were obtained as standardized to the world standard population. We included 29 studies, 8 Persian articles and 21 English articles, from different provinces and geographical areas of the country. We used comprehensive meta-analysis (CMA) software for this approach.

**Results:** ASRs were obtained based on the random model, and were 7.24 (95% CI: 6.01-10.9) and 6.18 (95% CI: 5.38-7.99), per 100,000 for men and women respectively. The random CRs for males and females were 5.11 (95% CI: 4.18-7.12) and 4.34 (95% CI: 3.58-5.01) per 100,000 respectively.

**Conclusions:** The rising incidence and mortality rates of colorectal cancer put demand on a systematic approach toward specific and national screening program in Iran. The more executed system for collecting cancer data, in all cities and rural areas of the country is one of the essential priorities.

## Survival time of patients with gastric cancer in Iran: a meta-analysis

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**Objectives:** Gastric cancer (GC) is the fourth prevalent cancer and the second cause of cancer-related deaths in the world. Various studies had different survival time report for patients with GC in IRAN. Thus, there is no general estimation available.

**Methods:** A meta-analysis study was conducted by domestic and

foreign valid databases as PubMed, Scopus, SID and Magiran, with "gastric cancer" and "survival time" keywords. Data were analyzed through random module by CMA software.

**Results:** A total of 9 articles, including 4381 subjects were selected. Gender distribution was 59.5% for male patients and 40.5% for female patients. Mean age was 59.1±9.2 years. The overall survival rate was 21.9±1.4 months, which was 10% more in females in comparison with males. The highest and lowest survival time were respectively in Tehran and Rasht. Survival time in patients below 55 years old was better than elderly patients.

**Conclusions:** Median Survival time in patients with GC in Iran is less than many countries in the world. Gender, age higher than 55 years and lower socio-economic status decrease the survival time.

## Celiac: disease of any age

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**Introduction:** Iron deficiency is the most common cause of anemia. A loss which varies according to age group comes first into consideration, rather than lack of absorption due to malabsorption, when evaluating the iron deficiency anemia. Menstrual bleeding is held responsible for this loss of iron in young women, while with the older age groups, the losses are due to gastrointestinal bleeding. We present here postmenopausal female patient with newly diagnosed celiac disease.

**Case report:** A 59 years old female patient was admitted to the internal medicine clinic with exhaustion and dyspepsia complaints. Medical history revealed that she has been having these complaints since her youth. She pointed out that she came to the hospital with the same complaints so many times over the years and she was always told that it was due to menstrual period and she had anemia. During these times, sometimes the patient had blood transfusion and sometimes iron preparations were prescribed. Tests showed Hb 9.4 g/dL, MCV 66.2 fL, RDW 17.3%, iron 7.8 mg/dL, total iron binding capacity 444.1 mcg/dL, ferritin 2.9 ng/ml and folate 1.4 ng/ml. Occult blood in the stool was negative and celiac disease was suspected and some tests were conducted: IgA tissue transglutaminase 8.33 (positive), tTG IgG 1.87 (positive). Upper endoscopy detected villous atrophy in duodenal bulb. Biopsy result was reported as Corazza Villanacci grade 2 A compatible with celiac disease. Patient's iron deficiency anemia and her complaints disappeared with a planned treatment and suggested diet.

**Discussion:** Celiac disease should be kept in mind, regardless of age, if there is combination of anemia and dyspeptic complaints.

## Mesalazine induced pancreatitis treated with mesalazine

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**Introduction:** Acute pancreatitis is a major disease that can cause morbidity and mortality. The annual incidence varies between

4.9 and 35 per 100,000. More than 300,000 patients each year in the United States are hospitalized with acute pancreatitis and about 20,000 cases are fatal. Disease sometimes can not be recognized especially when it is very mild or very severe and in these cases preventable causes can be avoided and it may cause death due to secondary attacks. 80% of the cases are mild cases which recover without serious morbidity, 20% is very severe. The most common causes of acute pancreatitis are gallstones and alcohol. Hypertriglyceridemia, hypercalcemia and drugs are among the less common causes. Mesalazine is one of the drugs that can cause acute pancreatitis.

**Case report:** A 58 years old female patient with a diagnosis of Sjogren syndrome, taking plaquenil 2x1 for 8 years, was diagnosed with ulcerative colitis (pancolitis) in the clinic she went after having complaints of bloody diarrhea up to 14-16 times in a day. Mesalazine 3 x 1000 mg treatment was started. She was admitted to the internal medicine department with complaints of nausea and abdominal pain during the fourth week of treatment. Epigastric tenderness was detected on physical examination and other findings were amylase 331 U/L, lipase 886 U/L. Abdominal ultrasound and abdominal computed tomography images were consistent with acute pancreatitis. There were no stones in the gallbladder, calcium and triglycerides was in the normal range, and no pathology was detected in the patient explaining the etiology. Considering autoimmune pancreatitis, performed magnetic resonance imaging could not clarify the etiology, either. IgG4 193 mg/l (39.2-864) was normal. She was diagnosed as acute pancreatitis due to mesalazine usage. Her mesalazine form was replaced with slow-release mesalazine which releases active drug slowly throughout the entire small intestine and colon. Amylase and lipase levels were observed back in the normal range and she showed improvement clinically, and radiologically. Slow-release mesalazine dosage was gradually increased to 4x1000 mg. The patient who achieved clinical improvement did not redevelop pancreatitis.

**Discussion:** Pancreatitis cases linked to mesalazine have been reported in the literature. Overall approach is that to cut the mesalazine and try another treatment. It should be kept in mind that slow-release mesalazine form can also be used as a different point of view.

### **Ischemia-modified albumin as a predictor of anastomosis dehiscence in intensive care patients after colorectal surgery**

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**Objectives:** Dehiscence of anastomosis is an infrequent but serious complication of colorectal surgery and a difficult task for intensive postoperative care. Until recently a suitable biochemical marker to identify high risk patients has not been available. Now the Albumin Copper Binding Assay (ACuB Assay) has been developed to improve the detection of ischemia-modified albumin (IMA), traditionally detected by cobalt binding assay. The aim of the presented work was to test the ability of the assay to predict the development of dehiscence.

**Methods:** Patients (n=96) suffering from colorectal cancer and undergoing surgery were enrolled in the study. In 5 patients, dehiscence of anastomosis developed (5.2%). Blood samples were drawn prior to and 2 hours after the surgery. The Albumin Copper Binding Assay was performed as described (1) to detect IMA using copper (II) ions and the fluorescent dye lucifer yellow. The results are expressed as the pre- and post-operative difference in fluorescence units (FU) per g of albumin (mean±SD). These values correlate with usually increased concentration of ischemia-modified albumin postoperatively, due to tissue ischemia.

**Results:** Patients suffering from dehiscence (374±165 FU/g) had a significantly higher concentration of ischemia-modified albumin compared to controls (94±239 FU/g, p=0.012). Using a cut-off value of 270 FU/g for discriminating positive vs. negative results, the diagnostic sensitivity was 100%, specificity 79.2% and efficiency 80.2%. The negative predictive value was 100% and positive predictive value 20%.

**Conclusions:** This recently developed method offers new diagnostic help in postoperative intensive care. In particular, the high negative predictive value may help to exclude patients not threatened by dehiscence of anastomosis. Possible analytical alterations of this promising assay may even improve its diagnostic efficiency.

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### **Hydrogen breath test to assess the effectiveness of non-absorbable antibiotic rifaximin in the treatment of ulcerative colitis**

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**Objectives:** Bacterial overgrowth (BO) often accompanies recurrent ulcerative colitis (UC). The aim of open prospective clinical study of the case-control was conducted in 42 patients with recurrent UC. The diagnosis of UC was confirmed typical clinical symptoms and endoscopic examination of data. In order to determine the extent of UC study was conducted using hydrogen breath testing (HBT).

**Methods:** BO was studied using the HBT in 40 patients with UC. Level of BO was assessed with hydrogen breath testing (HBT) with the help of the device Gastro plus (Bedfont Scientific Ltd., UK). The partial pressure of hydrogen (PPT) has been defined in the basal conditions, further each 30 minutes during 3 hours after intake lactose. Graphico-mathematical analysis has done, the results were compared with clinical symptoms (diarrhea, constipation, alternating diarrhea and constipation, pain and gaseousness).

**Results:** Of the 40 patients with UC, 19 (47.5%) presented small intestine bacterial overgrowth (SIBO) and 32 (80%) BO of colon. In 29 (72.5%) patients was registered with at two typical peak rate of partial pressure of hydrogen to 60 and 120 minutes of research that the indicating SIBO and BO of colon. After of basic therapy (mebeverine 600 mg/day, dietary fiber supplementation (at least 20 g/day), and antibiotics (rifaximin and ciprofloxacin) re-breath test was performed. 22 patients received rifaximin

1.200 mg/day for 7 days. The remaining 18 patients received two 7 days cyclical treatment with ciprofloxacin 1000 mg per day. After treatment with rifaximin in 22 patients, 17 (77.3%) showed a negative "breath test" one week later as well as a significant reduction of symptoms, thus confirming the relationship between SIBO and many of the symptoms claimed by patients. Cyclical treatment with ciprofloxacin in 18 patients was accompanied by similar results in 6 (33.3%) cases.

**Conclusions:** In patients with US recorded a high frequency of BO explains the severity of clinical symptoms of recurrence. Treatment with topical nonabsorbable antibiotics is accompanied by a significant clinical effect.

## Effect of correction of nutritional deficiency and prognosis of remission in inflammatory bowel diseases

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**Background:** Development of nutritional deficiency (ND) due to the loss of nutrients, water and electrolytes with frequent stools, nutrients malabsorption, anorexia and increased catabolism is typical for patients with IBD relapse.

**Objective:** To determine the frequency and structure of ND in patients with IBD relapse and to evaluate the therapeutic effect of nutritional support (NS) of nutritive mixtures during the course of therapy.

**Methods:** Two-phase 3 step study with prospective monitoring in patients with IBD was conducted during 3 years in the period from 2010 to 2012. The first phase was carried out using a one-time screening scales MUST and NRS, further in phase 2, the NS structure was refined. 520 patients with IBD were examined: 410 with ulcerative colitis (UC) and 110 with Crohn's disease (CD). Results: The 1st, 2nd and 3rd degree of ND was detected in 111 (27.1%), 96 (23.4%) and 42 (10.2%) patients with UC, respectively. 2nd and 3rd degree of ND was recorded in 48 (43.6%) and 29 (26.4%) cases in patients with CD, respectively. At the second stage of the study, 80 patients with UC were randomized into 2 major groups, depending on the degree of NN, were divided into groups A (2d degree of ND) and B (3d degree of ND). On basic therapy, patients of the 1st group received a diet with a high amount of protein (HAPD) and increased calorage (2500 kcal/day), while to the patients of the 2nd group in addition to the basic therapy, nutritional mixtures: peptamen and modulen IBD (Nestle) in the amount of 1/3 of the daily calorage were prescribed. Efficacy of treatment was evaluated on the 3rd, 4th, 12th week. At the third stage of the study, during 3 years, the long-term results were studied using index of the relapse frequency (IRF). Pick of the IRF was in the 1st group and by the end of the study it was 15 (75%) and 17 (85%) cases, respectively. In the second group IRF was significantly lower: 9 (45%) and 12 (60%) ( $p < 0.05$ ).

**Conclusions:** In patients with UC and CD relapse ND of the 1st and 3rd degree was recorded an average of 20.3% and 35%, respectively. Use of NS provides a low rate UC relapse, and thus stable remission of the disease.

## Regional peculiarities of the course of Crohn's disease depending on the patients' age

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**Objective:** The aim of this study was to investigate age differences among patients with Crohn's disease (CD) in the population of Perm and Perm region.

**Material and methods:** There are 51 patients with CD in Perm regional clinical hospital from 2008 to 2014.

Results: All patients were divided into 3 age groups: the 1 group – 18-29 years old, the 2 group – 30-45 years and the 3 group – over 45 years. A recurrent form of the disease was observed in 10 cases (47.6%) in the 1 group and in 9 cases (52.9%) in the 2 group, whereas, the 3 group an acute form was noted in 6 cases (46.1%). By severity in 1 group had a mild form of the disease was noted in 8 cases (38.1%) in the 2 and the 3 group we noticed a severe course form of a 10 cases (58.8%) and 8 cases (61.5%). According to the localization of the pathological process among patients in the 1 group, in most cases there are isolated lesions of the small intestine (enteritis) in 11 cases (52.4%) in the 2 group – associated lesion of the colon and small intestine 7 cases (41.2%) in the 3 group – 6 colitis cases (46.1%). Systemic manifestations among patients in the 3 group were observed in 3 cases (23%), in the 1 group in 2 cases (9.5%) and in the 2 group in 3 cases (17.6%). The incidence of complications of the underlying disease was also higher in the 3 group of patients in 7 cases (53.8%).

**Conclusions:** The more severe forms of the disease were observed in persons older than 45 years; they have also significantly more common systemic manifestations and complications of the underlying disease.

## Duplex scanning of the liver's vessels as a method of studying the fibrosis

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**Objective:** To study the kind of relationships between the condition of hepatic vessels and the expression of fibrosis.

**Material and methods:** The study included 3 groups of patients. The first group – 20 patients with chronic viral hepatitis C (CHC), the second group – 32 patients with nonalcoholic steatohepatitis (NASH) and the third group – 20 patients with alcoholic steatohepatitis (ASH). The condition indicators of lineal and hepatic arteries were studied at all the patients. For this purpose the ultrasonic device Philips Envisor C HD was used in the mode of duplex scanning. The density of liver's tissue and the fibrosis stage were studied with the help of liver's ultrasonic elastography device Fibroscan F-504 (France). During the assessment of the liver's tissue density, criteria of the fibrosis stage for different etiological variants of hepatitis were used. Biopsy under ultrasonic control was a reference method. The

results were marked statistically with the type's description of quantities placement, middle values and their deviations. Also correlation and regression analysis were held.

**Results:** as the result of the group patients' investigation, the connection between indices' functioning of the liver's vessels and the degree of its fibrosis authentically differs. Thus, in the group with virus hepatitis the degree of fibrosis correlated with the size of lineal vein's diameter (F0-1:  $r=0,49$ ,  $p=0,041$ ; F1-4:  $r=0,65$ ,  $p=0,042$ ). In the group with nonalcoholic steatohepatitis (NASH) statistically significant reliability about interrelation of hepatic vessel's indicators and fibrosis degree wasn't received at all. Patients with alcoholic steatohepatitis (ASH) many interrelations between studied parameters were revealed. It allowed making an equation of multiple regressions for this group of patients in order to forecast the fibrosis degree according to ultrasonic duplex scanning of liver's vessels. Here you can see the following equation:  $IF = -1,17 + 0,11 \times MSBS - 0,11 \times EDBS + 0,16 \times MBS$ , where IF – the index of fibrosis, MSSB – maximum systolic blood stream speed in the lineal artery, EDBS – end-diastolic blood stream speed in the lineal artery, MBS – middle blood stream speed in the lineal artery. Moreover due to IF we are able to distinguish F0-1 from F3-4 ( $p=0,045$ ).

**Conclusions:** In practice for the estimation of the liver's fibrosis stage the investigation of hepatic vessels' condition must be used regularly, especially for those patients, who have CHC or ASH. At increase in groups of supervision this way can become the alternative of liver's biopsy.

## Prokinetics are effective in gastroesophageal reflux disease by improving delayed gastric emptying. A pilot study

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**Objectives:** Previous studies have shown that patients with gastroesophageal reflux disease (GERD) have slower rates of gastric emptying than control subjects. However, the involvement of delayed gastric emptying (DGE) in the pathophysiology of gastro-esophageal reflux disease (GERD) remains debated. The aim of this study was to investigate whether treatment with prokinetics in addition to PPI therapy would improve clinical symptoms in dyspeptic GERD patients with or without delayed gastric emptying.

**Methods:** 30 consecutive patients refractory to PPI over 6 month period were included in the study. DGE by Gastric Emptying Scintigraphy was defined when gastric emptying time (T1/2) > 70 min. Patients were divided according to presence of dyspepsia into dyspeptic group (n=12) and non-dyspeptic group (n=18). Mosapride citrate in addition to esomeprazole 40 mg was administrated for 4 weeks. Symptoms were evaluated using a standardized questionnaire before and after treatment.

**Results:** There was no statistical difference in age and gender between dyspeptic group and non-dyspeptic group ( $p=0.92$  and  $p=0.23$ , respectively). Prevalence of esophagitis was similar between dyspeptic group and non-dyspeptic group (58% vs 39%,  $p=0.31$ ). DEG was detected 75% in dyspeptic group and 28% in non-dyspeptic group ( $p=0.01$ ). Symptom improvement

was greater in dyspeptic group than non-dyspeptic group (75% vs 33%,  $p=0.02$ ).

**Conclusions:** Gastric emptying in dyspeptic patients with GERD is significantly slower than in non-dyspeptic patients regardless of esophagitis. Combination therapy with prokinetics in addition to PPI improves typical GERD symptoms in dyspeptic patients with GERD.

## Drug-induced liver injury in an Israeli hospital

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**Objectives:** Drug induced liver injury (DILI) is a common but underreported problem. A recent large Islandian study reported a prevalence of 19.1:100,000 with augmentin reported as the most common drug to cause DILI. The aims of the study are to evaluate the prevalence of DILI and the most common drugs that cause DILI, and to evaluate the use of Naranjo Score and CIOMS/RUCAM scale for DILI (at least a score that matches "possible drug injury" in both tests).

**Methods:** All medical files with the diagnosis of "Drug induced liver injury" were evaluated and those patients that were defined by both criteria as "possible" having DILI were chosen.

**Results:** 78 patients were admitted due to DILI in 2003-2014. The prevalence was 1.625:100,000 person-years or 0.18:1000 admissions. Statins (34.6%) were found to be the most common drug associated with DILI. Antibiotics (17.9%) were the second most common. Augmentin (11.5%) was the most common antibiotic to cause DILI. Chemotherapy (12.8%), anticonvulsive drugs (7.7%), NSAID (5.1%), antipsychotic drugs (6.4%) and others were less common causes for DILI.

**Conclusions:** DILI is a common problem in Israel, but is probably under diagnosed and under reported (at least in our hospital). The most common drugs for long term use that causes DILI are statins. Augmentin is the most common short period used drug that causes DILI. Using both Naranjo Score and CIOMS/RUCAM scale may offer more reliability to the diagnosis of DILI.

## Epidemiology of upper GI bleeding in southern Israel

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**Objectives:** Upper GI bleeding is a very common cause for admission to ER with a high rate of death (8-10%). The aim of

the study: to evaluate prevalence, main causes, risk factors and mortality among patients admitted for GI bleeding in our hospital.

**Methods:** All medical files of patients with diagnosis of "Gastrointestinal Bleeding" were evaluated by a resident and information was collected by an EXCEL file.

**Results:** 448 patients were admitted to ER during the years 2003-13. The prevalence of GI bleeding was 112:100,000 adult patient-years. Male/female ratio was 2:1. Females were 10.4 years older than males in average. ASA score was 3 in most patients. Peptic disease was the most common cause for bleeding with duodenal ulcer first (22.5%) and gastric ulcer second (13.6%), erosive gastritis (10%), varices (7.5%), esophagitis (4.9%). Melena was the most common manifestation (49.3%) more than hematemesis (26.5%). 58% of patients were admitted to surgery department and 38.6% to internal medicine ward only 3% were admitted to ICU. Mortality was 9.9%. Hemostasis during endoscopy was needed in 16.3% of patients. Second look endoscopy was done during hospitalization in 12.1% of patients. Surgery was performed in 5.1% of patients.

**Conclusions:** 1) GI bleeding is a common problem in Israel; 2) Peptic ulcer is still the most common cause for GI bleeding; 3) Mortality is still high in GI bleeding and higher prevalence of admitting severe bleeders to ICU (and not to Internal Medicine departments) may help.

## Streptococcus intermedius bacteremia and hepatic abscess

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**Introduction:** Streptococcus intermedius is a member of the Streptococcus anginosus group of bacteria that comprises normal microbiota of the gastrointestinal tract and oropharynx. Despite being regarded as a harmless apathogenic commensal, Streptococcus intermedius is associated with abscess formation and rarely endocarditis.

**Case report:** A 70 years old Caucasian male presented to our emergency with fever (38-40°C), malaise, dull non-radiating right-sided abdominal pain, nausea, vomiting and poor appetite with seven days of evolution and progressive worsening. He had history of hypertension, dyslipidemia, type 2 diabetes and gallstones with previous episodes of cholecystitis. Laboratory findings showed leukocytosis (24.8×10<sup>9</sup>/l), partly based on the neutrophil count (86%), elevation of C-reactive protein (274.8 mg/l), aspartate aminotransferase 102 IU/l, alanine aminotransferase 115 IU/l and total bilirubin 1.68 mg/dl. Culture of urine was negative and was isolated in blood cultures Streptococcus intermedius. An abdominal computer tomography scan was performed which revealed a hypodense hepatic lesion with 9 cm of diameter with poorly defined and irregular contours suggestive of abscess. After 14 days of antibiotic therapy with piperacillin-tazobactam held aspiration biopsy and percutaneous drainage of the abscess which confirmed a pyogenic liver abscess caused by Streptococcus intermedius. There was a significant clinical, imaging and laboratory improvement and was discharged to home medicated for another seven days with

amoxicillin + clavulanic acid. It was assumed that the abscess was associated with episodes of cholecystitis and three months later was submitted to laparoscopic cholecystectomy which had no complications.

**Discussion:** Pyogenic hepatic abscesses are uncommon conditions that present diagnostic and therapeutic challenges to physicians. Frequency of pyogenic liver abscess is higher in diabetics than in the general population and they are often associated with recurrent cholangitis or presence of biliary stones. If left untreated, these lesions are invariably fatal. Because symptoms are often nonspecific, a high index of suspicion is required.

## Screening and dynamic evaluation of disorders of motor-evacuation function of the stomach ultrasound techniques

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**Objective:** To evaluate the prevalence of motor-evacuation function of stomach disorders by ultrasound among patients of therapeutic profile.

**Material and methods:** The study involved 90 patients who were hospitalized in a therapeutic clinic, diseases of internal organs. The mean age of patients was 46,9±2,2 years, among them men – 77.5%, women – 22.5%. According fibrogastroduodenoscopy (FGDS) and ultrasound determined criterion 4 motor-evacuation disorders of the stomach: the presence of hiatal hernia, duodenal and gastroesophageal reflux disease, failure of the cardia.

**Results:** The analysis of the results of the ultrasound revealed violations of the motor-evacuation function of the stomach in 92.5% of cases. Young patients (WHO classification) amounted to 37.5%, middle age – 45%, elderly – 17.5%. Violations of the motor-evacuation function of the stomach on the results of ultrasonography were presented in 15% of cases of hiatal hernia, in 17.5% of cases of duodenal reflux, in 37.5% – gastroesophageal reflux and incompetence of cardia – in 37.5% of cases. In comparison with the data obtained in violation of FGDS motor-evacuation function of the stomach were presented hiatal hernia in 17.5% of cases (p=0.763), duodenal reflux in 12.5% of cases (p=0.533), 37.5% – gastroesophageal reflux (p=1.000) and the failure of the cardia was diagnosed in 80% of patients in contrast to the results of US, where it is installed 37.5% of cases (p=0.0009).

**Conclusions:** Thus, these data suggest a high frequency of motor-evacuation disorders of the stomach in patients with pathology of internal organs. When comparing the criteria motor-evacuation disorders of the stomach on the results of FGDS and ultrasound found no differences in the frequency of their symptoms than the index indicating the failure of the cardia, where the "gold standard" for determining this disease is intraesophageal pH-meter (Russian clinical guidelines in gastroenterology, 2008). In contrast, from the endoscopic, ultrasound examination of the stomach has a number of advantages, such as non-invasive procedures, highly informative, easy to study, harmless to the health of the patient and the absence of contraindications. This method



of diagnosis to optimize pharmacological treatment as non-invasive ultrasound examination can be carried out many times in the dynamics. All of this suggests the need for clinicians of the method of diagnosis in order to identify screening motor-evacuation disorders of the stomach, to prevent the development of complications in the gastrointestinal tract in patients with pathology of internal organs.

### **Additional markers in diagnostics of gastroesophageal reflux disease with pulmonary manifestations and its combination with asthma: surfactant protein D and alveolar macrophages phenotype**

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**Objectives:** Among main components in pathogenesis of asthma (A) and pulmonary manifestations of gastroesophageal reflux disease (GERD) are immune response disorders depending largely on the balance of alveolar macrophages (AM) functional phenotypes. One of significant regulatory components of AM activity is surfactant protein D (SP-D). The aim of the study to analyze AM phenotype, quantitative and qualitative compound of SP-D in broncho-alveolar lavage fluid (BALF) in GERD with pulmonary manifestations and GERD and A combination.

**Material and methods:** Analysis of AM phenotype in patients with GERD (n=15, 46,4±4,2 y.o.), combination of GERD and A (n=16, 49,3±3,6 y.o.) and healthy volunteers (HV) (n=10, 51,8±3,5 y.o.) was performed by flow cytometry (Beckman Coulter FC500) by expression of M1 and M2 AM phenotypes CD markers (CD25, CD80 and CD163, CD206, respectively) and cytokine production of pro-, anti-inflammatory (M1, M2) and bivalent M1/M2 cytokines in culture medium (CM) of AM (BenderMedSystems, BMS810FF). Quantitative analysis of SP-D in BALF was performed by ELISA. Qualitative assessment of SP-D oligomeric forms in BALF was performed by western blot analysis using tris-acetate gels (Invitrogen, NuPAGE, # EA03752BOX).

**Results:** AM phenotype analysis in patients with GERD, GERD and A vs. HV showed that pooled M1/M2 ratio of AM CD markers and cytokine production was 2.16 and 2.52, 0.91 and 0.84 vs. HV, respectively. The results indicate shift of AM towards M1 phenotype vs HV in GERD and towards M2 phenotype vs HV – in GERD and A. In GERD patients SP-D level was 2.66 times decreased vs patients with GERD and A (155.8±18.1 ng/ml vs 414.7±50.2 ng/ml, p<0.05) and 3.42 times decreased vs. HV (155.8±18.1 ng/ml vs 533.2±21.1, p<0.05). Qualitative analysis of SP-D oligomeric forms in GERD and GERD with A showed predominance of monomeric forms vs HV with monomeric and multimeric SP-D oligomers.

**Conclusions:** In GERD with pulmonary manifestations and combination of GERD and A, AM phenotype and quantitative and qualitative composition of SP-D in BALF vary against HV and each other. Shift of AM phenotype towards M1 vs healthy and significant maximum decreased SP-D level in BALF are

typical for GERD with pulmonary manifestations, whereas shift of AM phenotype towards M2 and less decreasing SP-D level in BALF are specific for combination of GERD and A. There were no significant differences in qualitative oligomeric composition of SP-D in BALF in GERD and its combination with A.

### **Alveolar macrophages phenotypic plasticity in patients with gastroesophageal reflux disease with pulmonary manifestations and its combination with asthma**

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**Objectives:** In spite of different points of view on etiology and variety of cellular and molecular pathogenetic components of pulmonary manifestations in gastroesophageal reflux disease (GERD) and combination of GERD and asthma (A) there is a key feature of inflammation and the immune response disorder in the form of Th1/Th2 imbalance in the disease pathogenesis. Considering the concept of Th1/Th2 immunity and M1/M2 programming in changing microenvironment macrophages can change their phenotype in the disease formation, i.e. they possess phenotypic plasticity (PP). The aim of the study: assessment of alveolar macrophages (AM) PP in GERD and its combination with asthma (A) and healthy volunteers (HV) under the influence of different serum (FBS) concentrations.

**Methods:** In vitro experiments were carried out on AM, isolated from BALF of patients with GERD (n=15, 46,4±4,2 y.o.), combination of GERD and A (n=16, 49,3±3,6 y.o.) and HV (n=10, 51,8±3,5 y.o.). AM phenotype was assessed by flow cytometry (Beckman Coulter, FC500) by cytokine production of pro- M1, anti-inflammatory M2 and bivalent M1/M2 cytokines in culture medium (CM) of AM (BenderMedSystems, BMS810FF). Phenotypic plasticity of AM was measured as percentage change of markers during 36 hours of AM reprogramming in the presence of 0%, 10%, 40% FBS, containing endogenous reprogramming factor – surfactant protein D.

**Results:** Analysis of M1 and M2 phenotypic plasticity in GERD and GERD+A against HV showed maximum of M1 phenotypic plasticity in GERD – M1/M2 index of the macrophages ability to change their phenotype towards M1 was 5.33 and this was 8.5 times increased vs GERD+A (p<0.05). Maximum macrophage phenotypic plasticity towards M2 phenotype was observed in combination of GERD with A and M1/M2 index of phenotypic plasticity was 5.45 times higher than in GERD.

**Conclusions:** The ability of AM to change their phenotype under the influence of microenvironment in GERD and GERD+A was changed as compared to HV. In GERD macrophages possess more possibilities to obtain M1 phenotype than M2, but in combination of GERD and A macrophages are more predisposed to obtain M2 phenotype. So the studied ability of macrophages to adapt their phenotype to the microenvironment and to reprogram the phenotype of the cells can be thought of as the base for new therapy approach in personalized medicine influencing the initial links of inflammatory response and Th1/Th2 imbalance even in initial stages of pathological process.

## Starting as a stroke, ending as Crohn's disease

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**Introduction:** Crohn's disease is an inflammatory condition of unknown etiology that can affect any portion of the gastrointestinal tract, from the mouth to the perianal area. In 80% of cases there is involvement of the small intestine, often in the terminal ileum. It is characterized by the presence of abdominal pain, diarrhea, weakness and/or weight loss. Usually, Crohn's disease has a peak of incidence between the ages of 15 and 30 years old. However it can also present for the first time in older patients.

**Case report:** We present a case report of a 70 years old woman with a history of hypertension, obesity and depressive disorders. After 15 days of moderate abdominal colic pain and diarrhea, with no mention of blood or mucus, the patient went to the emergency department, where she was treated with ciprofloxacin. Four days later, she presented at the emergency department with dysarthria and loss of muscle strength on the right side of her body, symptoms that appeared suddenly. The patient was admitted to the Internal Medicine department with the diagnosis of cerebrovascular accident. Head computed tomography showed a temporal area of hypodensity on the left side. Laboratory tests showed acute kidney injury and mild leukocytosis. At the end of the third day at the hospital, there was a full recovery of neurological deficits reported at admission. Meanwhile, the diarrhea persisted. Infectious etiologies were excluded. An esophagogastroduodenoscopy and colonoscopy with biopsy were performed, revealing gastric ulcers, nonspecific duodenitis and ulceration of the ileal mucosa, compatible with Crohn's disease. As an outpatient, she began oral corticosteroid therapy. A few weeks later, she had a relapse, reason why she was started on azathioprine, with clinical and histological improvement.

**Discussion:** With this presentation we would like to remember that it is also common a peak onset of symptoms of Crohn's disease between the ages of 60 and 80 years old, so it reiterates the importance of a careful history taking in elderly patients with persistent diarrhea, even when it is not what led to the hospital admission.

## Does a physiotherapeutically coordinated exercise programme have a positive effect on irritable bowel syndrome?

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**Objective:** Irritable bowel syndrome (IBS) is an inorganic disease of the gastrointestinal tract. Affected people suffer from subtype A, type B or type C. Those affected usually have had a long medical history and have gone through a multitude of medical exams before arriving at this diagnosis. In therapeutic practice various measures are undertaken. Amongst other things physical activity is recommended and named in the DGVS guidelines

(German society for gastroenterology, digestive and metabolic diseases). Still there is a lack of concrete recommendations regarding kind, intensity and duration of such activities, which in turn was the starting point for our degree dissertation, entitled 'Does a physiotherapeutically coordinated exercise programme have a positive effect on irritable bowel syndrome?'

**Methods:** In a pilot study one intervention group consisting of three patients (2 female, 1 male) performed: 1) Regular physical activity for 20 min. twice a week ergometer training; 2) Strengthening exercises for the anatomically enclosed and functionally influential structures (M. iliopsoas, M. transversus abd., trunc musculature); 3) Activation of the pelvic floor; 4) Regulation of muscular tonus: relaxing and stretching of M. quadratus lumborum und M. iliopsoas combined with breathing techniques. The intervention took place as an individual therapy once a week for a duration of 45 min. over a 5 week period. The effect was evaluated using the IBS-SSS as well as the daily monitored Bristol Stool Form Scale.

**Results:** A total of two patients completed the study. The IBS-SSS showed clinically relevant improved scores from 345 points to 120 points and 280 to 100, respectively. Due to limited subjects, there was no significant correlation of the physiotherapeutic exercise programme and the improvement of the IBS-SSS (p-value of 0.147). The progression of the Bristol Stool Form Scale was depicted using descriptive statistical tools. Over the course of five weeks both patients showed a tendency towards normal values.

**Conclusions:** Thus an individual, physiotherapeutically coordinated exercise programme has a positive effect on IBS. Since the IBS-SSS-point values of both patients could be strongly reduced, it can be concluded in accordance with the literature (Betz et al., 2013) that there was an improvement of the symptoms and consequently clinical relevance. Further studies are recommended.

## Bacterial overgrowth syndrome and modification of protocol treatment of severe ulcerative colitis

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**Objectives:** The ambiguity of chronic mechanisms of ulcerative colitis (UC) determines the feasibility of improving the protocol of the disease diagnosis and treatment. To this end, an open study has been conducted concerning the evaluation of efficiency of incorporating of basic protocol of the UC therapy by noninvasive method of diagnosis of bacterial overgrowth syndrome (BOS) and directional selective decontamination with the use of rifaximin (R) (alpha normix, Alpha Vasserman, Italy).

**Methods:** A prospective, randomized, open study of 29 patients with the severe flow of UC (average duration 6.7±3.6 years) has been conducted. The UC diagnosis is verified through complex examination: the degree of activity was assessed by Mayo index (MI). All patients before treatment had respiratory

digital hydrogen test with lactulose (RHTL) with the help of electrochemical gas analyzer Gastro+ (Bedfont Scientific Ltd., UK). The hydrogen partial pressure (HPP) was assessed in basal conditions, then, every 30 minutes, for 3 hours. Results of graphic and mathematical analysis of (RHTL) were compared with bacteriological examination of feces, stating the presence and extent of BOS. The basic therapy included: salofalk 3 g/day and azatioprin 2.5 mg/kg/day. Patients were divided into two groups according to the method of simple randomization: I group – 13 patients, received metronidazole (M), 0.75 g/day for 20 days; II group – 16 patients had two 6-day courses with the interval in 7 days, a topic antibiotics R in the daily dosage – 1200 mg. Clinical efficiency of the therapy was assessed according to RHTL data on the 24th day of treatment.

**Results:** In 24 (82.7%) patients with UC was registered a typical peak of the triple gain of (HPP) to the 140th minute of study, which stated the existence of BOS of the 2nd degree. 24-day course therapy was followed by positive effect: in the I st group, the decrease of MI was recorded for 2 and 3 points in 6 (46.2%) and in 7 (43.8%) patients, respectively. In the II nd group: in 12 (75%) patients, the decrease of IM was recorded for more than 3 points. Results of RHTL showed a decrease of BOS after the treatment: in the I st group of patients, PDV constituted on average  $2.85 \pm 1.4N$ , in the II group –  $1.3 \pm 0.3N$ .

**Conclusions:** The use of RHTL registers a high frequency of SIBR in UC patients for the period of the disease relapse. The use of repeated courses of therapy R is significantly more efficient than the long-term use of M.

### Evaluation of the fecal neutrophil gelatinase-associated lipocalin in patients with different ulcerative colitis behavior

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**Objectives:** Fecal neutrophil gelatinase-associated lipocalin (NGAL) is a novel noninvasive surrogate marker of inflammation. Evaluation of NGAL in different clinical variants of ulcerative colitis (UC) is important. We aimed to evaluate the fecal concentration of NGAL in different courses of inflammatory bowel disease (IBD).

**Methods:** We prospectively included 72 patients with UC (exacerbation – 67, remission – 5) and 15 healthy controls. Fecal NGAL was determined by ELISA in fecal specimens. The average age of patients with UC was  $37 \pm 1$  years, in the control group –  $31 \pm 2$  years. Severity of UC was assessed by Mayo score: mild UC was seen in 22 (33%), moderate – 28 (42%), severe – 17 (25%). Location of UC was next: proctitis – 5 (7%), left-sided colitis – 27 (40%), total colitis – 35 (53%).

**Results:** Fecal NGAL level was increased in active UC – 4668 (1298; 7792) ng/ml ( $p < 0.05$ ), in remission – 3004 (1136; 4444) ng/ml ( $p > 0.05$ ) compared with healthy controls – 181 (169; 720) ng/ml. In severe UC fecal NGAL was higher – 6044 (4605; 9632) ng/ml than in moderate UC – 4963 (2198; 7780) ng/ml ( $p > 0.05$ ) and mild UC – 2194 (786; 4668) ng/ml ( $p < 0.05$ ). In total colitis fecal NGAL was higher – 5008 (1388; 8928) ng/ml than in left-

sided colitis – 4607 (1708; 6792) ng/ml ( $p > 0.05$ ) and proctitis – 1132 (965; 8730) ( $p > 0.05$ ). Fecal NGAL correlated with the stool consistency ( $r = 0.25$ ;  $p < 0.05$ ) and the weight loss ( $r = 0.27$ ;  $p < 0.05$ ), also with the erythrocyte sedimentation rate ( $r = 0.44$ ;  $p < 0.05$ ). ROC-analysis defined the threshold of fecal NGAL as a marker for determining an active phase of inflammation in UC – 1029 ng/ml, to which were empirically determined sensitivity of 80%, specificity of 93%, and AUC – 0.94. Thus, the findings suggest that studied indicator have high resolution in identifying IBD.

**Conclusions:** Fecal NGAL is a novel non-invasive marker to distinguish active UC from healthy individuals with a high sensitivity, specificity and AUC. Fecal NGAL might be used as one of the noninvasive biomarkers of intestinal inflammation.

### A rare cause of hepatic cirrhosis: Osler-Weber-Rendu disease

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**Introduction:** Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal-dominant disorder which affects 1 in 5-8000 people. Arteriovenous malformations are also characteristic lesions which may occur in pulmonary, cerebral and hepatic circulations.

**Case report:** 71 years old male admitted to hospital with complaining of swelling at lower extremities and recurrent nose bleeding. He was diagnosed as Osler-Weber-Rendu syndrome 20 years ago. In physical examination, bilateral inspiratory crackles at the lung bases, hepatosplenomegaly, pitting edema at lower extremities, multiple erythematous macular lesions on palms, nail bed and face, multiple erythematous papulonodular lesions on the tongue and oral mucosa were detected. Blood tests were as follows: hematocrit 9.7%, MCV 86 fL, platelet count 170.000 uL, aspartate transaminase 23 U/L, alanine aminotransferase 15 U/L, prothrombin time 13.2 sec., alkaline phosphatase 105 U/L, gamma glutamyl transferase 22 U/L, albumin 1.8 g/dL, globulin 1.9 g/dL, bilirubin total 0.79 mg/dL. Albumin was detected at normal range in urine. Thorax computed tomography (CT) scans showed bilateral pleural effusion but did not show arteriovenous (AV) malformations. Portal Doppler ultrasonography showed multiple venous collaterals in liver parenchyma. Multiphasic contrast-enhanced helical CT scans of the liver showed enlarged hepatic artery, portal vein and enlarged spleen with several collateral vessels in the splenic hilum as well as in the porta hepatis. Cirrhosis like surface changes (contour nodularity, hypertrophy of left hepatic lobe and parenchymal heterogeneity, etc.) were noted. Ascites was not detected. Hepatic arteriography showed diffuse telangiectases but no signs of AV shunt were documented. High-output cardiac failure was not detected by transthoracic echocardiography. Other causes of hepatic dysfunction (hepatitis B and C, alcoholic cirrhosis, Wilson's disease, etc.) were excluded. Portal hypertension and hepatic dysfunction, result from diffuse telangiectases leading to perfusion abnormalities in the liver parenchyma, was thought in this case.

**Discussion:** Because of there is still no consensus about

screening, diagnosis and treatment; highlighting the importance of the disease and sharing different cases is significant. As in this case, when determining the etiology of cirrhosis, rare causes also should be considered.

## A rare malignancy: primary malignant peritoneal mesothelioma

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**Introduction:** Malignant mesothelioma is a tumor originating from mesothelial cells with most common type pleural (90%), and second most common type is peritoneal (6-10%). Primary malignant peritoneal mesothelioma is a rare cancer of the peritoneum which is very difficult to diagnose and treat. Studies show that natural or industrial asbestos exposure increases the frequency of the disease. Especially asbestos exposure in the houses that were built with asbestos-containing materials is important part of the etiology.

**Case report:** A 77 years old female patient had an ongoing non-specific loss of appetite and abdominal pain complaints for 1 month. She applied to the hospital when she had swelling in her stomach for the last 20 days. Upper gastrointestinal endoscopy and colonoscopy were normal. Ascites was detected in physical examination. Abdominal ultrasonography showed free fluid in abdomen. Paracentesis revealed gelatinous ascites. Serum ascites albumin gradient was <1.1. Free fluid in abdomen, increase in nodular thickness in several places of the peritoneal surface and omental cake appearance was detected in abdominal tomography which was performed to investigate the etiology of ascites. PET CT showed no abnormal findings except the image compatible with omental cake in the mesentery. Patient was evaluated by oncology and women's health clinic however, there was not any finding explaining the etiology of ascites. Patient was diagnosed with primary malignant peritoneal mesothelioma after performing biopsy of the peritoneum with ultrasound. The detailed medical history revealed that, in the area where the patient is living, asbestos was used in the walls of the houses. Patient was discharged with planned treatment by medical oncology clinic.

**Discussion:** Diagnosis and treatment of malignant peritoneal mesothelioma is difficult. This illness should be kept in mind especially if the patient is living in high risk areas and have complaints compatible with the illness.

## Effectiveness of ultrasonography in the early diagnosis of gastroesophageal reflux disease

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**Objectives:** Earlier we and other investigators have shown that sonographic evaluation of abdominal segment of esophagus

can help in diagnosis of gastroesophageal reflux disease (GERD). Analysis of scientific literature has revealed absence of publications on sonographic assessment of other esophageal segments in GERD patients. The purpose of this study is to analyze if it is possible to find any morphofunctional changes in cervical segment of esophagus in GERD patients by sonography.

**Material and methods:** 36 patients with verified GERD and 12 healthy subjects without any esophageal disorders during gastroduodenoesophagoscopy were included in the study. Scanner Philips EnVisor HD with linear probe 12-3 MHz was used for ultrasonography. Exam was performed on an empty stomach. In decubitus position at the level of thyroid isthmus we have evaluated structure and thickness of mucosa and muscular layer of esophagus, presence of fluid and character of its movement, measured internal esophageal dimension. Then in upright position time of path of drink of standard chicken broth along esophagus was measured. After intake of 400 – 800 ml of chicken broth all measurements were repeated in decubitus position.

**Results:** Amongst all analyzed parameters statistically significant differences were detected in two. Internal esophageal dimension in patients was larger than in healthy subjects and time of path of drink of standard chicken broth through esophagus was less (4.95 vs 4.45 mm post fast and 10.1 vs 9.5 mm after test meal; 1.84 vs 2.32 s post fast and 1.66 vs 2.68 s after test meal, respectively).

**Conclusions:** Changes in two parameters in patients with GERD most likely are functional, not structural. They are related to esophageal tonic and motor activity disturbances. Ultrasonography of cervical segment of esophagus can be useful in detection of GERD and in follow-up.

## Severe alcoholic hepatitis. Prognostic scores and lipid peroxidation

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**Objectives:** Severe alcoholic hepatitis is associated with high mortality (50% in some series). Multiple scores to detect these severe cases have been developed. Moreover, a fundamental aspect of the pathogenesis is lipid peroxidation and the formation of neoantigens that contributes to increased liver damage. The aim of this study is to determine the best score to predict mortality. The relationship between lipid peroxidation and the scores was also analyzed.

**Methods:** 62 patients with severe alcoholic hepatitis (Maddrey DF  $\geq$ 32) were successively included. Maddrey DF, MELD, MELD-Na, ABIC and Glasgow scores were calculated at admission and a week. Also the Lille Model was computed. Finally, MDA levels were also measured at admission and a week.

**Results:** The mean age was 51.9 years (SD  $\pm$ 10.7). Maddrey DF and MELD, both one week after admission, were associated

with mortality (log rank =8.406 p=0.004; LR=13.34, p<0.001, respect) and ABIC and Glasgow scores too (LR=12.299, p<0.001; LR=11.692, p=0.001, respect). Just MELD-Na was associated with mortality at admission and after one week (LR=6.241, p=0.012; LR=13,599, p<0.001, respect.). Lille Model also predicted mortality (LR=5.746; p=0.017). MDA levels, both at admission and after one week, were also associated with mortality (LR=7.894, p=0.005; LR=10.163, p=0.001, respect.). MDA levels were correlated with all the indices calculated at admission and at one week, except for a non significant trend between ABIC at admission and MDA at admission and at one week; between Glasgow score at admission and MDA a week; and between Glasgow score a week and MDA at admission.

**Conclusion:** All scores after the first week were associated with mortality at 180 days. At admission, only MELD-Na also predicted it. In our sample, MELD-Na at one week was the strongest predictor of death at 180 days. Furthermore, MDA levels, both at admission and at the first week, were related with prognosis and also directly correlated with all scores, a result that underscores the relevance of lipid peroxidation in the evolution of this disease.

## Efficiency of legislative measures to restrict the sale of alcohol in the Sakha Republic (Yakutiya)

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**Background:** Alcohol consumption in industrialized countries is the cause of chronic pancreatitis (ChP) in 50-80%. Currently, 6-7 new cases of (ChP) per 100000 populations are registered annually depending on geographic region. Alcohol is the most important risk factor of disease. In order to reduce alcoholism substantial measures were taken. The Decree of the President of Republic of Sakha (Yakitia) «On measures for prevention of alcohol abuse in the Republic of Sakha (Yakitia)» from November 1, 2010 banned retail sale of alcohol beverages from 20:00 in the evening of the current day until 14:00 on the following day in the territory of Yakutia. Than a federal law of the Russian Federation was passed on July 18, 2011 and some legislative acts of the Russian Federation were adopted.

**Objective:** To estimate the dynamics of hospitalization of patients with (ChP) alcoholic etiology in gastroenterological department of Yakutsk City Clinical Hospital after the adoption of measures for the prevention of alcoholism at the regional and federal levels.

**Material and methods:** Medical records analysis for the period 2007-2013 years. Statistical processing by program «BIOSTAT».

**Results:** 6403 patients were admitted to the department for the reporting period, 778 patients (12%) with ChP. The number of these patients decreases year by year: 132 patients (14,5%) – in 2007 year; 82 (8,7%) – in 2013 year. Women prevailed among the hospitalized from 2007-2011 (57-59%), however since 2012 men prevail (51%).

**Conclusion:** Reduction in the number of cases of chronic pancreatitis is connected with the introduction of measures for restriction of sale of alcoholic products at the state level.

## Overlap syndrome of cholestatic liver diseases and autoimmune hepatitis

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**Introduction:** No historical symptom defines any of the overlap syndromes. The three main categories of autoimmune liver diseases are autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC), each regarded as a distinct entity with constellation of specific clinical, biochemical, immunological, and histological profiles.

**Case report:** A 69 years old woman was admitted to our department with asthenia, pruritus and rash. The patient had history of type 2 diabetes mellitus (with diabetic retinopathy), cholecystectomy and acute pancreatitis two years before. She denied alcohol abuse. The physical examination revealed only telangiectasia in malar region. Laboratory tests showed mild thrombocytopenia, significant cholestasis and elevation of aminotransferase levels. Immunological tests revealed positive antinuclear (1:320) and antimitochondrial antibodies (1:640) with negative anti-smooth muscle and liver kidney microsomal type 1 antibodies. An abdominal computed tomography showed hepatomegaly with hypertrophy of the caudate lobe and left lobe compatible with liver cirrhosis. The liver biopsy revealed portal fibrosis, interface hepatitis and bile duct proliferation. Patient initiated ursodeoxycholic acid 1 g/day according to standard of care. Due to weak biochemical improvement, immunosuppressive therapy was initiated with prednisolone 30 mg/day and azathioprine 50 mg/day. Significant improvement of the analytical parameters was observed.

**Discussion:** The initial diagnosis was primary biliary cirrhosis, but the precarious response led to initiate immunosuppressive therapeutic. The patient responded favorably. The final diagnosis was overlap of primary biliary cirrhosis and autoimmune hepatitis.

## Studying paracentesis: performed tests and etiology

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**Objective:** The goal of this study is to describe the features of patients with recently diagnosed ascites in a third-level hospital and its causes.

**Methods:** Review of patient records with a first episode of ascites that undergo diagnostic paracentesis and analysis of ascitic fluid (AF) within 18 months (January 2010 – June 2011).

**Results:** 39 patients with ascites were included. Their mean age was 61±17 years [21-94], and 53% were women. Medical history: active alcohol abuse 10%, heart failure 15%. AF analysis: median 315 cells/mm<sup>3</sup> [8-4060] with lymphocytic predominance (66±29%), total proteins 3.1±2.1 g/L, albumin 1.8±1.1 g/L, glucose 122±40

g/dL. Cultures were taken in 77% of the cases, only 1 came back positive and was considered a contamination. Ziehl-Nielsen staining and mycobacterial culture were performed only on 20% of the AF, all of them resulting negative. Cytological study was done on 59% of the samples, 21% of them were positive. Serum values: 54% had bilirubin <2 mg/dL, 28% had albumin >3.5 g/L and 87% an INR <1.7. Other complementary tests performed were abdominal ultrasonography (41%), abdominal CT-scan (62%) and oral gastroscopy (26%). These tests revealed: primary neoplasia 32%, metastasis 31%, signs of portal hypertension 28%, liver nodularity 23%, peritoneal implants 15%, esophageal varices 13%, portal hypertensive gastropathy 10%, portal thrombosis 8%. Liver CNB/FNAB was performed in 4% of the cases. The cause of ascites was: neoplasia 51% (ovary 35%, pancreas 25%, colorectal 15%, others/unknown 10%, stomach 5%, endometrium 5%); liver disease 28% (64% chronic alcoholic liver disease, 37% acute hepatitis: 2 cases due to drugs, 1 due to HBV and 1 due to autoimmune disease); heart failure 10%; acute pancreatitis 5% and other causes 6%. The median survival was 4 months.

**Conclusions:** The most common causes of a first episode of ascites in a patient without a history of cancer or liver disease were neoplasms and previously non diagnosed chronic alcoholic liver disease. Among the neoplastic causes, the most important are ovarian and pancreatic cancer, which means the diagnosis of these diseases is done in advanced stages.

### **Prolapsing antral gastric polyp: a rare cause of gastric outlet obstruction**

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**Introduction:** Gastric polyposis is an increasingly diagnosed disease due to the use of endoscopy. However gastric outlet obstruction caused by a prolapsing antral gastric polyp is a rare entity. We describe a case of dynamic pyloric obstruction by a gastric polyp.

**Case report:** An 81 years old woman, hospitalized by anorexia, intermittent postprandial vomiting and weight loss of 17 kg started 7 months before. The upper endoscopy showed a 2.5 cm antral polyp. In abdominal computed tomography scan was observed a doubtful gastric wall thickening so a diffuse gastric neoplastic disease was suspected. Therefore an upper gastrointestinal series (barium X-rays) was performed showing an antral image compatible with polyp and demonstrated its prolapse through the pylorus to the duodenal bulb. The patient totally recovered after endoscopic polypectomy. Taking into account all these findings a dynamic pyloric obstruction by gastric polyp was confirmed. Pathologic examination showed fundic gland polyp.

**Discussion:** The dynamic pyloric obstruction caused by gastric polyp is rarely described in the literature and is associated with large antral polyps. Currently the diagnosis and therapy are usually made by upper endoscopy. In this case it was necessary using upper gastrointestinal series (barium X-rays) for intermittent prolapse demonstration, not observed in upper endoscopy. The authors emphasize the rarity of the phenomenon and its demonstration by a classical radiographic method.

### **Alpha-Klotho levels, liver function and short term mortality in a cohort of alcoholic patients**

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**Objetives:** Fibroblast growth factor 23 and its cofactor alpha-Klotho have been extensively studied in their role in regulating bone metabolism. However, increased FGF23 levels have recently been associated with increased cardiovascular risk in patients with chronic kidney disease. Just like renal disease, alcoholism is a pro-inflammatory condition that is related to increased mortality. The aim of this study is to analyze short term mortality among alcoholic patients admitted to our hospital.

**Methods:** 60 alcoholic patients aged  $58 \pm 11$  years were followed-up after being admitted to our hospital. Liver function was assessed using Child score. Patients underwent laboratory testing and levels of FGF-23,  $\alpha$ -Klotho and sclerostin were determined.

**Results:** We followed up patients for a minimum of 1 month and a maximum of 14 months (median: 8 months). During this time period, 15% of patients (9 cases) died. Those who died had higher levels of  $\alpha$ -Klotho ( $Z = -3.05$ ,  $p = 0.002$ ) and FGF-23 ( $Z = -2.32$ ,  $p = 0.02$ ) than survivors. When comparing patients with  $\alpha$ -Klotho levels above and below the median, it was found that patients who died had significantly higher  $\alpha$ -Klotho levels (Log rank  $\chi^2 = 9.67$ ,  $p = 0.002$ , Breslow  $\chi^2 = 8.495$ ,  $p = 0.004$ ). No differences were found between patients who died and survivors regarding FGF23 and sclerostin levels that were above or below the median. A correlation was also found between high  $\alpha$ -Klotho levels and low prothrombin activity ( $\rho = -0.75$ ,  $p < 0.001$ ), low albumin ( $\rho = -0.59$ ,  $p < 0.001$ ), and high bilirubin ( $\rho = -0.64$ ,  $p < 0.001$ ). By logistic regression analysis comparing mortality with  $\alpha$ -Klotho levels, age, hypertension, and diabetes, it was found that the only parameter independently related to mortality was  $\alpha$ -Klotho. However, when Child score was included in the analysis, only Child score and hypertension were selected as having independent predictive values for mortality.

**Conclusions:**  $\alpha$ -Klotho levels were higher among patients who died. Hypertension and Child score had independent predictive values for mortality. There was a correlation between high  $\alpha$ -Klotho levels and worse liver function which explains why Child score displaces  $\alpha$ -Klotho levels as a predictor of mortality.

### **Evaluation of structural and functional cardiac changes in patients in relation to the severity of alcoholic cirrhosis**

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**Objective:** To evaluate structural and functional cardiac changes in patients with alcoholic cirrhosis in relation to the severity of liver disease.

**Methods:** Study included 80 patients (mean age 53,1±12 years) with alcoholic liver cirrhosis (LC) without history of cardiovascular and respiratory disease. According to the Child-Pugh score, 12 (14,8%) patients had class A disease, 22 (27,2%) and 46 (59,2%) patients had class B and C cirrhosis severity, respectively. ECG with QTc assessment, echocardiography with assessment of left ventricular ejection fraction (LVEF), left ventricular diastolic function; measurement of left ventricular myocardial mass index (LVMI) and systolic pulmonary artery pressure (SPAP) were performed. Plasma values of NT-proBNP were evaluated in 60 patients.

**Results:** Left ventricular ejection fraction was normal (mean value 65,3±5,8%) in all patients (n=80). Left ventricular hypertrophy (LVH) (LVMI 149,8±20 g/m<sup>2</sup>) and LV diastolic dysfunction were observed in 33 (40,7%) and 58 (71,6%) patients, respectively. The mean SPAP value was 19,9±10,7 mmHg (min 5 mmHg; max 52 mmHg). SPAP elevation above 30 mmHg was observed in 13 (16%) patients, in whom it measured 38,2±5,7 mmHg. QTc prolongation was detected in 11 (13,6%) patients, averaging 0,46±0,08 s. Median NT-proBNP value was 621,5 pg/ml (min 33 pg/ml; max 3849 pg/ml), NT-proBNP elevation (>125 pg/ml) was observed in 47 (58%) patients. NT-proBNP level positively correlated with the number of points on the Child-Pugh score (r=0,27, p<0,05). There was no relationship between the severity of cirrhosis and LVMI (Child-Pugh class: A 121,2±22 g/m<sup>2</sup>; B 114,6±36,6 g/m<sup>2</sup>; C 119,9±33,2 g/m<sup>2</sup>, p>0,05), SPAP (Child-Pugh class: A 15,6±10,1 mmHg; B 19,9±11,2 mmHg; C 21,2±10,4 mmHg, p>0,05) and QTc (Child-Pugh class: A 0,53±0,17 sec, B 0,45±0,04 sec, C 0,46±0,03 sec, p>0,05).

**Conclusions:** Patients with alcoholic LC frequently demonstrate structural and functional cardiac changes such as left ventricular hypertrophy, diastolic dysfunction and QTc interval prolongation. Although there was no significant increase in SPAP, mild pulmonary hypertension was present in 13% of patients. NT-proBNP elevation was observed in more than half of the patients and directly correlated with the severity of cirrhosis.

## Left ventricular global longitudinal strain in patients with alcoholic liver cirrhosis

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**Objectives:** Liver cirrhosis (LC) is characterized by the development of hyperdynamic circulation with an increased ejection fraction (EF) at rest and decreased myocardial contractility in response to hemodynamic stress. We aimed to evaluate left ventricular (LV) systolic function and LV global longitudinal strain in patients with alcoholic LC at rest.

**Methods:** Study included 80 patients (mean age 53,1±12 years) with alcoholic LC and without history of cardiovascular and respiratory disease. According to the Child-Pugh score 12 (14,8%), 22 (27,2%), and 46 (59,2%) patients had class A, B, and C liver disease, respectively. All patients in addition to standard clinical examination underwent echocardiography (Vivid 7 (GE)) with the assessment of the left ventricle ejection fraction (LVEF) and LV global longitudinal strain (GLS) (2-dimensional

speckle-tracking analysis). The reference value of GLS was set up at 18,6±0,1%.

**Results:** LVEF in all patients was normal (65,3±5,8%). There was no association between LVEF and Child-Pugh class of liver cirrhosis: A – 62±3,4%, B – 66±6%, C – 66±6% (p=0,09). Impaired global LV longitudinal strain (mean GLS 14,4±3%) was observed in 27 patients (52,9%) with a normal ejection fraction. Global deformation of the LV myocardium was not associated with the severity of liver cirrhosis: class A, B, and C Child-Pugh patients had mean GLS values of 16,3±4,2%, 17,5±5%, and 18,3±4,6%, respectively (p=0,52).

**Conclusions:** In patients with alcoholic liver cirrhosis no changes in LV contractility at rest were observed with the use of the standard echocardiographic criteria. However, more than half of the patients demonstrate abnormal LV global longitudinal strain, assessed by using speckle-tracking method. GLS is not associated with the severity of LC.

## The new metabolic index of insulin resistance diagnosis in patients with non-alcoholic fatty liver disease

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**Objectives:** Non-alcoholic fatty liver disease (NAFLD) is considered as the hepatic component of the metabolic syndrome and is associated with insulin resistance (IR), abdominal obesity, impaired glucose and lipid metabolism, hypertension. The combination of NAFLD and IR gets worse the glucose metabolism, increases the blood atherogenic lipids and the risk of atherosclerosis and cardiovascular disease. Early diagnosis of IR in NAFLD patients allows for timely correction and the primary prevention of cardiometabolic risk. We aimed to estimate the diagnostic value of the new metabolic index (MI) in the early diagnosis of IR in NAFLD patients.

**Methods:** 494 patients aged 20-65 years (213 male and 281 female) with NAFLD were examined in 2007-2010. In accordance with the aminotransferase levels all patients were randomized into two groups: with non-alcoholic steatosis (283 patients) and with nonalcoholic steatohepatitis (211 patients). We determined the blood parameters of lipid and glucose metabolism. IR was calculated using the HOMA-IR ratio and the triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) ratio. IR was recorded at rates of HOMA-IR>2.6 and TG/HDL-C>1.37 in mmol/L or 3.5 in mg/dL. According to the developed method for screening diagnosis of IR, we proposed the new MI using glucose and lipid parameters. The index was calculated by the formula:  $MI = [TG(mmol/L) \times Glucose(mmol/L)] / (HDL-C)^2(mmol/L)$ . IR was determined at rates of the MI>7.0.

**Results:** The MI using shows that IR detection in NAFLD patients was significantly higher than using the other indices: in patients with non-alcoholic steatosis for MI – in 66.4% compared with 47.9% for HOMA-IR and 43.1% for TG/HDL-C. The most often IR detected in patients with steatohepatitis: 93.9% versus 89.8% in HOMA-IR and 53.7% in TG/HDL-C. Averages the MI levels were significantly higher in steatohepatitis compared with steatosis and correlated with TG (r=0.43, p<0.05), HDL-C (r=0.36, p<0.05),

aspartate transaminase ( $r=0.56$ ,  $p<0.05$ ), alanine transaminase ( $r=0.4$ ,  $p<0.05$ ), body mass index ( $r=0.44$ ,  $p<0.05$ ).

**Conclusions:** Our results suggest that the MI reveals signs of impaired insulin sensitivity in the earlier stages of NAFLD. Being a simple, inexpensive, and reproducible marker the MI can be recommended in clinical practice to screen for IR in patients with NAFLD for further in-depth examination.

## Levofloxacin induced severe hepatitis

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**Introduction:** To address the case of an old lady who developed a severe drug induced liver injury related to levofloxacin non transplant candidate.

**Case report:** 87 years old woman with remarkable cardiovascular risk factors and renal insufficiency who came disorientated and somnolent after a respiratory chest infection treated with levofloxacin since 48 hours before the admission. She presented hemodynamically stable, afebrile, and punctuating 14-15 on Glasgow scale with a minimum flapping tremor. Abdominal exam showed Courvoisier sign, related to a harsh and elastic 3-4 cm mass in the upper right quadrant. Labs revealed total bilirubin 1.9 mg/dL, GPT 3731 U/L, CK 568 U/L, LDH 4340 U/L, CRP 7.8 mg/dL, mild anemia, a WBC of 9000 leukocytes with an elevated neutrophil rate, 87.000 platelets and coagulopathy (represented as a prothrombin index of 26% and INR 2.9). CT scan showed a porcelain calcified gallbladder, and mild enlargement of the biliary tract. All potential causes of hepatitis were excluded and we reach the diagnosis of levofloxacin caused hepatitis. We then reported the case to the drug surveillance system and achieved its confirmation. In spite of potentially accomplishment of surgical criteria, transplant was underestimated because of comorbidity, as well as prophylactic cholecystectomy. After suspending levofloxacin, and instauring support treatment with fluids and vitamin K, the patient underwent both clinical and analytical recovery.

**Discussion:** Although it is not a common cause, levofloxacin induced liver injury is reported on the literature. It is worldwide assumed that the treatment of choice when it leads to fatal hepatitis is transplant. Several scores establish this indication (King's College criteria, Clichy criteria, MELD score). However, it has been observed on several series an increase in mortality when liver transplant is performed as well as full recovery with only accurate support treatment. Given the great success of our lady without the supposed gold standard treatment, it seems necessary the development of validate criteria for transplant in this situations. Patients with clear indication for it will benefit from an optimized care.

## Carcinoid syndrome — case report

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**Introduction:** Carcinoid tumors are rare neoplasms, most commonly found in the gastrointestinal tract and responsible for the production of neuroendocrine mediators. The carcinoid syndrome is even rarer, present only in 5-7% of the tumors, and consists of a set of symptoms typical of the release of these mediators in bloodstream. The aim of this work is to draw attention to inclusion of this syndrome in the differential diagnosis with numerous benign conditions with the same symptoms.

**Case report:** 65 years old man, Caucasian and autonomous. No medical history of known diseases or chronic medication, and without documented allergies or alcoholic habits. Resorted to hospital emergency service by abdominal pain, diarrhea, weight loss and postprandial flushing. The physical examination revealed facial telangiectasias and nodular hepatomegaly of stony consistency. Analytically, it was found alteration in liver tests (aspartate aminotransferase 95 U/L, alanine aminotransferase 162 U/L, gamma-glutamyl transpeptidase 915 U/L) with normal values of albumin, platelets and coagulation. The abdominal CT scan showed solid heterogeneous hepatic lesions compatible with metastases. In the cecum was observed an image with contrast uptake in the arterial phase with 23x1 cm. Determination of urinary adrenaline, noradrenaline and dopamine was normal. The neuron-specific enolase (NSE) was 23.3 ug/L, acid 5-hidroxiindolacetic (5-HIAA) was 99.9 mg/24h and chromogranin A >50 nmol/L. The upper gastrointestinal endoscopy was normal. Colonoscopy revealed a polypoid and infiltrative lesion with 40 mm in the ileocecal transition, whose histology revealed a well-differentiated neuroendocrine tumor with Ki67 <1%. Patient was treated with octreotide 20 mg monthly with clinical improvement and it was scheduled surgical resection of the tumor lesion.

**Discussion:** Despite the carcinoid syndrome be a rare and late manifestation of the tumor, it is still possible to provide an improvement in the quality of life of the patient, with good control of symptoms with somatostatin analogue in conjunction with surgery. In tumors of the small intestine, the surgical excision of the lesion should be the therapeutic option, even when there is evidence of metastases, as in the presented case. This strategy may prevent complications such as intestinal bleeding, perforation or obstruction.

## Hepatitis B virus reactivation: the importance of immunosuppression

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**Introduction:** Reactivation of hepatitis B virus (HBV) infection is a serious complication of immunosuppression, which can be effectively identified and prevented. The aim of this work is to highlight the importance of HBV screening and prophylaxis of its reactivation in case of immunosuppression.

**Case report:** 78 years old man, Caucasian and autonomous for daily activities. As associated comorbidity, he had rheumatoid arthritis treated weekly with methotrexate and sporadic cycles of steroids, without clinical follow-up or analytical control for



over 5 years. He had also diagnosed ischemic heart disease, hypertension and a total hip prosthesis. He was polymedicated in particular with analgesia, which included tramadol, paracetamol and celecoxib. Denied alcoholic habits, unprotected sex, drug abuse and introduction of new medication. Patient was unaware of having any drug allergies. Patient went to hospital emergency service by jaundice, dark brown urine, asthenia and anorexia with 10 days of evolution. Without other associated symptoms, including abdominal pain, fever, vomiting or itching. Analytically, it was found elevation of transaminases 10 times the normal value, gamma-glutamyl transferase 419 U/L and total bilirubin 19.7 mg/dL. Determination of acetaminophen was <2 and autoimmunity was negative. The ultrasound showed no hepatic space-occupying lesions or bile duct dilatation. The serology for cytomegalovirus and herpes virus was negative. The HBs and HBe antigens (HBsAg and HBeAg, respectively) were positive, with anti-HBs and anti-HBe negative, anti-HBc IgM positive and HBV-DNA 8688248 IU/l. The serology was negative for the other hepatotropic viruses. It was assumed a possible reactivation of HBV infection, with suspension of methotrexate and initiation of 0.5 mg of entecavir with analytical and clinical improvement. In the patient's follow-up, it was observed HBeAg to anti-HBe seroconversion.

**Discussion:** We describe a case of how reactivation of HBV infection can cause serious clinical repercussion. Identification of patients with HBV infection before initiation of the immunosuppressant therapy is extremely important. Reactivation can be prevented by administration of antiviral therapy (entecavir, tenofovir or lamivudine) to HBsAg-positive patients at the beginning of chemotherapy or immunotherapy.

## Acute mesenteric ischemia: an unusual case of abdominal pain

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**Introduction:** Acute mesenteric ischemia is a syndrome caused by inadequate blood flow through mesenteric vessels, resulting in ischemia and eventual gangrene of the bowel wall. Although relatively rare, it is a potentially life-threatening condition. In Portugal is a rare clinical entity responsible for only 0.1% of hospital admissions but is associated with high mortality. The enormous scientific progress and the development of new technologies in recent decades have not diminished significantly their mortality. Conventional surgical techniques of intestinal revascularization remain as gold standard. The generalization of abdominal computed tomography facilitated early diagnosis and faster therapeutic intervention.

**Case report:** A 72 years old Caucasian man, presented in the emergency room with acute abdominal pain, fever (39°C), associated with nausea and signs of intestinal occlusion. Known personal history of chronic liver disease etiology of ethanol, hypertension, atrial fibrillation, chronic obstructive pulmonary disease and obesity. Medicated in ambulatory with candesartan, omeprazol, mononitrate isosorbide, rosuvastatin, digoxin, aspirin, budesonide, formoterol, salbutamol and etorocoxib. Analytically: Hb 11.8 g/dL, leukocytosis 27300, neutrofilia

93%, CRP 43.5. X-ray abdominal – irrelevant changes. First abdominal computed tomography showed irrelevant changes. Started empiric antibiotic with meropenem EV and measures for intestinal occlusion. After 3-4 days with no improvement repeated abdominal CT scan showing marked distention of the jejunum as well as intra-peritoneal free liquid without expansion ileum or colon. He went first look surgery: ileum-colic resection (ileum and ascending colon) jejunostomy, and interneer in intensive care unit. Stabilized and went on second look surgery for intestinal transit restoration. Featuring a favorable evolution of his medical condition.

**Discussion:** Acute mesenteric ischemia is a rare abdominal emergency that is characterized by a high mortality rate. Generally, acute mesenteric ischemia is due to an impaired blood supply to the intestine caused by thromboembolic phenomena. A prompt diagnosis is a prerequisite for successful treatment. The treatment of choice remains laparotomy and thromboendarterectomy, although some prefer an endovascular approach. A second-look laparotomy could be required to evaluate viable intestinal handles. Although the prognosis of acute mesenteric ischemia due to an acute arterial mesenteric thrombosis remains poor, a prompt diagnosis, aggressive surgical treatment and supportive intensive care unit could improve the outcome for patients with this condition.

## Spontaneous bacterial peritonitis – a death sentence

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**Objectives:** Patients with liver cirrhosis are predisposed to infections. The most common is spontaneous bacterial peritonitis (SBP), the infection of the pre-existing ascitic fluid without known secondary abdominal source. Diagnosis is based on clinical suspicion and analysis of ascitic fluid, especially white cell count and culture in blood culture bottles. The aim of this study was to evaluate the clinical features, the most frequent agents and the mortality among in-patients with SBP.

**Methods:** Retrospective study of admissions from 2010 to 2014 in internal medicine department with the diagnosis of SBP. The diagnosis criteria were the presence of ascitic fluid absolute polymorphonuclear leukocyte count  $\geq 250$  cells/mm<sup>3</sup> without an evident intra-abdominal, surgically treatable source of infection. On consulting clinical registries, the following parameters were evaluated: sex, age, etiology of the cirrhosis, SPB agent, re-admissions and mortality.

**Results:** In that period of time, 41 patients were admitted with SPB diagnosis: 85% were male with a mean age of 60 years. In 93% of the patients alcohol abuse was the cirrhosis etiology. Culture positive SBP was present in 48% of the cases – in 88% a single agent was found (43% – *Escherichia coli*, 24% – *Streptococcus*, 19% – *Enterococcus*, 5% – *Staphylococcus*, 5% – *Salmonella* and 5% – *Klebsiella*) and the remainder 13% had a polymicrobial culture. Re-admissions occurred on 17% of cases: 5 patients twice and 2 patients three times. 32% of the patients died during

the hospital stay and mortality in less than a year after hospital discharge was 39%. Data regarding prophylactic therapeutics were difficult to achieve because either patients lack of compliance or prescription absence – therefore it was not included in the study. **Conclusions:** Most patients in this study died during the hospitalization or in less than a year after discharge. The recurrence rate was not as high as expected mainly because of this high mortality rate. These aspects reinforce the prognosis severity of SPB and the need to prompt treatment to modify clinical course of patients and mortality rate.

### **Clinical efficacy of biological therapy anticytokine achieving of stable remission in patients with severe ulcerative colitis**

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**Objectives:** Ulcerative colitis (UC) is considered as an immune reaction with an increased production of cytokines and damage of mucous membrane of colon. Our purpose – to evaluate the clinical efficiency of induction course (IC) of biological infliximab therapy (BIT) in patients with a severe UC.

**Material and methods:** 18 patients with UC were examined; they were 27-39 years old with a severe form of UC (11.3±1.8 points of Mayo index). Patients were prescribed to intravenous infusion of infliximab in a dose of 5 mg/kg of body weight on days 0, 2 and 6 of the treatment week. The evaluation of efficiency was conducted with the use of the reduced questionnaire of Mayo (QM) on the 2, 4, 6, 12 and 24 week after IC. The positive response for ICR was evaluated at QM lower than for 4 and more points. Final evaluation of efficiency IC BIT was conducted on the 48-th week of the observation with the use of endoscopic, histological and complete questionnaire of Mayo.

**Results:** A positive response for BIT is registered in 2 weeks in 6 (33.3%) patients, in 4 weeks in 9 (50%) and in 6 weeks in 15 (83.3%) patients respectively. All patients with UC underwent therapy by azathioprine at a daily dose of 150 mg. In a state of clinical response, to week 12, 16 (88.8%) patients were observed. IC was continued for 2 patients due to the high level of QM according to a supporting biological therapy and they were excluded from the main group observation. By week 48 of observation, 14 (77.8%) patients were in clinical remission of UC. Average index QM in the group constituted 2.03±0.04 points. In 3 (16.7%) patients, by week 24, aggravation of the state was registered (QM=4.3±0.8 points). Undesirable phenomena and (or) adverse effects on IC weren't registered. In 7 (38.9%) cases after IC, intermittent leukocytosis was registered with a moderate shift of leukogram to the left. A similar effect in the use of BIT was registered for the first time and requires the following evaluation.

**Conclusion:** Using biological anticytokine therapy provides long-term remission in patients with severe ulcerative colitis. Strategy for the early use of biological therapy is appropriate to consider in cases of severe ulcerative colitis patients with early age group.

### **Frequency of disaccharidase deficiency in patients with severe ulcerative colitis**

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**Objectives:** The role of lactose malabsorption in ulcerative colitis (UC) is controversial. The aim of this study was to compare the prevalence of lactose malabsorption in a group of UC patients with severe ulcerative colitis and a control group and to modify lactose consumption in view of the results.

**Methods:** Lactose malabsorption (LM) was studied using the hydrogen breath test (HBT) in 34 patients with UC and 24 controls after ingestion of 25 g of lactose. A questionnaire on ingestion of milk products was also administered. Level of LM was assessed with hydrogen breath testing (HBT) with the help of the device Gastro plus (Bedfont Scientific Ltd., UK). The partial pressure of hydrogen (PPT) has been defined in the basal conditions, further each 30 minutes during 3 hours after intake lactose. Graphico-mathematical analysis has done, the results were compared with clinical symptoms (diarrhea, pain, belching and flatulence).

**Results:** Of the 34 patients with UC, 23 (67.6%) presented lactose malabsorption compared with 9 of the 24 (37.5%) controls (p=0.032). 22 patients (46%) had been advised to completely eliminate lactose from their diets. 10 patients (29.4%) had been recommended the use of laktazar, 2 capsules with meals 3 times a day for 1 month. Lactazar (Farmstandart, Russia) contains 3,450 units of the enzyme lactase. After a course of basic therapy (oral mesalazine 2 g/day and dietary fiber supplementation (at least 20 g/day), eliminate lactose from their diets and laktazar) the level LM was detected in only 34.2% of patients.

**Conclusions:** When UC recorded a high level of LN. This fact encourages the use in the treatment of patients with reduction in milk version of the diet and laktazar (6900 units) for at least 4 weeks.

### **Plasma citrulline as a marker of paralytic ileus**

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**Objectives:** Plasma citrulline is a biomarker of enterocyte mass. In patients with short bowel syndrome, citrulline concentration is positively correlated with remnant small bowel length. It has been demonstrated that plasma citrulline concentration is a simple and reliable biomarker of enterocyte mass in patients with chronic small bowel pathologies. Plasma citrulline concentration is mainly determined by the balance between gut citrulline synthesis and kidney citrulline degradation. The aim of this study was to verify plasma citrulline concentration changes after large intestine resection as a model of small bowel injury.

**Methods:** The cohort included 117 patients treated by resection

of the large intestine for colorectal carcinoma. 12 bowel complications were observed – 5 paralytic ileus, 5 dehiscences of anastomosis, 1 subfrenic abscess and 1 hemorrhage. Plasma citrulline was determined by HPLC method. Samples were drawn before (day -1) and daily during 5 days after operation (day 0, 1, 2, 3, 4). Group of patients – without bowel complications, ileus and other bowel complications were compared. The data were statistically analyzed by software SigmaStat –One Way repeated measures ANOVA. Data are presented as median (25%; 75%).

**Results:** Plasma citrulline concentration changes were compared during 6 days of investigation in a group of patients without bowel complications as follows: day -1: 34.4 (28.3; 43.8), day 0: 27.9 (22.6; 35.5), day 1: 20.7 (16; 25.8), day 2: 21.1 (16.3; 25.3), day 3: 24.1 (19; 29.5), day 4: 25.8 (20.6; 32) umol/l. Ileus group: day -1: 27.6 (21.8; 39), day 0: 29.2 (19.5; 33), day 1: 14.9 (13.3; 18.5), day 2: 18.9 (12.5; 23), day 3: 17.8 (10.9; 20.3), day 4: 18.2 (9.7; 19.8) umol/l. Other bowel complications: day -1: 34 (29.2; 52.7), day 0: 27.6 (22.7; 36.9), day 1: 19.9 (17.8; 35), day 2: 20.8 (15.4; 34.3), day 3: 18.8 (18.5; 39.9), day 4: 19.1 (15.9; 34.3) umol/l. The significant differences in day 3 and day 4 in groups of ileus vs. patients without bowel complications were observed. Significances were not observed in groups without complication vs. other bowel complications.

**Conclusions:** The plasma citrulline concentration seems to be a sensitive marker suitable for monitoring of patients suffering from ileus reflecting the synthetic activity of enterocytes. It enables to monitor small bowel damage by significant decrease of its plasma concentration.

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## Intermittent fever and lymphadenopathy in a 55 years old male

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**Case report:** A 55 years old Caucasian man was presented to our clinic for a second opinion on a 13-month-history of intermittent fever, weight loss and fatigue. He had a medical history of rheumatic fever (1999) and seronegative rheumatoid arthritis for which methotrexate was prescribed (2014). At presentation, his medication was meloxicam ( $\pm 3$  times a week). On physical examination, several small and soft lymph nodes (<1 cm) were palpable bilaterally in the axillary and inguinal regions. Blood analysis showed an erythrocyte sedimentation rate (ESR) of 69 mm/h, a C-reactive protein (CRP) level of 97 mg/l with a normal total leukocyte count ( $9.5 \times 10^9/l$ ) and differentiation. Blood cultures remained negative. Serology tests for syphilis, EBV, CMV, HIV, Bartonella henselae, Brucellae, Coxiella burnetii, Leishmania species, Histoplasma capsulatum, Toxoplasma (T.) gondii and Cryptococcus neoformans were negative or not compatible with a current infection. A tuberculin sensitivity and quantiferon assay were negative. Echocardiography showed no signs of endocarditis. On a CT-scan of the thorax and abdomen, general lymphadenopathy with small lymph nodes (<2 cm) and mild splenomegaly (cranio-caudal diameter of 13

cm) were observed. Examination of a specimen from an axillary and inguinal lymph-node biopsy revealed a granulomatous inflammation without evidence of a malignancy and with negative microbiology results for Chlamydia trachomatis, T. gondii and Mycobacterium tuberculosis simplex (PCR) and negative acid-fast staining. Analysis of a bone-marrow biopsy specimen did not demonstrate signs of malignancy, granuloma or histiocytic proliferation. An esophagogastroduodenoscopy and small-bowel-biopsy with specific instructions to look for Whipple's disease were performed. Histopathological examination of the small-bowel-biopsy specimens revealed normal villi with diffuse infiltration by periodic acid-Schiff (PAS)-positive, foamy macrophages. The diagnosis Whipple's disease was made and the patient was treated with ceftriaxone 2 g od for 2 weeks followed by trimethoprim-sulfamethoxazole 960 mg bid scheduled for one year. Recently, i.e. 3 weeks after the start of the treatment, the symptoms had disappeared, the CRP level normalized and the ESR declined to 16 mm/h.

**Discussion:** Here, we report an atypical case of Whipple's disease, illustrating the difficulty to recognize it in the absence of gastro-intestinal manifestations, which are the most common symptoms of this rare disease.

## Clinical effectiveness of non-invasive diagnosis of Crohn's disease

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**Objectives:** In the last two decades ultrasonography (US) has had a growing role in the diagnosis of Crohn's disease because this method is cheap, non-invasive, and comfortable for the patients and has sufficient diagnostic accuracy. But it is debated whether US should be used regularly in all patients or only in cases when intra-abdominal complications are suspected. In this study we decided to verify if routine use of US in all patients with Crohn's disease can really give additional important diagnostic information.

**Material and methods:** 30 patients with Crohn's disease underwent standard US examinations of small and large bowels. We have evaluated diameter, thickness, compressibility and wall structure of the gut, changes in haustration and peristalsis, bowel contents, presence of extra-intestinal structures.

**Results:** In all cases US was able to detect distinct changes in normal gut anatomy and function. In 12 patients (1st group) signs of diffuse bowel lesions were found (dilatation of lumen, increase in wall thickness and echogenicity). In 4 and 8 patients of this group decrease or increase in peristalsis was detected. In 14 patients (2nd group) segmental nonstenotic lesions were found (7 patients with lesion of cecum and ascending colon and 7 with lesion of descending and sigmoid colon). In this group of patients we detected reduction of peristalsis, diffuse wall thickening, haustras flattening, and loss of normal wall stratification. In 4 patients (3rd group) typical signs of stenotic lesions were revealed.

**Conclusion:** Intestinal US can give additional important diagnostic information in all patients with Crohn's disease.

## Proteomic analysis of the interaction of apoptosis and intestinal microbiota in patients with ulcerative colitis

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**Objectives:** The incidence rate of ulcerative colitis (UC) in Russia is 5–30 cases per 100,000 per year. Molecular pathways of the UC development are not clear. The purpose of the work was to study the molecular interactions of apoptotic pathway in patients with UC.

**Methods:** The clinical trial included 32 patients with UC. The clinical presentation of UC depends on the extent of involvement: distal colitis, extensive colitis; the severity of disease. The diagnostic workup for UC: clinical examination; laboratory – erythrocyte sedimentation rate (ESR), thrombocytosis, C-reactive protein (CRP), stool culture; abdominal ultrasound, colonoscopy with biopsy. Mucosal specimens were graded according to grade 0,1,2,3. Methods of proteome research was assumed 1-,2-DE/MALDI-TOF-TOF-MS. Patients accepted mesalazine rectal 2 g/day, mesalazine orally 3-4 g/day and rectally 1-2 g/day, prednisolone 1 mg/kg/day p.o./i.v., azathioprine 2,5 mg/kg/day; infliximab 5 mg/kg i.v. with azathioprine 2,5 mg/kg/day, methotrexate 25 mg/week i.m./s.c. depending on UC activity. "Statistica 12.0" was applied.

**Results:** We have revealed distal colitis in 28 patients, extensive colitis in 4 patients, registered mild (n=15), moderate (n=10), severe activity (n=7) of UC and grade 1 (n=15), 2 (n=13), 3 (n=4) of UC activity. Laboratory tests: anemia, the increase of ESR and CRP, thrombocytosis, the increase of *Escherichia coli*, *Proteus* spp., *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp., *Bacteroides* spp., *Clostridium* spp. and the reduction of *Bifidobacterium* spp., *Lactobacterium* spp. in feces. We have found bowel wall thickening (n=32), continuous disease spread (n=32), concentric pattern of mucosal involvement (n=32), pseudopolyps (n=9). 29 patients achieved the UC remission, 3 patients had relapses.

**Conclusions:** Proteomic analysis has demonstrated the cascade with caspases 8, 9, 10, the release of cytochrome C from mitochondria, which interacts with Apaf-1, causing activation of caspase-9 in UC colon mucosa. TNF- $\alpha$  activates of initiator

caspase-2, -8, and -10 in apoptotic pathway. The NF- $\kappa$ B pathway induces cellular inhibitors of apoptosis, which function as specific caspase inhibitors in UC colonic mucosa.

## Enteral parasites detected by stool exam, colonoscopy or abdominal imaging study during 10 years' health checkup: a Korean single center study

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**Objective:** The aim of our study was to study the status of enteral parasites detected by stool exam in a single health checkup center for 10 years and to explore the efficacy of organ specific exams such as abdominal ultrasonography (US) or computed tomography (CT), or colonoscopy for detecting enteral parasites.

**Methods:** Data about 197,406 stool samples collected from 99,451 subjects in a single health checkup center for 10 years were analyzed.

**Results:** 3,472 (1.73%) stools were positive for parasitic ova. Sort of parasitic ova were as follows: clonorchiasis 1,508 (0.76%), metagonimiasis 959 (0.49%), trichiuriasis 855 (0.43%), ascariasis 142(0.072%), trichostrongylosis 5 (0.0025%), taeniasis 2 (0.001%), enterobiasis 1 (0.00051%). Overall detection rate of parasitic ova by stool exam peaks in the second year. Detection rate of clonorchiasis was significantly higher among initial examination subjects than reexamination subjects. However, this differential detection rate between initial examination subjects and reexamination subjects were not shown in subjects with other parasitic ova. Colonoscopy was performed in 258 (30.18%) trichiuriasis subjects, and among them, colonoscopy revealed adult worm in 23 (8.91%) subjects. Abdominal US or CT was performed in 1,505 (99.8%) clonorchiasis subjects, and among them, only 37 (2.46%) subjects showed images compatible with clonorchiasis.

**Conclusion:** Our data suggest that stool exam during health checkup may reduce the burden of silent but carcinogenic clonorchiasis, and abdominal US, CT or colonoscopy may not be an alternative to a stool exam for screening enteral parasites during health checkup.

# Hematology

## Iron overload – a global perspective

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**Objectives:** Iron is a crucial element in biologic systems. Nevertheless, its excessive accumulation is toxic. Hereditary hemochromatosis is a prototype of this mechanism: a biallelic mutation in HFE gene causes a tendency to constant iron enteric absorption, regardless of its body stores. There are other forms of iron overload, classified as acquired hemochromatosis that may be caused by several diseases processes, like alcoholic liver disease and non-alcoholic steatohepatitis, among other causes. The main goals of this study are: to characterize a cohort of patients with iron overload, studying the main differences between acquired and hereditary hemochromatosis (diagnostic tests and clinical presentation).

**Methods:** The authors realize a retrospective observational study based on a cohort of patients with identified iron overload followed up in Hepatology consultation of an Internal Medicine department. The following variables were analyzed: age, sex, iron biochemistry profile (serum ferritin, transferrin saturation), HFE gene status, causes of acquired hemochromatosis, hepatic iron concentration (HIC) by magnetic resonance images (MRI) and direct organ injury.

**Results:** A total of 70 patients were included (49 males and 21 females), with a median age of around 40 years old by the time of diagnosis. It was observed a strong correlation in ferritin, transferrin saturation and HIC by MRI in hereditary hemochromatosis. This group showed superior mean values of that parameters comparison to acquired hemochromatosis patients. The HFE genes associated with significant iron overload and elevated HIC were H63D and C282Y mutations, particularly in homozygosis. A strong positive correlation was confirmed between HIC by MRI and hereditary hemochromatosis. This fact, associated with the simplicity, inexpensive and efficient treatment (periodic blood removal - phlebotomy), indicates that a quick diagnosis leads to premature treatment which reduces the impact of the disease. The RMI represents also a beneficial and preferable diagnosis procedure due to its non invasive method. Otherwise, MRI's reveals poor performance in acquired hemochromatosis, suggests that this diagnostic procedure is ineffective in cases of suspected acquired iron overload.

**Conclusions:** There is a significant number of patients having acquired hemochromatosis, with a very important contribute from dysmetabolism and alcoholic liver disease. The elevated ferritin levels and transferrin saturation showed a best performance in these cases.

## Renal infarction: a rare manifestation of thrombophilia

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**Introduction:** Thrombophilias are conditions associated with a hypercoagulable status with inherent risk of arterial and venous thrombosis and high morbidity and mortality. They can be of genetic (gene mutations) or acquired origin, such as smoking, diabetes mellitus, dyslipidemia or hormonal contraception. A thrombotic event, venous or arterial, when occurring in a young patient or in an unexpected location must lead to a more thorough investigation.

**Case report:** The authors present the case of a 39 years old woman, smoker and on oral contraceptive therapy, with a previous history of acute arterial ischemia of the right limb due to occlusion of the superficial femoral artery. The patient was admitted through the emergency room with acute abdominal pain located in the left flank. The blood tests were unremarkable and a CT scan was performed, which showed an infarction of the lower third of the left kidney, apparently due to occlusion of multiple branches of the renal artery. A full body scan was performed, which excluded neoplasia. A trans-esophageal echocardiogram revealed a large and very mobile thrombus in the descendent thoracic aorta, which was believed to be the origin of the emboli that led to the renal infarction. A thrombophilia study was also performed, which revealed normal levels of protein S, protein C, a normal test for protein C resistance, normal genotype for prothrombin G20210A and negative antiphospholipid antibodies. The search for MTHFR mutations 677 and 1298 as well as PAI-1 was performed, revealing heterozygosity on all mutations. Other cardiovascular factors such as dyslipidemia, diabetes mellitus and hypertension were excluded. The patient suspended the oral contraceptive therapy, was encouraged to quit smoking and started anticoagulation with warfarin, achieving good INR control. She has not had another thrombotic event after 36 months of follow-up. A control transesophageal echocardiogram was performed showing an organized thrombus with smaller dimensions. A follow-up of renal function has also shown preserved function.

**Discussion:** A thrombotic factor may, by itself, not lead to a thrombotic event. However, this case shows that a combination of thrombophilias may lead to a highly hypercoagulable state and the formation of arterial thrombi. The diagnosis is sometimes challenging, but the management of such conditions is crucial to prevent the progression of thrombotic events, which are associated with great morbidity.

## Light chain multiple myeloma – regarding a clinical case

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**Introduction:** Hypercalcemia is a common electrolyte disorder. The most common causes are primary hyperparathyroidism and

malignant neoplasms. Considering that the therapeutic approach is different, differential diagnosis is imperative.

**Case report:** We present the case of a 80 years old Caucasian woman who was admitted with the diagnosis of acute lower respiratory tract infection, empirically treated with amoxicillin/clavulanic acid and azithromycin. Laboratory findings included microcytic hypochromic anemia (9.5 g/dL) and leukocytosis ( $17,8 \times 10^9/L$ ) with neutrophilia, C-reactive protein 6.9 mg/dL, urea 113 mg/dL, creatinine 1,6 mg/dL, hypercalcemia (13.2 mg/dL), parathyroid hormone (PTH) 9.3 pg/mL, normal levels of calcitonin and vitamin D. Chest radiography showed a left clavicle fracture (without traumatic context). Skull and body computed tomography scans showed osteolytic lesions in multiple bones of the skull, chest, abdomen and pelvis, with soft tissue component. Further investigation revealed an elevated  $\beta_2$ -microglobulin (7.2 mg/dL), gamma bands in serum protein electrophoresis, Bence Jones proteins in urine immunofixation and elevated serum kappa light chains (13800 mg/L). The myelogram, very difficult to obtain, demonstrated 19% clonal plasma cells, which was consistent with the diagnosis of multiple myeloma.

**Discussion:** Hypercalcemia was treated with isotonic saline IV hydration, IV biphosphonates, diuretics and prednisolone. The case was discussed with hematologist: the patient was not considered suitable for chemotherapy or autologous stem cell transplant, and was admitted to a palliative care unit.

## Mediterranean Kaposi sarcoma related hemophagocytic lymphohistiocytosis

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**Introduction:** Hemophagocytic lymphohistiocytosis (HLH) is a relatively rare, yet underdiagnosed condition characterized by a pathologic and unabated activation of the immune system. Case report: We present a case of a 71 years old patient with a history of Mediterranean type Kaposi sarcoma presenting to our department with cough, fever, anemia and thrombocytopenia. He reported similar hematological findings for several years and that he had been treated with corticosteroids with a presumptive diagnosis of rheumatic polymyalgia. Having tried a course of antibiotic treatment he was referred to us for investigation. On admission he had profound thrombocytopenia ( $16.000/\mu l$ ), significant anemia (Hb 9.9 g/dL), hypertriglyceridemia (250 mg/dL), hyperferritinemia (2986 ng/ml), elevated CRP (260 mg/dL) and creatinine (1.7 mg/dL), high fever, hepatosplenomegaly and mild jaundice. All cultures were negative and the patient had 5 out of the 8 criteria for the diagnosis of HLH. Bone marrow aspiration verified the existence of hemophagocytosis. He was started on high doses of corticosteroids (1 mg/kg/day), immunoglobulin (0.5 g/kg) and etoposide (100 mg/day). His condition unfortunately deteriorated fast and he succumbed.

**Discussion:** HLH is characterized by an over-activation of macrophages and a suppression of NK cell activity, leading to a cytokine storm; an inflammatory process affecting every

system and leading to multi-organ failure. Predisposing conditions include hematological malignancies, solid tumors, autoimmune diseases, while triggering factors include infections and medications. Diagnosis is based on a set of criteria, but they are not absolute; in cases with high suspicion, patients should receive treatment. Ferritin levels are almost always elevated and serve as a disease progress indicator. Kaposi sarcoma is a malignant condition arising from vascular endothelium and caused by infection with herpes virus 8, also known as Kaposi sarcoma herpes virus (KSHV). A relationship between KSHV and HLH has been described in HIV patients and it is hypothesized that KSHV affects lymphocytes triggering them to release cytokines and set HLH in motion. HLH is a potentially catastrophic condition with multisystemic involvement. Due to its rarity and lack of convenient diagnostic criteria, it is of utmost importance that physicians maintain a high degree of suspicion when treating patients with refractory high fever and hyperferritinemia.

## Invalidating kyphosis due to vertebral fractures complicating a multiple myeloma: a case report

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**Introduction:** Multiple myeloma (MM) is a B cell malignancy characterized by important alterations of physiologic bone turnover. It can cause significant bony resorption and vertebral involvement is extremely common. Myelomatous vertebral metastasis cause compression fractures and can lead to kyphosis and sagittal imbalance.

**Case report:** A previously healthy, 52 years old male presented with complaints of fatigue for the last 10 months and significant back pain especially at the lumbar spine and ribs radiating to the upper limb. On physical examination, patient was noted to be afebrile, and his blood pressure was 120/80 mmHg. He had pale conjunctivae. He has high respiratory frequency at 32 cycles/min and the lungs were clear on auscultation. Significant kyphosis was noted and no focal neurological deficit was found. Examination of the extremities revealed edema of the lower limbs. Laboratory analysis revealed a normal white blood cell count, hemoglobin of 7.9 g/dL, creatinine of 224  $\mu\text{mol/l}$  giving a creatinine clearance 29 ml/min and a high total serum calcium of 3,74 mmol/l. Urinalysis was significant for 2+ proteinuria and 2+ hematuria. Serum protein electrophoresis did not show any M-spike but a hypogammaglobulinemia 3.8 g/l. Besides, the serum immunoelectrophoresis revealed the presence of a monoclonal gammopathy with free kappa light chains. Urine immunoelectrophoresis revealed kappa light chains at 3.6 g/24h. Bone marrow biopsy showed obvious 30% of bone marrow area was replaced by plasma cells. Radiography of the thoracic spine objectified exaggerated thoracic kyphosis associated with a single antero-posterior regular settlement of a dorsal vertebra with cortical respected without involvement of the posterior wall. The computed tomography of the spine

showed a kyphosis with an angle of curvature in the sagittal plane 90 associated with a cuneiform compaction of T4 to T8 condensed with a heterogeneous pattern of the vertebral body associated with a bulge of the posterior vertebral wall narrowing the central spinal canal about 30%. The diagnosis of multiple myeloma complicated by vertebral fractures inducing invalidating kyphosis was retained. Since the patient is young, a bone marrow transplant was decided and treatment with thalidomide dexamethasone was introduced. No surgical treatment was decided for him. While he was kept in the hospital, he presented a respiratory distress with polypnea and pulmonary congestion. On physical examination, he was afebrile and the auscultation showed sounding rales in both lung fields. The intubation was impossible because of the deformation. The patient expired.

**Discussion:** Carcinomas that metastasize to the bone are characterized by a new bone formation following bone destruction. The lytic process observed in MM is different since it may still have progression of skeletal event without the repair of osteolytic lesions even when patients respond to anti-MM therapies. The obsession is the possible complications such as cord compression, urinary retention, ileus, intractable pain, and pulmonary compromise.

## Primary systemic amyloidosis with massive isolated lymph node involvement: a case report

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**Introduction:** Systemic AL amyloidosis (AL) is a disorder in which light chains form fibrillar deposits, may involve almost any organ system in the body. However, neck lymph node involvement is rare, with only six previous cases reported. We report a case history of a patient whose diagnosis of primary systemic AL amyloidosis with cervical, axillary, mediastinal, retroperitoneal, splenic, and inguinal lymph nodes localizations with a pulmonary involvement.

**Case report:** A previously healthy, 67 years old male presented with complaints of fatigue for the last 2 years associated with weight loss, sweat and significant cervical polyadenopathy. On physical examination, patient was noted to be afebrile, and his blood pressure was 130/80 mmHg. The lungs were clear on auscultation. Examination of lymph nodes noted polyadenopathies in the neck (submental and submandibular, jugular and occipital nodes) whose largest dimensions was 2 cm in major axis. No focal neurological deficit was found. Laboratory analysis revealed a normal white blood cell count, hemoglobin of 12.2 g/dL, creatinine of 75  $\mu$ mol/l and a total serum calcium of 2,28 mmol/l. Urinalysis was normal. The tuberculin skin test (TST) was positive. Serum protein electrophoresis showed an oligoclonal spike with hypergammaglobulinemia at 19 g/l. Besides, the serum immunoelectrophoresis revealed the presence of a double monoclonal gammopathy with IgM/kappa and IgG/lambda. Urine immunoelectrophoresis did not reveal light chains neither Bence Jones protein. Bone marrow biopsy

showed that 5 to 11% of bone marrow area was replaced by plasma cells. Medullary bone biopsy showed an hypoplastic marrow without tumor invasion. Thoraco-abdominal-pelvic CT scan also objectified retroperitoneal, splenic, and inguinal lymph nodes localizations with pulmonary parenchymal and mediastinal lymph necrotic as making mention tuberculosis lung disease. Since TST was positive, and necrotic mediastinal lymph appearance, the patient was treated by tuberculosis treatment. But there was no regression of lymphadenopathy at the clinic and the CT scan control. Therefore, the diagnosis of tuberculosis was eliminated. Meanwhile, histological analysis of lymph node biopsy and biopsy of the salivary glands confirmed the presence of amyloid deposits AL kappa. The diagnosis of primary systemic AL amyloidosis with cervical, axillary, mediastinal, retroperitoneal, splenic, and inguinal lymph nodes localizations with a pulmonary involvement was retained. So, the patient was then treated with melphalan prednisone but he seemed to be unresponsive to medical therapy since the CT scan control showed the same lesions.

**Discussion:** AL amyloidosis usually has a bad prognosis. Lymph node involvement is rare. The prognosis is even more severe because we do not have a recommendation for treatment.

## Chronic myelomonocytic leukemia: a patient presenting with rare extramedullary involvement

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**Introduction:** Even though high lysozyme levels are consistently elevated in chronic myelomonocytic leukemia (CMMoL), lysozyme-induced kidney injury (LIKI) is a rare cause of renal failure. Filtered lysozyme appears to be a direct tubular toxin and lysozymuria has been proposed to be a valuable tool for detection of tubular damage. Polyneuropathy secondary to CMMoL is also infrequent and may be due to autoimmune mechanisms.

**Case report:** A 74-year-old male with a recent diagnosis of chronic myelomonocytic leukemia was admitted for rapidly progressive renal failure (RPRF), associated with gait impairment due to muscle weakness and pain in lower limbs. After exclusion of prerenal and postrenal causes of RPRF, the workup revealed high inflammatory markers, polyclonal hypergammaglobulinemia, nephrotic proteinuria and high serum and urinary lysozyme levels. Renal biopsy confirmed the diagnosis of lysozyme-induced kidney injury. An electromyography also revealed a sensorimotor axonal polyneuropathy. Magnetic resonance imaging of the renal arteries revealed no stenosis or dilatations. The patient was started on prednisolone and azacitidine. Improvement of limb symptoms and a decrease in monocyte count, renal function values, inflammatory markers and proteinuria were seen afterwards.

**Discussion:** We describe a case of lysozyme-induced kidney injury and axonal polyneuropathy, presumably both secondary to CMMoL, where prednisolone and azacitidine seem to have been very helpful in treating extramedullary leukemic involvement.

## Glucose 6 phosphatase dehydrogenase deficiency

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**Introduction:** Glucose-6-phosphatase dehydrogenase (G6PD) deficiency is a rare X-linked recessive hematological disorder that predisposes patients to hemolysis under certain circumstances. Patients express low levels of G6PD, impairing glutathione formation and thus rendering erythrocytes highly susceptible to oxidative stresses. Overall prevalence is low, with higher rates reported among populations surrounding the Mediterranean basin or their descendants. We present the case of a late-onset hemolytic crisis associated with G6PD deficiency.

**Case report:** A 45 years old Brazilian woman of Portuguese descent presented with severe jaundice after the ingestion of a large amount of fava beans. Past medical history was unremarkable and the patient denies previous episodes of jaundice. Laboratorial workup showed decreased hemoglobin and erythrocyte count as well as elevated indirect (unconjugated) bilirubin, high LDH levels and decreased haptoglobin, all consistent with acute hemolysis. G6PD levels were near the lower end of normal range, while testing for other causes of acute hemolysis was negative. The patient was admitted for monitoring and intravenous hydration. After complete regression of jaundice and normalization of bilirubin levels she was discharged with iron, folate and cyanocobalamin supplementation.

**Discussion:** G6PD is a key enzyme in maintaining intracellular levels of glutathione, thus providing cells with reducing power and resistance to oxidative stresses. While several foods and drugs are responsible for inducing highly oxidative states, fava beans are the classic cause of hemolytic crises in G6PD-deficient individuals. The likelihood of a crisis is related not only to the level of G6PD activity but also the level of exposure. During hemolytic crises, due to the predominance of enzyme-rich reticulocytes and heightened destruction of G6PD-deficient erythrocytes, enzymatic activity levels may be falsely normalized. Repeated testing several weeks after improvement of jaundice is mandatory for definite confirmation of diagnosis. Despite its low prevalence, G6PD deficiency should be considered in the differential diagnosis of acute hemolysis, particularly in individuals of Mediterranean descent. In these populations, G6PD activity levels should be tested before administration of highly oxidative drugs, such as synthetic anti-malarials.

## A catastrophic outcome of a case of acquired hemophilia A

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**Introduction:** Acquired hemophilia A is a rare autoimmune disorder caused by an autoantibody to factor VIII (FVIII) predisposing to severe hemorrhage. Delayed diagnosis and delayed obtention of hemostasis may be fatal. We report a case

in which the delay of introduction of bypassing agents (BA) or recombinant activated factor VII (RaFVII) was fatal.

**Case report:** 77 years old women patient with a history of hypertension treated, hospitalized for the appearance of spontaneous multiple bruises three weeks before with indirect signs of bleeding (hemoglobin (Hb) falling from 12 to 8.2 g/dL).

**Clinical examination:** it was noted multiple superficial bruises on both thighs with a large hematoma of the right calf. There were no signs of meningeal irritation or rectal bleeding or melena. Biology: TCK 88 seconds without lupus anticoagulant, anti-cardiolipin antibody or antinuclear antibody. The factor VIII was severely decreased (<1%) with the presence of anti-factor VIII antibodies. It was also noted a slight peak monoclonal gammopathy on the electrophoresis (4.5 g/l immunoglobulin (Ig) A kappa with a deficit of IgG and IgM to 4 g/l and less than 0.21 g/l respectively. Hb after transfusion 10.3 g/dL. A thoraco-abdominal-pelvic (TAP) and lower limb CT scan: no neoplasia but diffuse infiltration of leg posteromedial compartment. Treatment consisted of 2 bolus corticosteroid with oral relay for 4 weeks with regular monitoring of factor VIII. RaFVII substitution was not initiated due to the lack of profound hematoma. We noted a significant regression of the leg hematoma and patient discharged. 10 days later, the patient arrived in emergency department with severe acute abdominal pain. Hb was 5 g/dL. TAPCT confirmed a psoas hematoma and peritoneal hemorrhage. Transfusion and short treatment RaFVII performed and the patient transferred to operating room where it was found, as expected, intraperitoneal flooding complicated with 2 cardiac arrests during the surgery then rapid death.

**Discussion:** This case illustrates the lack of experience of emergency units with the management of acquired hemophilia, focuses on the importance of early treatment with repeated and or continuous BA or RaFVII in profound organ hemorrhage and confirms the catastrophic results due to any invasive or surgical procedure carried out before obtaining a perfect hemostasis, in the false hope of saving the patient.

## Iron deficiency and restless legs syndrome in blood donors. A prospective study

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**Background:** Restless legs syndrome (RLS) is strongly linked to iron deficiency. Regular blood donation may lead to iron deficiency. Contradictory results in previous studies are found; some studies suggest an increased risk of RLS in blood donors, and others fail in finding any relation.

**Objectives and methods:** We designed a prospective study in two Blood Donation Units of the Public Health-Care System, to study iron metabolism and the prevalence of RLS symptoms in blood donors. All blood donors underwent a physical examination including blood pressure, body mass index (BMI) and capillary hemoglobin (Hb) test, discarding those with Hb < 12 g/dL. The study was approved by the hospital Ethics Committee. Sample recruitment underwent a four issues questionnaire about RLS symptoms and a blood test to analyze serum ferritin levels.



Results: 179 blood donors were included in the study, 101 women (56%), and 78 men (44%). Mean age was 43.2 years, IC 95% (41.5-44.9) and mean BMI was 25.9 kg/m<sup>2</sup>, IC 95% (25.2-26.5). Blood donors were divided in two groups: first time donors (n=44, 24.6%) and regular donors (n=135, 75.4%); the average in donating time (in years) was 10.9, IC 95% (9.3-12.5). Mean serum ferritin levels were 48.7 µg/L, IC 95% (40.1-57.3) in women, and 131.8 µg/L, IC 95% (110.1-153.5) in men. 79 donors (44.4%) had serum ferritin levels <50 µg/L, with predominance of women (n=50, 64.9%) and regular donors (n=66, 49.3%). 7 donors (4%), all of them regular donors, had serum ferritin levels <12 µg/L. Mean serum ferritin levels in first time donors were 136.5 µg/L, IC 95% (101.9-171.1) and 79.7 µg/L in regular donors, IC 95% (67.6-91.8), p=0.007. 28 donors (15.4%, 18 women) answered 'yes' to at least one of the questionnaire issues. 15 donors answered 'yes' to 3-4 questions (53.6%). Women had a non-significant higher risk to have at least one RLS symptom (p=0,053). We did not find any association between low serum ferritin levels and RLS symptoms (p=0.97), neither between serum ferritin <50 µg/L and RLS symptoms (p=0.88).

**Conclusions:** It is not usual to assess iron metabolism in blood donation units, where the only item which can discard donation is Hb. Normal Hb values can coexist with iron deficiency and unleash RLS. Nevertheless we could not demonstrate this second item. In our study there is a high prevalence of low serum ferritin levels, but this does not increase RLS prevalence. Women donors have lower ferritin values, and a higher risk to have RLS symptoms.

## Hypoferritinemia in blood donors

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**Background:** Continuous blood extractions decrease significantly iron deposits. Despite this fact, it is not usual to assess iron status in Spain blood donation units, where the only item in iron metabolism which can discard donation is the presence of hemoglobin (HB) levels under 12g/dL.

**Objectives and methods:** We designed a prospective study in two Blood Donation Units of the Public Health-Care System, to study iron status. We also analyzed if the iron deficiency could have discarded the donation. The study was approved by the hospital's Ethic Committee. All blood donors underwent a physical examination including blood pressure, body mass index (BMI) and capillary hemoglobin test. All donors with HB <12g/dL were excluded. Sample recruitment, underwent an additional blood test to determine serum ferritin levels and transferring saturation. Donors with hypoferritinemia were followed-up and received treatment with iron supplements.

**Results:** 179 blood donors were included in the study, 101 women (56%), and 78 men. Mean age was 43.2 years IC 95% (41.5-44.9) and mean BMI 25.9 kg/m<sup>2</sup>, IC 95% (25.2-26.5). Blood donors were divided into: first time donors (n=44, 24.6%) and regular blood donors (n=135, 75.4%), where the mean years donating was 10.9, IC 95% (9.3-12.5). Mean serum ferritin levels were 48.7 µg/L, IC 95% (40.1-57.3) in women, and 131.8 µg/L, IC 95% (110.1-153.5) in men. 79 donors (44.4%) had serum ferritin

levels <50 µg/L, with predominance of women (n=50, 64.9%) and regular donors (n=66, 49.3%). 7 donors (4%), had serum ferritin levels <12 µg/L, all of them regular donors. Mean serum ferritin levels in first time donors were 136.5 µg/L, IC 95% (101.9-171.1) and 79.7 µg/L in regular donors, IC 95% (67.6-91.8), p=0.007. An association between serum ferritin levels and high BMI was found (Rho Spermán 0.298, p<0.001).

**Conclusions:** Hypoferritinemia in usual blood donors could unleash anemia and eliminate potential blood donors from the donating system. Some authors promote a systematic use of iron supplements in donors, but this strategy may also be related to side effects. Regular blood donation may reduce iron stores to ferritin concentration <50 µg/L. Women donors have lower serum ferritin values, in contrast to high BMI, which have higher serum ferritin levels. We recommend to assess iron status in high-risk donors, in order to initiate prompt supplementation which could avoid altruist blood donors losses and help to maintain blood donation habits.

## Adult T-cell leukemia: a rare etiology of thrombocytopenia among elderly patients

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**Introduction:** Adult T-cell leukemia/ lymphoma (ATLL) is a malignant proliferation of activated, mature T lymphocytes. This is a rare type of lymphoproliferative syndrome which is typically associated with human T-cell lymphotropic virus (HTLV-1). Diagnosis is based on clinical and laboratory findings, namely through immunophenotyping. The initial presentation is usually insidious, delaying diagnosis and consequently treatment. Prognosis is not favorable and death usually occurs within 12 months following diagnosis.

**Case report:** We present the case of an 86 years old woman, born and resident in Lisbon, Portugal whose past medical history included chronic kidney disease due to hypertensive nephropathy and post-nephrectomy due to renal cell carcinoma. She was well until pancytopenia was found in a routine blood test, prompting admission to hospital for further investigation. A bone marrow aspirate was obtained, showing severe lymphocyte infiltration (60% of total cellularity), without any changes in the other cellular populations, namely erythrocytes and granulocytes. Immunophenotyping identified a mature lymphocyte population (55%) suggestive of ATLL (CD3+/ CD4-/ CD8+/ CD2+/ CD5+/ CD56+). Viral serologies, including HTLV-1 were negative. Thoraco-abdomino-pelvic CT scan did not show peripheral lymphoid involvement. Rapid onset of kidney function and hematological compromise with profound pancytopenia, pulse corticosteroids were initiated with little benefit. End-stage kidney disease was established and initiation of dialysis was discussed with the patient who refused it. She would die 5 days following diagnosis.

**Discussion:** ATLL has a distinct geographical distribution due to its strong association with HTLV-1 infection and its occurrence among elderly patients, particularly in the absence of a typical epidemiological context is exceedingly rare.

## Bilateral pulmonary embolism: pathogenic role of hyperhomocysteinemia and raised factor VIII

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**Introduction:** Venous thrombotic phenomena are a frequently encountered problem in clinical practice. Traditional modifiable risk factors are associated with blood flow changes and/ or vascular wall injury while genetic defects affecting elements of either the clotting or fibrinolytic cascade lead to a pro-coagulant tendency.

**Case report:** We present the case of a healthy 26 years old woman who developed left sided-pleuritic chest pain, fatigue and gradually worsening dyspnea. At the Emergency Department, hypoxemia and hypocapnia were noted and laboratory tests revealed greatly raised D-dimer. Chest angio-CT showed bilateral pulmonary embolism on the inferior pulmonary branches. Doppler assessment of both lower limbs excluded deep vein thrombosis. Besides excess weight (BMI – 28 kg/m<sup>2</sup>) and use of low estrogen dose contraceptive pill, other traditional risk factors were excluded. Additional investigation showed hyperhomocysteinemia, raised von Willebrand and factor VIII. Immunological and genetic screenings were unremarkable. Low-molecular weight heparin followed by warfarin was started without incidents and the patient was discharged clinically stable. Supplementation with folic acid and weight loss program were also initiated. Contraceptive pill was stopped. Three months after presentation, the patient remained well, with effective weight loss (BMI – 25 kg/m<sup>2</sup>) and normal homocysteine. Factor VIII remained high but at a lower titer. Chest angio-CT performed three months after presentation showed completed resolution of previous imaging findings. One-year after presentation, all serological findings, including factor VIII levels were normal, hence warfarin was stopped and the patient kept under twice-yearly follow-up to monitor homocysteine and factor VIII levels. Discussion: Besides activated protein C resistance, mutations on the prothrombin gene and protein C or S deficiency, new phenotypes associated with increased thrombotic risk have been emerging. Elevated factor VIII levels have been identified as a pro-thrombotic phenotype as opposed to hyperhomocysteinemia which has been recognized as a cardiovascular risk factor but is not associated with increased risk of venous thromboembolism.

## Acquired hemophilia: a rare form of hemorrhagic blood dyscrasia

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**Introduction:** Acquired hemophilia (AH) is a rare and potentially severe type of hemorrhagic blood dyscrasia associated with the presence of inhibitors directed against circulating clotting

factors, more commonly against factor VIII (fVIII). Besides the idiopathic form, AH may be secondary to cancer or auto-immune conditions. Definitive diagnosis is rendered difficult by the absence of characteristic personal or familial history and by the wide range of clinical presentations compared to what is usually found among the hereditary forms. Treatment goal is to correct clotting abnormalities by eliminating circulating autoantibodies.

**Case report:** We present the case of a 73 years old man with past medical history of atrial flutter under treatment with warfarin. He developed hemoptysis which was interpreted as secondary to warfarin but due to its persistence in association with epistaxis, extensive skin bruising and dyspnea to minimal exertion, he attended the local Emergency Department. On examination, several hematomas were noted but no other relevant findings were observed. Blood tests revealed microcytic anemia and prolonged prothrombin (INR: 5.6) and activated thromboplastin time (APTT >100 sec) with normal platelet count and normal fibrinogen. Thoraco-abdominopelvic CT did not show intra-abdominal bleeding and excluded lymphadenopathies or other signs suggestive of cancer. fVIII was greatly (<1%) and factor VIII inhibitors (fVIIIi) found to be present in high titer (491 BU). Immunological screening was otherwise negative. Following pulsed methylprednisolone, a slight decrease of APTT and fVIIIi (273 BU) were initially noted but due to extensive, rapidly progressive muscular hematomas and severe anemia despite multiple blood transfusions, high dose activated factor VII (afVII) was started with little benefit. A six-day course IV IgG in addition to prednisolone 1 mg/kg/day was initiated with gradual hematological improvement and clinical stabilization even after afVII was stopped. Accompanying fVIII increase, fVIIIi titers decreased and became negative 8 weeks after presentation under steroid tapering regimen. The patient remains well and has resume oral anticoagulation with rivaroxaban with no further hematological relapses 4 months after diagnosis.

## AL amyloidosis and multiple myeloma – a clinical case

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**Introduction:** AL amyloidosis (ALA) is due to extracellular deposition of fibril-forming proteins derived from monoclonal immunoglobulin (Ig) light chains (LC). ALA is the most common type of systemic amyloidosis in developed countries with an estimated incidence of 6 to 10 cases/million inhabitant/year and its association with multiple myeloma (MM) is unusual. Presenting symptoms usually include asthenia and dyspnea. Amyloid deposition in viscera results in restrictive cardiomyopathy, nephrotic range proteinuria and hepatomegaly. Diagnosis relies on pathological exam showing Congo red-positive amyloid deposits, with typical green birefringence under polarized light.

**Case report:** A 69 years old woman was admitted with hepatomegaly, weight loss and asthenia. Laboratory analysis revealed elevated serum alkaline phosphatase, creatinine and beta 2 microglobulin levels and a nephrotic range proteinuria. Serum electrophoresis and immunofixation presented with IgG lambda monoclonal gammopathy and quantitative elevation

LC levels. Hepatic imaging showed regular hepatomegaly and liver biopsy revealed extracellular amorphous Congo red positive deposits. Bone marrow biopsy had 30% infiltration with plasma cells and amorphous extracellular deposits. Late gadolinium-enhancement cardiac magnetic resonance described concentric left ventricle hypertrophy and a pattern of amyloid deposition. The diagnosis of MM and systemic ALA with liver, renal and cardiac involvement was assumed and the patient started corticotherapy and was referred for Hematology to begin chemotherapy. 4 months later the patient was readmitted for general edema, ascitis, dyspnea and renal function deterioration. Supportive therapy for heart failure was optimized. One week after hospital discharge the patient returned for palliative care due to poor performance status and died.

**Conclusion:** AAL is a systemic disease seldom related to MM and early diagnosis and chemotherapy is important for improving its generally poor prognosis. Prognosis is determined by the extension of amyloid tissue deposition and cardiac involvement is the main prognostic factor.

### **Bullous fixed drug eruption in a patient with metastatic renal cell carcinoma induced by iodinated contrast. A case report**

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**Introduction:** Hypersensitivity reactions due to iodinated contrast are well known under clinicians however little is known of fixed drug eruptions.

**Case report:** A 70 years old male was treated for metastatic clear cell renal cell carcinoma with pazopanib, a tyrosine kinase inhibitor targeting several receptors, but main site of action is the vascular endothelial growth factor receptor 2 (VEGFR2). Pazopanib impairs angiogenesis by abrogating the VEGFR2 to exert its function, by binding to the intracellular domain of the receptor. He uses the antitumor medication now on a stable dose, without remarkable toxicity. Computed tomography (CT) scanning is done at regular intervals in order to perform response evaluation. Within 24 hours of performing the CT scan the patient develops a blood blister on digit III of the left hand which dries out after approximately 4 days and disappears completely. This phenomenon occurred each time with the bullous fixed drug eruption at exactly the same location and it also occurred if the contralateral arm was used to infuse the contrast medium. Laboratory investigations were unremarkable, including parameters evaluating coagulation. Furthermore anti-basement membrane zone antibodies, anti-intercellular substance antibodies, desmoglein-1 and -3 antibodies and BP180 and 230 specific auto-antibodies were all negative. A biopsy will be taken at the next occurrence and data will be available at the meeting. Bullous fixed drug eruptions are a rare entity and have not been described before as a result of contrast.

**Discussion:** Our patient was diagnosed with a fixed drug eruption caused by iodinated contrast. This rare phenomenon although the scarce knowledge on this entity might result in underreporting as well.

### **Anemia of inflammation, an important entity**

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**Introduction:** Anemia of inflammation (AI), formerly called anemia of chronic disease (ACD), is a clinical syndrome characterized by the development of anemia in patients with infectious, inflammatory, and neoplastic diseases. Recent reports find that this kind of anemia can also be associated with other conditions including the diabetes mellitus, trauma, sepsis, among other pathologies. Characteristically, AI corresponds to normochromic/normocytic, mild to moderate anemia, iron levels (Fe) serum low. The main pathological mechanisms involved in AI are altered iron metabolism, decrease in the production and survival of red blood cells and inadequate erythropoietin (EPO) response.

**Case report:** A 59 years old man is referred for evaluation of a hypoproliferative normocytic anemia with hemoglobin of 7 g/dL. His past medical history is significant for a mitral valve replacement 6 months ago. Recently, he has developed fever and generalized fatigue. His examination is unremarkable except for a temperature of 38°C and a 3/6 systolic ejection murmur over the mitral valve. Laboratory evaluation reveals a decreased serum iron, low total iron-binding capacity (TIBC), and low iron saturation percentage. Serum ferritin is 57 ng/mL and the Westergren sedimentation rate (WERS) is elevated at 100 mm/h. Blood cultures subsequently return positive for methicillin-resistant *Staphylococcus aureus*. Echocardiogram confirms subacute bacterial endocarditis of the prosthetic mitral valve. The patient is placed on vancomycin and ferrous sulfate. 5 weeks later, the hemoglobin increases to 11.5 g/dL.

**Discussion:** AI is the most common cause of anemia in patients with underlying inflammatory diseases. Multidisciplinary approach was necessary for a complete diagnosis and treatment. Treatment should be directed at the underlying medical condition. If anemia is severe and the patient is symptomatic, EPO can be considered. Therefore AI, one of the most common diseases in clinical practice, imposes the need for the hematologist, the general practitioner, the internist and other specialists to be familiar with this entity.

### **Hemoglobin sickle cell disease in adulthood: paradoxically milder, paradoxically severe?**

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**Introduction:** Isolated splenic vein thrombosis is rare; while acute splenic sequestration crisis (ASSC) associated with sickle cell disease (SCD) is considered a disease of pediatric age. Hemoglobin sickle cell (HbSC) disease, a milder variant of SCD is associated with normal splenic function; ASSC is rare and tends to occur in later years.

**Case report:** We describe a case of a 30 years old female, with the diagnosis of sickle cell anemia HbSC variant with 1-2 minor vasoocclusive and hemolytic events per year. No splenic crisis or splenomegaly had been formerly documented. The patient was admitted with a vasoocclusive crisis, described as left thoracic and lower leg pain. Within 24 hours rapid drops of 40 g/L of hemoglobin and platelet count was accompanied by fever, tachycardia, hypotension, lethargy and diffuse abdominal pain. Echography and computerized tomographic imaging documented various areas of splenic and hepatic infarctions accompanied by a 4 cm splenic vein thrombus. No other intra-abdominal venous thrombi were documented. In light of the diagnosis of ASSC complicated by isolated splenic vein thrombosis, blood transfusion support was initiated and the patient was submitted to emergent splenectomy. An enlarged spleen measuring approximately 19x13x7 cm, with macroscopic evidence of multiple subcapsular, parenchymal infarcts and splenic vein thrombus was removed. Anticoagulation was initiated as soon as proper hemostasis was guaranteed. Remainder of hospitalization was uneventful. Given the rarity of this complication in HbSC disease, with the accompanying splenic vein thrombosis, further workup to exclude other pro-thrombotic states was undertaken. Although laboratory testing for systemic lupus erythematosus (SLE) was positive (positive ANA, anti-Ro/SSA and anti-La/SSB antibodies and antiribosomal P protein antibodies), the patient did not fulfill the Systemic Lupus International Collaborating Clinics criteria for the classification of SLE, in fact antinuclear antibody positivity has been shown in association with SCD. Antiphospholipid antibodies assays and paroxysmal nocturnal hemoglobinuria testing were negative. Factor V Leiden and prothrombin gene were normal. No antithrombin, protein C or protein S deficiencies were documented.

**Discussion:** The authors present this case as a reminder of the heterogeneous, rare and late complications of SCD, as well as the basal hypercoagulable state amplified further by increased sickling, endothelial dysfunction and circulating pro-coagulant micro-particles in acute disease.

## A “simple” back pain – apropos of a clinical case

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**Introduction:** Burkitt's acute lymphocytic leukemia (ALL) is a rare type of adult ALL, difficult to distinguish from disseminated Burkitt's lymphoma (BL) involving the bone marrow; BL and Burkitt leukemia are classified as different manifestations of the same disease. This tumor is highly proliferative and tends to involve the central nervous system (CNS) at diagnosis or early during the disease course – with many different possible clinical manifestations, sometimes easily confounded with other etiologies.

**Case report:** 24 years old Caucasian male, engineering student and basketball player. No relevant personal or family medical history. Admitted to the emergency department due to sudden-

onset cervicgia with dorsal radiation, after physical exercise; he was discharged with analgesic medication. Symptomatic worsening occurred, with progressive loss of strength and sensibility in the lower limbs, inability to walk and urinary retention. On observation: bilateral lower limb paresis (muscle strength 2/5); no other relevant findings. Blood testing: hemoglobin 10.7 g/dL, leukocyte count (WBC) 4.1x10<sup>9</sup>/L, platelets 60000, lactate dehydrogenase (LDH) 2108 U/L. Spine magnetic resonance imaging (MRI): compressive intracanalicular haematoma D2 - L2. He was admitted to the internal medicine ward of his local hospital, with rapid worsening of paresis and subsequent onset of fever without obvious infectious origin. The patient was transferred to a hematology ward for further study. Dry-tap marrow aspiration and biopsy: Burkitt-like acute lymphoblastic leukemia, CD20+, Philadelphia chromosome negative, FLT3 negative e MYC positive. Intrathecal and systemic chemotherapy (ChT) was started with hyper-CVAD regimen (cyclophosphamide, vincristine, doxorubicine and dexametasone); lumbar puncture did not reveal malignant cells in the cerebrospinal fluid. Subsequent neutropenic fever appeared, resolved with meropenem. Due to the vast spinal hematoma, placement of an Ommaya catheter was considered for optimal intrathecal ChT, but was ruled out due to high risk of hemorrhage. After repeated ChT cycles, progressive symptomatic remission was observed, with sustained recovery of limb strength and walking ability.

**Discussion:** The authors reiterate not all “typical” presentations translate into common diagnoses. It is vital that the physician maintain critical thinking and approach each patient's symptoms with care – even when appearing simple, they may hide serious conditions requiring urgent treatment.

## Cytomegalovirus infection: on the gateway for hematological malignancy

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**Introduction:** Primary cytomegalovirus (CMV) infection in the immunocompetent host rarely causes serious illness. Uncommonly, it can result in a mononucleosis syndrome, indistinguishable from primary Epstein-Barr virus infection. The overall seroprevalence for CMV in developed countries is 30-70%.

**Case report:** 45 years old male, previously healthy, with a 1-week history of night sweats and anorexia was admitted for observation. He reported no fever, dyspnea, diarrhea, vomiting or dysuria. His physical examination was unremarkable. During his internment daily fevers were reported, with temperatures as high as 40°C. Leukocytosis with activated lymphocytes was noted. Red-cell indexes, erythrocyte sedimentation rate and results of renal function tests were normal, C-reactive protein was mildly elevated (6 mg/dL) and liver enzymes levels were abnormal (AST 80 U/L, ALT 68 U/L, FA 97 U/L, GGT 142 U/L). Antibodies for human immunodeficiency virus types 1 and 2 and tests for syphilis and acute EBV infection were negative. A seroconversion of low-avidity IgG to CMV together with IgM for

CMV revealed an acute primary CMV infection. Proteinogram revealed a monoclonal gammopathy IgA kappa. A myelogram was performed and revealed a monoclonal gammopathy of undetermined significance with a total of 10% of plasmocytes. Bence Jones proteinuria was detected. Bone marrow biopsy shown granulomatous myelitis and reactive plasmocytosis. The chest radiograph was normal. The patient was discharged and then lost to follow up.

**Discussion:** In developed countries, delayed exposure is causing an increasing incidence of infections in middle-aged adults. Previous studies have shown that monoclonal gammopathy is common among patients with primary CMV infection, either immunocompetent or immunocompromised, even though it is usually transient. Even so, this association may indicate a causal relationship between CMV infection and pathogenesis of plasma cell malignancies.

## Cold agglutinin disease: a presentation of acute myelomonocytic leukemia

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**Introduction:** Cold agglutinin disease (CAD) is a form of autoimmune hemolytic anemia (AIHA) that usually affects the elderly and is characterized by particular clinical and pathological features.

**Case report:** 72 years old male, with a past medical history of chronic kidney disease on dialysis, left nephrectomy following clear cell renal carcinoma, sigmoid colon adenocarcinoma, type 2 diabetes mellitus insulinotreated, hypertension, hyperuricemia and benign prostatic hyperplasia. He was admitted with one month of fatigue, dizziness and several episodes of lipothymia. In emergency department he was febrile (T 39°C), icteric sclera and pale skin. He also had a lesion with herpetic features on his nose. His lab tests revealed normocytic anemia (Hb 6,8 g/dL), leukocytosis, 2% myeloblasts, 27% neutrophils, platelets 35000, total bilirubin 1,3 mg/dL, CRP 9,8 mg/dL, LDH 4840 IU/l, beta-2-microglobulin 35 mg/dL. At this point the hypotheses were cold antibodies hemolytic anemia in context of lymphoproliferative disease versus viral infection. Search for cryoagglutinins came out positive for anti-I antibodies and anti-I with high temperature. His blood cultures were negative. Her serological tests were positive for Herpes zoster and negative for HIV, HBV, HCV and CMV. The patient underwent transfusional support and was put on high dose corticotherapy with methylprednisolone. His thoracic, abdominal and pelvic CT scan revealed multiple mediastinal adenopathies, splenomegaly (19 cm) and apparently a spleen subcapsular infarction on its medium third. His imagiological assessment was consistent with systemic disease - lymphoproliferative disease. He suddenly developed dyspnea and peripheral desaturation recognized as volume overload and was put on urgent dialysis. His clinical situation aggravated during the session leading to non-reversible cardiac and respiratory arrest. The diagnosis of acute myelomonocytic leukemia was confirmed postmortem, using a myelogram sample taken on first day of hospitalization.

**Discussion:** Like most of the autoimmune diseases, the real etiopathogenesis of CAD remains unknown. However, from the clinical point of view, this type of AIHA can appear as an isolated process, as well as a part of other autoimmune disease and even as the initial presentation of a lymphoproliferative disease.

## Multiple myeloma presenting with relapsing hypoglycemia

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**Introduction:** Hypoglycemia is characterized by a reduction in blood glucose concentration to a level that induces adrenergic or neuroglycopenic symptoms and reversal of these symptoms when glucose is restored to normal (Whipples' triad). The insulin autoimmune syndrome (IAS), or Hirata's disease, is a rare cause of hypoglycemia characterized by a high titer of anti-insulin autoantibodies, usually polyclonal, without prior insulin administration. The intermittent and unpredictable release of bound insulin results in spontaneous hyperinsulinemic hypoglycemia, associated with relatively low C-peptide levels. We describe an unusual case of relapsing hypoglycemia in a patient diagnosed with multiple myeloma.

**Case report:** A 69 years old patient presented with one-year history of dizziness, tremor and gait instability, and fasting hypoglycemia for the last month. He had no history of diabetes mellitus. On physical examination, there was nothing remarkable while blood studies revealed anemia and monoclonal gammopathy. Computed tomography and magnetic resonance imaging of the abdomen were done in order to exclude insulinoma and they were normal. A 72-hour fasting glucose test was performed. In 10 hours the patient developed symptomatic hypoglycemia (serum glucose 48 mg/dL). At the same time serum insulin level was high at 142 µIU/ml while C-peptide levels were normal at 1,0 ng/ml. Bone marrow biopsy confirmed the diagnosis of multiple myeloma. Treatment of multiple myeloma led to discontinuation of hypoglycemic episodes.

**Discussion:** Reported mainly in Japan, IAS is associated with autoimmune diseases such as Graves's disease, rheumatoid arthritis, or sulfhydryl containing drugs. A strong correlation with HLA-DR4 has been noted. However, few case reports associate IAS with plasma cell dyscrasias. In these cases, a clonal proliferation of plasma cells produced a monoclonal insulin-binding antibody. It is speculated that in response to a meal, high plasma glucose levels evoke insulin secretion, a substantial proportion of which binds to the monoclonal antibody, being not biologically available. The resultant hyperglycemia promotes further insulin release. Postprandially, as glucose concentration declines, the bound insulin is released, resulting in high serum insulin levels, thus inducing hypoglycemia. Conclusion: IAS should be considered in any patient evaluated for hypoglycemia. Monoclonal

gammopathy should be investigated as a possible cause of this syndrome.

## **Congenital abnormalities of inferior vena cava and deep venous thrombosis**

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**Introduction:** Congenital protein C and S deficiency is well known to be associated to thrombotic events in young patients and deep venous thrombosis is considered to be the most frequent clinical manifestation in these cases. On the other hand, anatomical anomalies of the cavoiliac territory are contributing factors for thrombotic events.

**Case report:** A 28 y.o. male patient with a previous history of hypertension, renal colic and a previous deep venous thrombosis in the right leg was admitted to ER complaining of left lumbar pain radiated to ipsilateral testicle. He was initially treated with analgetics with no relief. The patient was slightly hypertensive and tachycardic and was saturating 94% on room air. Lab tests showed: DD 4.21 mcg/ml with normal complete blood count, hemoglobin and chemistry panel. An abdominal CT was ordered showing thrombosis of the inferior vena cava, infrarenal and iliac veins as well as bilateral femoropopliteal thrombosis. Interestingly, the left renal vein and inferior vena cava were both hypoplastic accompanied of important collateral circulation. Sodium heparin was initiated, then switched to low weight heparin with 24 hours. He was released on oral anticoagulation which was 1 year pursued. 2 months after discontinuation a complete coagulation study was performed. In this respect, protein C and S deficiency was found, thus long-term anticoagulation was prescribed.

**Discussion:** Congenital anatomic abnormality of the inferior vena cava (IVC) is an important risk factor for the development of spontaneous venous thrombosis in young adults. A number of congenital IVC anomalies have been described, and the prevalence of IVC anomalies in the general population has been estimated to be between 0.07 and 8.7%. These abnormalities are often asymptomatic, and identified incidentally in patients undergoing imaging investigations for other reasons. It is likely that many, if not most, cases of congenital IVC abnormalities remain undiagnosed and of little or no consequence to affected individuals. However, there is a subset of patients with congenital IVC anomalies who present with clinically significant deep vein thrombosis (DVT) as in our case. Because the mainstay of diagnosis of DVT is ultrasound with venous Doppler, which does not readily identify IVC anomalies, these anomalies may be underdiagnosed in patients presenting with spontaneous DVTs. Previous estimates of the prevalence of IVC anomalies among young adult patients with DVTs have been in the range of 5% in patients under 30 years of age. Besides, in protein C and S deficiency is a leading cause of thrombophilia and a risk factor for developing DVT.

**Conclusion:** young patients with recurrent deep venous thrombosis should undergo a complete coagulation screening even more in the present of infrequent anatomical vein variations.

## **Prasugrel-associated acquired thrombotic thrombocytopenic purpura**

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**Introduction:** Thrombotic thrombocytopenic purpura (TTP) is defined by a severe deficiency of ADAMTS13, but the diagnosis of TTP remains based on clinical judgment since ADAMTS13 measures are often not available for several days and different methodologies may yield different results. Deficiency of ADAMTS13 can be hereditary or acquired, as a result of inhibition of ADAMTS13 activity by an autoantibody. TTP is unique among the primary TMA syndromes for minimal abnormalities of kidney function, despite microthrombi observed throughout the kidney. TTP typically has more systemic manifestations of organ injury than the other primary TMA syndromes. In TTP, abnormalities of the central nervous system, heart, pancreas, thyroid, adrenal glands, intestinal mucosa, and other tissues may occur.

**Case report:** 64 y.o. male patient with previous medical history of type 2 diabetes mellitus and hypertension was admitted because of ST elevation acute coronary syndrome. Fibrinolysis was effective and stents were placed. He was discharged on oral prasugrel 10 mg. 36 days later he was re-admitted owing to abdominal pain, vomiting, purpuric skin lesions, hypotension and oliguria. He was suspected to have appendiceal gangrene and subsequently underwent surgery. Lab tests showed anemia, severe thrombopenia, acute renal failure, increase CK, LDH, total bilirubin, lactic acid as well as CRP and procalcitonine. No results consistent with disseminated intravascular coagulation were found. Prasugrel was taken off upon arrival and antibiotics were indicated. Inflammatory markers, renal function and platelets recovered within 48 hours but after that a systemic clinical worsening was noted. Laboratory and clinical findings included 6% schistocytes, negative Coombs test, severe thrombopenia and neurological impairment. Plasma exchange was initiated but the patient died 6 days after. The autopsy revealed thrombi in the microcirculation mainly affecting the adrenal glands, spleen, heart, bone marrow and intestine. Subendothelial deposits or wall vessel disturbances were not described.

**Discussion:** TTP is rarely associated to drugs even though clopidogrel and prasugrel have been implied. A study carried out in US between 1991 and 2011 stated that clopidogrel was most commonly associated to TTP (197 cases), followed by ticlopidine (97 cases) and prasugrel (14 cases). Interestingly, TTP is mainly described to appear early after the drug initiation. In this case there was no other cause for TTP, clinical features initially improved when the drug was taken off, ADAMTS13 activity was inferior to 10% and genetic studies ruled out hereditary TTP. Inflammatory markers and function renal tests went down after surgery, no leukocytosis was found in contrast to increase hemolytic markers in the absence of lab findings consistent with disseminated intravascular coagulation (DIC). Plasma exchanged is considered to be an adequate treatment in the management of acquired TTP and survival reaches 78% of patients.

**Conclusions:** Prasugrel probably brought about TTP as there were no other laboratories or histological findings consistent with sepsis or DIC. However inhibitory autoantibody to the ADAMTS13 couldn't be determined.

## Antibody-negative pernicious anemia

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**Introduction:** Pernicious anemia is caused by an autoimmune gastritis, characterized by atrophy of the gastric mucosa, which leads to diminished gastric acid and intrinsic factor secretion and vitamin B12 malabsorption. It accounts for 20–50% of the causes of vitamin B12 deficiency in adults. Serum antiparietal cell antibodies are present in 85–90% of the cases and anti-intrinsic factor antibodies exist in 50% of the cases. Vitamin B12 deficiency usually develops gradually, and symptoms may not occur until it is severe.

**Case report:** A 44 years old previously healthy man presented with a 4-month history of asthenia and anorexia, with dyspepsia and diarrhea in the last 2 months. Blood tests showed macrocytic anemia (Hb 7.3 g/dL, MCV 124.5 fl), high LDH (5864 U/L), AST (76 U/L) and total bilirubin (1.7 mg/dL). Peripheral blood smear showed anisopoikilocytosis and hypersegmented neutrophils. Additional blood tests showed low reticulocytes (8x10<sup>9</sup>/L), normal serum iron (145.5 ug/dL) and ferritin (224 ng/ml), low total iron binding capacity (168 ug/dL), high transferrin saturation (87%), low vitamin B12 (63 pg/ml) with high homocysteine (60.8 umol/L), normal folates and low haptoglobin (<8 mg/dL). After excluding causes of intestinal malabsorption, pernicious anemia was suspected. Antiparietal cell antibody was positive and anti-intrinsic factor antibody was negative. Treatment with intramuscular cobalamin was started with clinical response. After one month of treatment he was asymptomatic and blood tests showed no anemia, normal mean corpuscular volume and normal peripheral blood smear. Antibody-negative pernicious anemia was assumed and lifelong treatment with cobalamin was started.

**Discussion:** In this case we report an exception to the classical diagnosis of pernicious anemia made in 50% of the cases by anti-intrinsic factor antibody. Antibody-negative pernicious anemia is assumed when there is clinical response to cobalamin treatment. Prompt detection and treatment of vitamin B12 deficiency is essential for hematologic recovery and to prevent the development of irreversible neurologic impairment.

## Kikuchi-Fujimoto disease: a rare condition with an atypical presentation happening in Europe

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**Introduction:** Kikuchi-Fujimoto Disease (KFD) is a rare benign, idiopathic, self-limited cause of lymphadenitis. It is known to be a condition causing necrotizing histiocytic lymphadenitis, most common in Asia. Its etiology is believed to be of viral origin, as Epstein-Barr virus, human Herpes virus 6 and 8. It tends to affect a young population under 30 years of age. Frequently manifests as a relatively acute onset of cervical lymphadenopathy associated with fever and a flulike prodrome. A definitive diagnosis requires whole lymph node biopsy. Immunoblast cell changes seen in lymph nodes mimic those of malignancy and are a source of diagnostic confusion.

**Case report:** The authors describe a clinical case of a 66 years old male, of Portuguese nationality, who was taken to the hospital emergency unit because of anorexia, behavioral changes and weight loss. In the emergency unit, blood tests showed low platelet and red blood cell count, with high erythrocyte sedimentation rate, associated with oligoanuric renal failure. The patient was admitted to the inpatient department for further investigation. The ultrasound showed normal kidneys and urethras. A computerized body scan tomography revealed multiple lymphadenopathies with hepatosplenomegaly, with no evident cause found imagiologically. From extended blood analysis, what stood out was polyclonal gamopathy compatible with infectious or inflammatory etiology. So a bone marrow and lymph node biopsy were necessary for the definitive diagnosis. Bone marrow was described with trilineage hyperplasia with granulocytic predominance and an exuberant plasmocytosis of reactive pattern. Lymph node biopsy results reported plasmocytosis with necrotizing lymphadenopathy, compatible with KFD.

**Discussion:** KFD almost always runs with a benign course and resolves in several weeks to months. Disease recurrence is unusual, and fatalities are rare. Although uncommon, should be featured in a list of differential diagnosis of tender lymphadenopathy, especially affecting the cervical region. Its treatment differs significantly from the other conditions that would be on that list, such as systemic lupus erythematosus, lymphoma and tuberculosis. This is important as the treatment of KFD is symptomatic and supportive, while the other conditions mentioned require prompt specific treatments.

## A rare presentation of prostate cancer

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**Introduction:** We report a case of myelophthisic anemia secondary to marrow infiltration by solid tumor.

**Case report:** A 74 years old male, smoker and with a history of type 2 diabetes came to emergency with a 15-day history of dyspnea with minimal effort and increased volume in lower limbs, accompanied by marked weakness and hyporexia of several weeks of evolution. On examination, he showed pale mucous membranes, basal crackles in both lungs and discreet edema in the lower limbs. In blood analysis highlighted: hemoglobin

9.9 g/dL, MCV 109.6 fL, MCH 37.6 pg, 31000 platelets /uL, with normal leukocyte count. Alkaline phosphatase was 2810 U/L, the rest of liver function was normal. A chest radiograph showed evidence of pulmonary congestion. Peripheral blood smear was performed, confirming the presence of thrombocytopenia and reticulocytosis (5.6%), macrocytic anemia with anisocytosis and presence of macro-ovalocytes. A complete blood analysis performed in Internal Medicine ward showed ferritin 1221 ug/L and PSA 107 ng/mL. Serological tests for HIV, HCV, HBV, HAV, parvovirus and cytomegalovirus were negative. A transthoracic echocardiography showed signs of dilated cardiomyopathy with an LVEF of 35%. A computed tomography (CT) of the chest and abdomen was performed, with findings consistent with primary prostate cancer with left iliac lymph node involvement and metastatic spread affecting the entire skeleton included in the study. Bone marrow biopsy was performed; the pathological examination of the specimen revealed massive infiltration by moderately differentiated adenocarcinoma of morphology and immunohistochemical profile compatible with primary prostatic origin. Final diagnosis: myelophthitic anemia as first manifestation of disseminated prostate cancer.

**Discussion:** The bone marrow fibrosis may be primary (myelofibrosis) or secondary (myelophthisis). Myelophthisis is a reactive process, which may be a reaction to the invasion of the marrow by tumor cells, but may appear in mycobacterial or fungal infections, HIV or sarcoidosis. The main solid tumors related to the development of myelophthisis are carcinomas of the breast, lung, prostate, thyroid, kidney and various sarcomas that share the characteristic of having a pattern of small, round blue cells. Myelophthisis is characterized by normochromic normocytic anemia, with characteristic leukoerythroblastosis in the peripheral blood smear. Prostate cancer is the second most common cancer in men. Most of them are asymptomatic, but may present as voiding syndrome. Although most of prostate cancer are diagnosed when the disease is localized, there are described cases of prostatic cancer diagnosed with metastasis. Myelophthitic anemia as first manifestation of advanced prostate cancer is a very unusual presentation, and there are few similar cases described in the literature.

## Hepatitis B virus screening for malignant lymphoma

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**Objectives:** The non-Hodgkin lymphoma shows a major ratio in malignant lymphoma in Japan. Chemotherapy (CTx) is the first choice. The rituximab administration is standard therapy for CD20 positive cases. Rituximab has side effect such as infusion reaction, but reactivation of the hepatitis B type virus (HBV) is an important problem. We reviewed the situation of the HBV infection check of patients that ML is diagnosed.

**Methods:** We intended for patient which ML was diagnosed in in this hospital from January, 2003 to December, 2012. The pretreatment HBV check factor is hepatitis B surface antigen

(HBsAg), hepatitis B surface antibody (anti-HBs), antihepatitis B core antibody (anti-HBc). When either anti-HBs or anti-HBc is positive, we measure viral load by HBV-DNA Taqman and do it with completion. In the case of HBV check is incomplete, additional HBV check followed as much as possible. We reviewed HBsAg, anti-HBs, a positive rate of anti-HBc, search rate of HBV-DNA Taqman, complete rate that we matched pretreatment complete rate, a follow-up survey. Also we investigated HBV reactivation rate of RCHOP or RCHOP like CTx.

**Results:** There were 446 cases, including male 243, female 203, median age of these was 68 years, about type of malignant lymphoma, Hodgkin's lymphoma (HL) - 39 cases, non-Hodgkin's lymphoma (NHL) - 401 cases, adult T cell lymphoma (ATL) - 6 cases (1.3%). In NHL, B cell type were 358 cases. Among 446 patients, it was 411 cases that was performed CTx or CTx + radiation therapy (RTx). HBsAg was examined in all cases, anti-HBs, anti-HBc was 351 cases, 261 cases respectively. The case searched three factors before CTx was 150 cases. It was 30 cases that it was searched HBV-DNA Taqman for the case that anti-HBs and/or anti-HBc were positive. Treatment needed situation were 5 cases. These 5 cases treated by antiviral drug (entecavir) and after 2 weeks, CTx performed. The case that was already given an antiviral drug with HBsAg positive for treatment was 4 cases. It was 107 cases after CTx that it was searched anti-HBs, anti-HBc or either. It was 2 cases after CTx to have needed the administration of antiviral drug. The cases that performed RCHOP or RCHOP like CTx was 278 cases. HBV reactivation rate was 0%.

**Conclusions:** Japan achieves the HBV rate of infection in 1997 that WHO proposes. 111 cases that were able to chase and 2 therapeutic necessary HBV infection was (1.8%) excised. In present, we do check in all cases and try for safe chemotherapies especially rituximab including one.

## Multiple neoplasms including myeloma and related plasma cell neoplasms

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**Objectives:** Last decade, the treatment outcome of multiple myeloma was improved drastically. The patients that can achieve CR are not rare. Naturally, the long term survivors increased. The long term survivors increased at an opportunity to meet with second malignancies. So, we investigated multiple neoplasms including multiple myeloma and related plasma cell neoplasms. **Methods:** In the case that hematologic malignancy was diagnosed in our hospital by 1988 from 2014. We intended for multiple neoplasms 301 cases including hematological malignancy. We reviewed 42 multiple neoplasms including myeloma and related plasma cell neoplasms. All patients were followed up until death or until December 2014. Survival was measured from the diagnosis of multiple cancers to time of death or last contact. So we reviewed and reported about age, gender, kind of hematologic malignancies, kind of co-exist malignancies, and the cause of death.



Results: There were 42 cases; median age was 71 years, about gender, male were 31 cases, female 11 cases. Type of multiple neoplasms, metachronous type were 29 cases, synchronous type were 13 cases, about number of malignancies, double neoplasms 36 cases, triple neoplasms 6 cases. The constitution of the disease is as follows, multiple myeloma 31 cases, macroglobulinemia 7 cases, isolated plasmacytoma 2 cases, monoclonal gammopathy undetermined significance 2 cases. Type of multiple neoplasms, metachronous type were 29 cases, synchronous type were 13 cases. About kind of co-exist malignancies, 42 cases 48 diagnoses, gastric cancer 12 cases, colon cancer 7 cases, myelodysplastic syndrome 7 cases, hepatocellular carcinoma 5 cases, acute myeloid leukemia 4 cases, malignant lymphoma 4 cases, lung cancer 3 cases, prostate carcinoma 3 cases, and pancreatic cancer, uterine body cancer, laryngeal cancer 1 case respectively. About cause of death, 26 cases were death cases, 18 cases died from multiple myeloma, 5 cases died from co-existent malignancies, 3 cases were accident.

Conclusions: As for the treatment of MM, it is common that MM therapy continue to the last. Prognosis was improved by the appearance of the new drug, decision of the treatment interruption is necessary. A method of the accurate evaluation of effect measurement is expected.

### **Influence on cardiac function of adriamycin in the treatment of malignant lymphoma**

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**Objectives:** The standard therapies of non-Hodgkin's lymphoma (NHL) are R-CHOP therapy. Key drug of CHOP therapy is adriamycin. In adriamycin to heart is toxic. The adriamycin has the limit of the dose. Sometimes cardiac function may decrease with in the limit. Even if treatment is successful, cardiac function may limit activity of daily life.

**Methods:** In the case that malignant lymphoma was diagnosed in our hospital by 2003 from 2012. 446 cases were eligible to our study. We intended for 243 cases that were diagnosed non-Hodgkin's lymphoma diffuse large B cell type (NHL DLBCL). In 243 cases 193 cases were received R-CHOP therapy that was standard regimen for NHL DLBCL. Adriamycine is included in R-CHOP therapy. 144 cases achieved complete response. We examined an ejection fraction comparing from previous R-CHOP therapy to after R-CHOP therapy.

**Results:** Of 144 patients, we examined 91 cases that measured EF in before and after. Median age was 68 years ranged from 33 years to 86 years; gender ratio was male 53 cases, female 38 cases. The median of courses was 8 course of RCHOP therapy. Cumulative dose were 400 mg/m<sup>2</sup>/body. This dose was within permitting dose. The case treated more than an allowable dose had nobody. It was 59 cases (65%) that EF had decreased in before and after therapy. There was not the case that performance status (PS) decreased by EF decrease.

**Conclusions:** 65% of cases that EF decreases are present. The EF observation after the treatment is necessary.

### **Assessment of sites of marrow and extramedullary hematopoiesis by hybrid imaging in patients with primary myelofibrosis**

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**Objective:** To assess the interest of non-invasive nuclear medicine procedures with the use of <sup>99m</sup>Tc and <sup>111</sup>In-Cl3 coupled to a SPECT/CT image acquisition to detect the sites of active or inactive hematopoiesis as well as the extent and intensity of the extramedullary hematopoiesis (EMH) in primary myelofibrosis (PMF).

**Material and methods:** We performed hybrid imaging (HIm) in 4 untreated patients with PMF and in 1 with essential thrombocytemia (ET) who was developing a secondary MF. Two tracers were employed: a) <sup>99m</sup>Tc marked nano-colloids to assess the reticulo-endothelial system. Whole body planar and focused SPECT acquisitions were made with a dual head gamma camera. The whole body acquisitions were made 1h and 6h after IV administration of <sup>99m</sup>Tc. A SPECT/CT was performed and multiplanar reconstructions were made.; b) <sup>111</sup>In marked transferrin scintigraphy (<sup>111</sup>In-Cl3), with SPECT/CT. Image acquisitions were made 48 and 72h after IV injection of <sup>111</sup>In-Cl3. Results: In patients with PMF we observed a low intensity fixation of both tracers in the axial skeleton (AxS) and conversely a hyperfixation at the level of the distal skeleton (DiS) and more in particular the limbs. In all the patients we observed a hyperfixation of <sup>111</sup>In-transferrin at the splenic level. This pattern is higher suggestive of PMF when it is associated to a lower fixation of this same radionuclide in the AxS.

**Conclusions:** Some questions remain unsolved as the mechanisms involved in the recruitment of DiS, in circumstances that these hematopoietic areas were progressively inactive since birth and replaced with adipose tissue. Is the reactivation of DiS a consequence of the homing of HSC that cannot seed in the physiological hematopoietic areas of an adult human, which takes part essentially in the AxS? Or is this the fruit of the reactivation of HSC (and their micro-environment) already present in these DiS of the skeleton but simply dormant. Interestingly in the patient with post-ET secondary MF who was starting the medullary fibrotic process, there was no hyperfixation at the DiS. Conversely a significant fixation with both radiopharmaceuticals was observed in the spleen and a lower fixation with <sup>99m</sup>Tc-nanocolloids was detected in the AxS. This may evokes a sequence of reactivation of some hematopoietic sites in patients with MF that perhaps starts by the spleen and then in a second time the DiS is «recruited». All this process is accompanied to a progressive decrease of the hematopoietic activity in the AxS.

## Factor VII deficiency

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**Introduction:** The lack of clotting factor VII is a rare haemostatic disorder, with prevalence in the general population of 1:500,000, which can be suspected with trivial changes in a test of hemostasis but may require prophylaxis in certain risk situations that requires correct identification. A variety of inherited disorders are associated with bleeding episodes per deficits of one or more coagulation factors.

**Case report:** Male patient, 14 years old, who consulted the emergency room with abdominal pain, the study was completed with abdominal ultrasound was normal and blood test that included blood count, biochemistry and coagulation in which it is objectively a prothrombin time (PT) prolonged 16.6 sec, suspecting coagulopathy, being requested a determination of coagulation factors in a quantitative deficit of factor VII of approximately 40% (factor VII is objective: VN 55-170%).

**Discussion:** We describe a rare case of factor VII deficiency. The disease is characterized by a quantitative or qualitative deficit of some component of this factor within the haemostatic cascade. It inheritance follows an autosomal recessive pattern; develop clinical bleeding, only when the deficiency is greater than 90%. There are no differences in prevalence by gender. The suspicion of this entity is established by isolated abnormalities of prothrombin time (PT) and must be confirmed with the quantification of the different coagulation factors. The molecular study only has indication in genetic counseling. It is a disorder that may require special treatment in the presence of high risk surgery or major bleeding, among which has been employed recombinant factor VII (rF VII a), the purified recombinant bleeding factors (rich in factor II, VII, IX, X) and fresh frozen plasma (rich in all clotting factors). We emphasize on the relevance of rF VII, because this one diminish biological risks of blood derivatives transfusions and decrease the effect of vascular overload. It is remarkable the prevalence of up to 4% thrombotic events related both to factor replacement treatments.

## Pancytopenia and vitiligo: keep pernicious anemia in sight

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**Introduction:** Pernicious anemia is associated with several autoimmune diseases. The association of pernicious anemia (manifested by pancytopenia) and vitiligo, however, is less frequent.

**Case report:** 72 years old male was admitted with 3 months of worsening chronic heart failure. He had skin lesions compatible with vitiligo in the face, thorax, hands and abdomen. We found no neuropsychiatric changes. Laboratorial investigation showed: hemoglobin level of 6.5 g/dL, MCV 120 fL, leukocytes 1750/

μL, platelets 78000/μL. The peripheral blood smear revealed policromatophilia, basophilic staining and hypersegmented neutrophils. Bone marrow examination showed a hypercellular marrow, with basophilic erythroblasts, signs of dyserythropoiesis, increased promyeloblasts and megakaryocytes with hypersegmented nucleus, typical of megaloblastic anemia. B12 vitamin was 163 pg/mL and folic acid was 8.5 ng/mL. Anti-intrinsic factor antibody was positive and anti-parietal cell antibody was negative. Thyroid function was normal and thyroid antibodies (TPOAb, TgAb, TRAb) were negative. Upper gastrointestinal endoscopy didn't reveal macroscopic changes. The diagnosis of pernicious anemia was admitted and intramuscular cobalamin was administered with complete normalization of the hemogram: hemoglobin 15.5 g/dL, MCV 85 fL, leukocytes 4650/μL, platelets 155000/μL.

**Discussion:** 2-8% of patients with pernicious anemia have vitiligo and approximately 1% of vitiligo patients have also pernicious anemia. The coexistence of megaloblastic anemia and vitiligo should make doctors aware of the possibility of atrophic gastritis as the etiology for the hematologic picture.

## Differential diagnosis of elevated pleural effusion adenosine deaminase activity levels: a case report

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**Introduction:** Adenosine deaminase activity (ADA) is one of the parameters usually evaluated during the investigation of a pleural effusion (PE). Elevated PE ADA levels are commonly associated with exudative PE in pleural tuberculosis (PT), rheumatoid arthritis and lymphoproliferative neoplasms. The cut-off point >40 U/L results in sensitivity and specificity >80% for PT but no clear value differentiates the several causes of lymphocytic PE. **Case report:** An 86 years old man with history of diffuse large B-cell lymphoma IIIA IPI-3 diagnosed 2 years earlier, heart failure, idiopathic chronic right exudative PE and pulmonary tuberculosis (TB) at the age of 20. He attended our hospital complaining of dyspnea and chest pain aggravated by efforts. Acute coronary syndrome was excluded. Chest X-ray not only showed a right PE overlapping the previous one but also a new left PE. Diuretic therapy was optimized but 2 days later he presented with dyspnea and lumbar back pain. He denied fever, cough, sputum and night sweats. On clinical examination left cervical enlarged lymph nodes were palpable; pulmonary murmur was bilaterally diminished with basal crackles, the abdomen was painful at the palpation of the left flank with no sign of organ enlargement. Hypoxemia and hyperlactacidemia were also stated. Laboratory tests showed anemia (Hb 9.7 g/dL), no leukocytosis and acutized chronic renal failure. A thoracocentesis was performed and the analysis of the serum-hematic pleural fluid (PF) showed a pH of 7.07, 7385 cells with 85% mononuclear predominance, ADA 556 U/L, low glucose levels, LDH 3449 U/L, protein levels 53.4 g/L, beta 2 microglobulin 6596. The PF culture was negative for bacteria and Mycobacteria as well as the polymerase chain reaction for Mycobacterium tuberculosis. Immunophenotyping of

the PF was positive for a B-cell monoclonal lambda population, which was compatible with the previous diagnosis of diffuse large B-cell lymphoma. Myelogram presented a CD4/CD8 lymphocyte inversion. The patient was proposed for a palliative therapeutic regimen but died at the hospital on day 8 of hospitalization.

**Discussion:** The literature states that either TB either lymphoma-related PE share clinical, radiological and laboratorial characteristics. ADA levels can be overlapped in these 2 conditions and to our knowledge there is no clear description of such a high ADA PE level and what it can represent in terms of differentiating them. As in this patient it is the combined use of immunophenotyping and cytology that allows the differentiation of a PE with elevated ADA levels.

## Unusual form of presentation of pernicious anemia: a case report

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**Introduction:** Pernicious anemia (PA) may be defined as a severe lack of IF due to gastric atrophy and, therefore cobalamin deficiency by malabsorption. It is a common disease in north Europeans but occurs in all countries and ethnic groups, frequently under-diagnosed. The overall incidence is about 120 per 100,000 population. The ratio of incidence in men and women among whites is ~1:1.6, and the peak age of onset is 60 years, with only 10% of patients being <40 years of age. However, in some ethnic groups, notably black individuals and Latin Americans, the age at onset of PA is generally lower. The disease occurs more commonly than by chance in close relatives and in persons with other organ-specific autoimmune diseases, like thyroid diseases, vitiligo, type 1 diabetes mellitus and Addison's disease.

**Case report:** The authors present a clinical case of a 59 years old woman, Caucasian, with an unremarkable medical background. Admitted in our hospital for rectorrhagia, with an evolution of 4 days. Also, with asthenia and nocturnal hyperhidrosis, anorexia and prior weight loss, with a month of evolution. No further symptoms were observed. Analytically with severe pancytopenia (hemoglobin 7,2 g/dL, leukopenia  $2.7 \times 10^9/L$ , neutropenia 1500, platelet counts  $74 \times 10^9/L$ ). Concerning to serum analysis, low vitamin B12 levels and a slight increase of total bilirubin were noticed. Given the diagnostic hypothesis, several exams were requested, among them, sternal puncture for myelogram with results suggesting megaloblastic anemia. The infectious serologies were negative, as the immunological study. The definitive diagnosis of pernicious anemia was confirmed by the positivity of the anti-intrinsic factor antibody and anti-parietal cells in the stomach. Patient began cyanocobalamin reposition, with favorable clinical evolution. Upon medical release, already asymptomatic and with hematological parameters improvement. In the follow up (one month later) showed normal analytic values.

**Conclusion:** The presentation of pernicious anemia under the form of severe pancytopenia is uncommon, whereby the authors intend to alert for its consideration in the differential diagnosis with other entities, namely acute myeloid leukemia or myelodysplastic syndrome.

## Adult hemophagocytic syndrome: prognostic analysis in 111 consecutive patients (REGHEM-GEAS-SEMI Spanish cohort)

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**Objectives:** HScore is a numeric scoring system recently proposed by Fardet et al in 2014, designed to estimate the risk of having hemophagocytic syndrome (HS) in adults. The aim of this study is to analyze the potential use of the HScore as a prognostic factor in a large cohort of Spanish patients with adult HS.

**Methods:** In June 2013, the Study Group of Autoimmune Diseases (GEAS-SEMI) created the National Registry of Adult Patients with HS. Patients were diagnosed according to the fulfillment of the Histiocytosis Society criteria proposed in 1991 and updated in 2004. The HScore includes 9 clinical, laboratory and histopathological criteria, and the score may range from 0 to a maximum of 337 points.

**Results:** In January 2015, the REGHEM registry included 111 adult patients with HS, 65 (59%) men and 46 (41%) women, with a mean age at diagnosis of 49.2 years (range 12-85 years); nineteen patients (17%) were not born in Spain (58% from Latin America, 21% from Africa and 16% from Asia). Tissue hemophagocytosis was confirmed in 97/107 (87%) cases. The main underlying diseases diagnosed before HS were autoimmune/rheumatological diseases in 36 (33%), chronic infections in 24 (22%) and neoplasia in 25 (23%) patients. The great majority of patients required ICU admission and death occurred in 59 (53%). The HScore was retrospectively calculated in 61 patients in whom all the criteria required could be applied: the mean HScore was 230,03 (range, 58-306). No significant differences for the mean HScore were found with respect to gender, age at diagnosis, underlying diseases, or severe internal organ involvement (pulmonary, renal or central nervous system). However, a higher mean HScore was found in foreign patients (257 vs 222,  $p=0.02$ ), in patients with concomitant infections with confirmed microbiological isolation (243 vs 214,  $p=0.022$ ) and in those who required vital support (248 vs 212,  $p=0.004$ ). Patients who died showed a higher mean HScore in comparison with survivors (241 vs 217,  $p=0.05$ ).

**Conclusions:** Hemophagocytic syndrome is a life-threatening multisystemic disease that often requires vital support in intensive care units. Despite this and the use of a complex therapeutic approach, half of the patients died. We found higher HScores in patients presenting with a complicated HS (concomitant infections, need for vital support and death). The use of the new HScore as prognostic factor may help to identify patients with a poor outcome.

## Clinical and therapeutic complexity of an adult T-cell lymphoma secondary to infection by human T-cell lymphotropic virus type I

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**Introduction:** The human T-cell lymphotropic virus type I (HTLV) is endemic in specific geographic areas. Although most individuals remain asymptomatic, infection is associated with the risk of developing adult T cell leukemia / lymphoma (ATLL). The presence of non-specific symptoms until an advanced stage and the aggressiveness of the disease that induces severely impaired cellular immunity explain that the survival rate after diagnosis is less than one year.

**Case report:** We present the case of a 52 years old woman, which came from São Tomé and Príncipe with the diagnostic hypothesis of left ovarian cancer. She referred significant weight loss, weakness, night sweats, pelvic pain, gradual groin mass and swelling of the left leg with 1 month of evolution. The physical examination revealed a mass in the groin and left iliac region, generalized edema of the left lower limb and normal gynecological examination. Laboratory tests revealed elevated inflammatory parameters, hypercalcemia and alterations suggestive of tumor lysis syndrome. Abdominal-pelvic CT identified large adenopathy conglomerates, the largest one in the groin and left iliac region with mass effect and diffuse edema in the soft tissues of the left lower limb. There was no evidence of deep venous thrombosis by Doppler ultrasonography. Incisional biopsy of the groin mass was performed, allowing the provisional diagnosis of high-grade lymphoma (Burkitt lymphoma vs large B-cell). While waiting for the final histological diagnosis, the patient developed fever, hypotension and high inflammatory parameters. We admitted septic shock with starting point at the biopsy incision, and large spectrum antibiotic therapy was started with gradual improvement. After definitive histological diagnosis of adult T cell lymphoma and positive HTLV I serology, CHOP chemotherapy was prescribed, followed by neutropenic sepsis. Bronchoscopy was performed and bronchoalveolar lavage diagnosed bronchopulmonary aspergillosis. The patient died from multiple organ failure.

## HIV-associated multicentric Castleman's disease: from a challenging diagnosis to an unknown treatment

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**Introduction:** Describe and discuss the diagnostic and therapeutic approach in a case of HIV-associated multicentric Castleman's disease (MCD).

**Case report:** A 34 years old woman was transferred from Guinea by anorexia, weight loss, fever, cough and lymphadenopathy since a year ago. HIV-1 infection was diagnosed and a myeloproliferative disease suspected by: severe anemia, generalized lymphadenopathy and monoclonal gammopathy (IgG-K). However the biopsies examinations did not support this diagnosis, the results supported only the HIV infection. The patient started antiretroviral therapy and 2 months later developed hepatosplenomegaly and starts periods of self-remission of: high fever, severe hemolytic anemia (hemoglobin 3.5 g/dL) and elevated C-reactive protein. New ganglion biopsies were obtained and continued to show characteristics of HIV infection. The hypothesis of MCD was though so IL-6 was measured (very high) and HHV8 identified in serum. In addition the patient developed skin lesions consistent with herpetic lesion, so we admitted manifestation of infection by HHV8 and valganciclovir was started. We performed a pathological review and finally established the diagnosis of MCD with identification of HHV8 in ganglia. We started therapy with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone, having notorious clinical improvement.

**Discussion:** Multicentric Castleman's disease in patients with HIV is rare but its incidence has been increasing. The case reported shows the difficulty in diagnose MCD, established only after several months of research and several nodal biopsies. Therapeutic approach is being investigated and it has been speculated that rituximab has an important role in eliminate infected B cells with HHV8.

## Pure red cell aplasia secondary to thymoma: an unusual presentation of an uncommon disease

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**Introduction:** Thymomas account for about 20% of mediastinal neoplasms. Symptoms are usually related to the size of the tumor and its effects on adjacent organs. However, in 5 to 15 percent of patients pure red cell aplasia occurs, resulting from an autoimmune-mediated hypoproliferation of erythrocyte precursors in the bone marrow. This paraneoplastic disorder is more common in older women. The authors intend to expose a report of this uncommon presentation.

**Case report:** The authors describe a case of a 63 years old female with known history of residual schizophrenia, under monthly-injected haloperidol. She was admitted to the emergency department with a clinical picture of vesperal fever and asthenia with one-week duration, with no other focalizing complaints. Physical examination was unsuspecting except for a pale skin and discrete tachycardia. Chest X-ray exhibited a widened superior mediastinum. Laboratorial examination revealed a normocytic/normochromic anemia (5.5 g/dL) with no other relevant findings. No history of blood loss. Further study revealed a hypoproliferative anemia with no signs of hemolysis and without iron, B12 vitamin or folate deficiency. Endoscopy and colonoscopy

exhibited no hemorrhagic lesions. Thoracic CT scan displayed a 10 cm mass in the anterior mediastinum. A CT-guided core biopsy of the mass was performed, with pathological examination revealing a thymoma. A medullogram was performed, revealing a hypocellular marrow with erythroid aplasia. A diagnosis of pure red cell aplasia secondary to thymoma was assumed. Therapy was instituted with methylprednisolone intravenous pulses (500 mg) for 3 days, followed by oral prednisolone 60 mg/day. Hemoglobin value stabilized at 10 g/dL following corticotherapy. Patient was referred to thoracic surgery consultation and is presently awaiting surgery.

**Discussion:** Despite constituting an infrequent entity, acquaintance with this etiology of anemia is noteworthy, stressing out the importance of a thorough investigation and the need for a precocious medical and surgical therapy.

### **Nephrotic syndrome as first manifestation of primary amyloidosis. A case report**

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**Introduction:** Amyloidosis is a multisystem, extracellular deposit disease, which implies a strong clinical suspicion and an early detection. The nephrotic syndrome is one of its first manifestations.

**Case report:** 43 years old woman with a history of Turner syndrome and hypothyroidism, hospitalized for an edema and anemia. On physical examination she was pale, emaciated, blood pressure 100/60 mmHg, tachycardia, decreased vesicular murmur in the bases on lung exam. Lower limbs with edema. Laboratory assessment on arrival: hemoglobin 9.8 g/dL, mean corpuscular volume 63,3 fL, total protein 4.9 g/dL, albumin 2.2 g/dL and urine with proteins 4+, normal renal function. Chest X-ray with bilateral pleural effusion. Diagnostic hypothesis: nephrotic syndrome (etiology: amyloidosis? autoimmune? infectious?), hypothyroidism and anemia. From the complementary assessment: nephrotic proteinuria (6.5 g/24h), TSH 10,2 UI/mL, normal FT4, positive celiac disease by antibodies and duodenal biopsy. Echocardiogram with mild depression of left ventricular function, right ventricular hypertrophy and pericardial effusion. With diuretic therapy there was remission of edema and pleural effusion. Thereafter, biopsy of abdominal fat showed amyloid deposits. Remaining autoimmune and serological study both negative. Cardiac magnetic resonance imaging showed myocardial infiltration consistent with amyloidosis. While waiting the identification of amyloid deposits, the patient was readmitted to hospital in shock, with hematochezia and edema. She died 24 hours after readmission.

**Discussion:** In this case, the authors present a patient's case with possible primary amyloidosis with renal, cardiac, pulmonary and digestive involvement. The outcome was rapidly fatal and it has not been possible to identify amyloid deposits type. There was not found correlation in the literature between amyloidosis and Turner syndrome.

### **Anemia in the elderly – a diagnostic challenge**

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**Introduction:** According to the Empire study, Portugal has a prevalence of 19.9% of anemia in adults. The elderly are a particularly important group, associated with significant morbidity and mortality. The etiology is varied and is often multifactorial.

**Case report:** Female, 84 years old, with relevant personal history of chronic kidney disease, hypertension, and previous hospitalization due to polypoid and erosive bulbitis, diverticula and tubular adenoma of the sigmoid with low-grade dysplasia. She was forwarded to hemotherapy consult for transfusion support. She was admitted in an internal medicine ward with an acute myocardial infarction (AMI) associated with acute anemia (Hb 5.2 g/dL). During hospitalization she remained hemodynamically stable with no visible blood loss except one clot in the faeces on day 3 of hospitalization. A capsule endoscopy was performed which revealed 3 polyps in the duodenum, one with red clot. In the analytical study, there was reticulocytosis, normal serum iron and a raised ferritin (5898.7 ng/mL). Initially bilirubin, LDH and haptoglobin were within normal limits. There was then a progressive elevation of bilirubin and LDH throughout hospitalization. An antiglobulin direct test was positive. Over 41 days of hospitalization 28 red cell concentrate units were administered via transfusion with a poor outcome despite starting corticosteroid therapy. A computed tomography scan was performed which revealed massive lumbo-aortic lymphadenopathy and hepatosplenomegaly. Biopsy of one of the lymph nodes was performed, which identified diffuse large B-cell lymphoma. The patient was sent to an oncology center.

**Discussion:** With this case report, the authors exemplify how challenging a diagnosis of anemia is in the elderly, and in this particular case complicated by chronic disease, anemia due to blood loss and hemolysis in lymphoma context.

### **Workup of anemia causes: the importance of an accurate diagnosis**

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**Introduction:** The correct diagnosis on first approach of severe anemia can be challenging. Several features can overlap between different anemia causes. A hemolytic component may act as a confounding factor during the workup of a newly found anemia. We aim to discuss the clinical steps to discovering the underlying cause of newly diagnosed anemia.

**Case report:** A 58 years old man presents to the emergency department with asthenia, pallor and increased fatigue, worsening the week before admission. On clinical examination, cutaneous

and mucosal pallor were found, with unremarkable findings on chest, abdomen and neurological examination. Blood tests revealed hemoglobin of 6.2 g/dL (normal range [NR] 13.5 to 18.0 g/dL), mean corpuscular volume of 111 fL (NR78-100 fL), mean corpuscular hemoglobin of 38.7 pg (NR 27-31 pg), with normal leukocyte count, platelet count of  $87.000 \times 10^3 / \mu\text{L}$  (NR 150.000-400.000  $\times 10^3 / \mu\text{L}$ ). Liver enzymology showed elevated aspartate aminotransferase (63 U/L, NR 0-38 U/L), unconjugated bilirubin (1.16 mg/dL, NR 0.0-0.3 mg/dL) and lactate dehydrogenase (2947 U/L, NR 240-480 U/L). Further testing revealed reduced haptoglobin (0.3 mg/dL, NR 30-200 mg/dL) and vitamin B12 (1.5 pmol/L, NR 19.1-119.3 pmol/L); the reticulocyte index was 0.3%, with hematocrit count of 17.9% (NR 42-52%). In peripheral blood smear anisopoikilocytosis and hypersegmented neutrophils were found. Immunoglobulins G, A and M and folic acid were normal, antinuclear antibodies and antiglobulin test were negative. Patient was admitted for further investigation and a bone marrow sample revealing hypercellular with large erythroid precursors, with no malignant cells was obtained. As patient's anti-intrinsic factor and anti-gastric parietal cells antibodies were positive, a sample of gastric mucosa was obtained showing a diffuse atrophic gastritis. Patient was started on parenteral vitamin B12 replacement therapy. A progressive regression of all clinical and laboratory findings was observed, with complete normalization within 3 months of treatment.

**Discussion:** Pernicious anemia has an increasing prevalence with age. A hemolytic component may cause delay of correct diagnosis as severe life threatening causes of hemolytic anemia should be ruled out. An efficient clinical investigation allows fast vitamin B12 replacement therapy, which rapidly reverses clinical and analytic findings.

### **Morphological dysplasia on bone marrow of patients with newly diagnosed multiple myeloma: an association not attributable to treatment**

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**Objectives:** The continuous development of cytogenetic and molecular techniques has not displaced the importance of bone marrow cytomorphology analyses for diagnosis of myelodysplastic syndromes (MDS). MDS were described in patients with multiple myeloma (MM) treated with alkylating agents. The aim of this study is evaluate the presence of morphological dysplasia on bone marrow aspirates of patients (P) with newly diagnosed MM still untreated. Relate these findings with age (A), sex (S), cytopenias (C), the symptomatology (s) and the proportion of marrow plasma cells (PC).

**Methods:** We studied by optical microscopy and May-Grünwald-Giemsa staining the morphology of bone marrow cells in P with MM diagnosed according to the criteria of the International Myeloma Working Group in the past five years in our center. We excluded of this analysis to 12P with MM and acquired factors associated with dysmyelopoiesis (deficit of maturation factors,

alcoholism or HIV). Finally, the dysmorphic on 200 erythroblasts, 200 granulocytes and 30 megakaryocytes on bone marrow was analyzed. 50P (22 men and 28 female) with MM were evaluated (35 symptomatic MM and 15 quiescent MM) newly diagnosed. Data were analyzed with SAS 9.2 statistical software using Chi2, Fisher test and t-Student in the comparative analysis of the variables. The tests were bilateral and significant when  $p < 0.05$ . Results: The median of A was 60 years (range 37-87) and mean PC at the time of diagnosis of MM was 36.5%. Of the 50P studied, 34 (68%) had C diagnosis and significant dysplastic features ( $\geq 10\%$  of dysmorphic in one or more hematopoietic cell lines) were detected in 26P being the prevalence of myelodysplasia in our series of 52%. Of these 26P, 11 had dyserythropoiesis, 9 dysgranulopoiesis and 12 dysmegacariopoiesis. 24P (48%) had no dysplasia features although 6 (12%) of them showed dysmorphic borderline significance (from 9 to 9.9%). No statistically significant association between myelodysplasia and A ( $p=0.06$ ), S ( $p=1.00$ ), C ( $p=0.05$ ), s ( $p=0.76$ ) and PC ( $p=0.062$ ) was detected.

**Conclusions:** 1) High prevalence of myelodysplasia in P with newly diagnosed MM; 2) our findings are not attributable to the therapy and that presented P had not received treatment for MM; 3) dysmegacariopoiesis was the most detected dysmorphia; 4) in this study no significant association between A, S, C, PC and myelodysplasia were observed; 5) prospective studies are needed to clarify these findings.

### **Autoantibodies: coexistence with alloantibodies and its association with pathologies underlying. Our experience**

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**Objectives:** It is already known the development of anti-erythrocyte autoantibodies in relation to certain drugs and certain diseases, primarily of neoplastic and autoimmune nature. In this sense, we propose to describe in our environment: the presence of autoantibodies associated or not, with alloantibodies and their association with previous or intercurrent pathologies, treatments or a history of blood transfusion to estimate the actual proportion of idiopathic cases.

**Methods:** Database Blood Bank area that encompasses our Center was reviewed and found 176 patients with autoantibodies. The study period was 60 months (from 01/01/2010 to 31/12/2014) and immunohematologic variables, analytical (hemoglobin) and clinical data were collected. The identification of antibodies was performed by screening and identification of irregular antibodies, direct antiglobulin test and study of the eluate or immunoadsorption, as appropriate. Anemia was defined according to the latest standards of the World Health Organization (WHO).

**Results:** 104 women and 72 men ( $n=176$ ) with a median age of 46 years (range: 2-90) autoantibodies were detected. 55 (31.3%) had transfusion history and 13 (7.4%) were pregnant. The nature of autoantibodies was: 122 (69.3%) + C3d- IgG, 46 (26.1%) + IgG + C3d, 5 (2.8%) and IgG-C3d + 3 (1.7%) IgG-

C3d-. 158 (89.8%) showed the autoantibodies eluted complex specificity and in 10 (5.7%) was unreactive. In addition, 42 (23.9%) had alloantibodies - mainly anti E (52.3%) specificity - simultaneously (18), rear (11) or prior to the identification of autoantibody (13). Mean hemoglobin at diagnosis was 10.5 g/dL and 139 (78.9%) had clinical history: 44 (25%) hematological malignancies, 39 (22.2%) autoimmune diseases 22 (12.5%) malignancies, 18 (10.3%) chronic infections with hepatotropic viruses and 6 (3.4%) intercurrent infections. Additionally, 10 (5.7%) had cardiovascular disease, 6 (3.4%) depended on hemodialysis, 5 (2.8%) were transplanted, 3 (1.7%) carried pacemaker, 2 (1.1%) orthopedic prostheses and 1 (0.6%) surgery bariatric. 25 (14.2%) were treated with immunosuppressive or immunoglobulins and 7 (4%) had no history of interest.

**Conclusions:** In our series, most presenting with regenerative anemia and have a history that justify the development of antibodies. Moreover, only 7 cases were idiopathic underscoring the importance of monitoring these individuals for possible early detection of hidden processes.

## Autoimmune hemolytic anemia and pathologies associated. Our experience

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**Objectives:** It is known the association between autoimmune hemolytic anemia (AIHA) and certain diseases, primarily neoplastic and immune nature but according to the literature about 50-60% of cases are idiopathic. We propose describe retrospectively, in our environment, the presence of previous or intercurrent pathologies in patients in which autoantibodies were identified to estimate the actual proportion of idiopathic cases.

**Methods:** Database Blood Bank area that encompasses our Center, found 170 AHAI patients (99 women and 71 men) with a median age of 46 years (range 2-90). The study period was 5 years (2010- 2014) and analytical variables (hemoglobin) and clinical data were collected. Anemia was defined according to the latest standards of the World Health Organization (WHO). Results: The mean of hemoglobin levels at diagnosis was 10.5 g/dL. Of all patients 43 (25,3%) had hematological malignancies (12 chronic lymphocytic leukemia, 12 myelodysplastic syndrome, 7 non-Hodgkin lymphoma, 6 acute lymphoblastic leukemia, 2 acute myeloblastic leukemia, 1 Hodgkin lymphoma, 2 multiple myeloma and 1 polycythemia vera), 38 (22.4%) autoimmune diseases (12 systemic lupus erythematosus, 6 antiphospholipid syndrome, 4 cryoagglutinins disease, 5 vasculitis, 4 diabetes mellitus type 1, 4 autoimmune hypothyroidism, 2 Sjögren syndrome and 1 rheumatoid arthritis), 20 (11.8%) cancer (6 colon, 4 prostate, 2 lung, 2 breast, 1 ovary, 1 bladder, 1 kidney, 1 liver, 1 esophagus and 1 melanoma), 18 (10.6%) had chronic infection for hepatotropic viruses (11 hepatitis C virus, 5 hepatitis B virus and 2 HIV) and 6 (3.5%) other intercurrent infections (1 Cytomegalovirus, 1 Staphylococcus

aureus, 1 Nocardia, 1 Bacteroides fragilis, 1 Mycoplasma and 1 Criptococcus). Additionally, 13 (7.6%) were pregnant women, 7 (4.1%) had cardiovascular disease, 6 (3.4%) were depended on hemodialysis, 5 (2.8%) were transplanted, 3 (3.5%) carried pacemaker, 2 (1.2%) orthopedic prostheses or 1 (0.6%) bariatric surgery. Only 8 (4.7%) patients had no underlying pathologies of interest.

**Conclusions:** We emphasize the low incidence of idiopathic cases (4.7%) associated with AIHA. Hematological malignancies, autoimmune diseases and cancer are the most frequently associated pathologies (59.4%) to this entity without forgetting the role of pregnancy and chronic or intercurrent infections in at diagnosis while stressing the high proportion of viral infections in the population studied.

## A 26 years old man with headache, fever and skin lesions

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**Introduction:** To report an unusual presentation of a case of systemic anaplastic large cell lymphoma (ALCL) which was misdiagnosed as a benign lesion over a 3 month period.

**Case report:** A previously healthy 26 years old male presented with a history of fever, headache and subcutaneous nodules on the scalp of 3 weeks' duration. The initial evaluation including physical examination, blood tests, brain CT and lumbar puncture was non-diagnostic. The patient's skin lesions were suspected to be multiple scalp trichilemmal cysts and the patient was discharged to ambulatory follow-up. Two months later, the patient was admitted again with worsening of symptoms and extension of the skin lesions to the trunk and both arms; a firm inguinal lymph node was noted on physical examination. Incisional biopsy from a skin nodule was performed; histopathology results were highly suspicious for cutaneous ALCL. An excisional lymph node biopsy revealed findings consistent with ALK-negative ALCL. A bone marrow biopsy revealed lymphoid infiltration. Lymphatic cells exhibited positive immunohistochemical staining for CD4 and CD30 and negative for CD3, CD8, CD20, EMA and clusterin, consistent with ALK(-) ALCL. A PET-CT showed pathologic FDG uptakes at cutaneous regions of the scalp and trunk, nasopharyngeal midline, sphenoidal sinus, lungs, inguinal lymph nodes and skeleton. HTLV-1 was negative. Brain and sinus MRI is planned to rule out contiguous CNS invasion from the sphenoid sinus. The histopathology examination confirmed the diagnosis of systemic ALCL. Dermatological and systemic evaluation ruled out other forms of CD30(+) lymphoid proliferation.

**Discussion:** This case illustrates the wide differential diagnosis of cutaneous lesions with CD30(+) lymphoid proliferation, varying from benign, nonspecific lesions to life threatening malignancies. We report an unusual presentation of an aggressive systemic ALCL in a young patient which was misdiagnosed as a benign lesion over a 3 month period. Our clinical case emphasizes the importance of performing a complete systemic work up and histopathological evaluation in cases of suspicious skin lesions.

## Axillary, subclavian and internal jugular venous thrombosis by protein S deficiency

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**Introduction:** Venous thrombosis (VT) with an annual incidence of 1-3/1000 individuals has multiple causes, genetic or acquired. The most frequent causes of VT in the young man are prolonged immobilization, trauma, thrombophilia and neoplasms. Hereditary thrombophilia (HT) includes, among others, the antithrombin (AT), protein C (PC) and protein S (PS) deficiencies. The prevalence of hereditary deficit of PS is estimated between 0.03 to 0.13% in the general population and 1-5 % in individuals with a history of VT.

**Case report:** A 26 years old male patient, native of Guinea Bissau, previously healthy was admitted with a 15 days history of edema, swelling and pain in the left upper limb and ipsilateral region of the neck, with no other abnormalities on physical examination. Doppler showed internal jugular, subclavian and left axillary veins thrombosis. Blood test showed a free (28%) and functional (50%) protein S deficiency. Complete study of prothrombotic factors, including antiphospholipid syndrome was negative. No evidence of neoplasia was found. Hereditary thrombophilia by PS deficit was assumed as the probable diagnosis. The patient started anticoagulation with enoxaparin, with resolution of swelling and pain after 4 days and was discharged on warfarin and aspirin.

**Discussion:** This case PS deficiency reflects a rare epidemiological profile of a low incidence disease in a less common anatomical location. In fact this situation is particularly rare in melanodermic patients and the most frequent location of VT is in the lower limbs (90%). Given the 9% annual rate of thrombosis recurrence in these situations, the absence of clear guidelines regarding anticoagulation time after the first episode of thrombosis or indications for primary prophylaxis are elements that stress the importance of discussing this field with clear room for improvement of available evidence.

## A case of follicular lymphoma

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**Case report:** A 55 years old Caucasian women was arrived at the Emergency Room with complaints of anorexia, asthenia, adynamia and >10% weight loss over the last 2 months. She also referred abdominal pain in the right flank in progression since the last week. Clinically, the most significant findings were small and painless bilateral axillary, posterior and lateral cervical and subclavicular lymphadenopathies, inaudible breath sounds at the base of the right lung, hepatomegaly and splenomegaly. Laboratory findings revealed anemia,

thrombocytopenia and elevated lactate dehydrogenase and serum B2-microglobulin. Serum protein electrophoresis was normal. CT-scan revealed right pleural effusion and ascitis, multiple axillary, mesenteric, aortic, pelvic and inguinal adenopathies and hepatosplenomegaly. She was admitted in the Internal Medicine ward with the assumption of lymphoproliferative disorder. Immunophenotyping studies confirmed the diagnosis of follicular lymphoma by detecting pathological B-cells BCL-2 positive and cytogenetics detected the t(14;18). Altogether, these studies allowed the classification of non-Hodgkin lymphoma of follicle centre B-cells, stage IV. The patient underwent a total of 6 cycles of treatment with RCHOP entering in complete remission.

**Discussion:** Follicular lymphoma represents 22% of non-Hodgkin lymphomas worldwide. Its most common presentation shows new painless lymphadenopathies with multiple locations of lymphoid involvement. The diagnosis is confirmed by the presence of B-cell immunophenotype and the existence of t(14;18), along with an abnormal expression of BCL-2 protein. Fortunately, it is one of the most responsive malignancies to chemotherapy as with adequate treatment, 50-75% achieves a complete remission.

## Prevalence of iatrogenic thrombocytopenias in an internal medicine service

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**Objectives:** Usually, thrombocytopenia is defined as a platelet number <150x10<sup>9</sup>/L and this is a frequent situation in patients admitted to an Internal Medicine service. In the vast majority, the causes are not well established, because there are many medications which can induce thrombocytopenia. The authors intend to identify all the patients admitted with thrombocytopenia and those who develop thrombocytopenia during the hospital course. In all the cases, we wanted to specify the causes, mainly the iatrogenic potential of some medication.

**Material and methods:** This is a retrospective study during 6 months which analyses the clinical files of all the patients admitted with thrombocytopenia in an internal medicine service. We also verified the problems at admission, thrombocytopenia-related signs and symptoms and the potential iatrogenic medication.

**Results:** The vast majority of patients that had thrombocytopenia at the admission (93,7%), were not hospitalized because of this. Instead, only 12 patients were admitted because of thrombocytopenia-related signs and symptoms and most of them were doing chemotherapy. 81% had grade 1 thrombocytopenia and 45% were doing potential iatrogenic medication. In 32% of the cases, the patients were discharged with normalized platelet levels.

**Conclusions:** Medications seemed to be an important cause of thrombocytopenia, almost in 50% of the analyzed cases. It is also necessary further investigation to specify if the thrombocytopenia is only iatrogenic or if it is related with the disease that motivated the hospital admission too.



## **Thromboembolic venous disease: mesenteric, portal and other venous thrombosis presentations. A retrospective study of six cases**

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**Objective:** To analyze the epidemiology, associated risk factors, clinical presentation, diagnostic methods, treatment, and evolution of patients diagnosed with superior mesenteric venous thrombosis, cerebral venous sinus thrombosis and other extrapulmonary thrombotic conditions in our hospital.

**Methods:** Retrospective and descriptive study. We review the medical records of cases with this diagnosis in our hospital from February 2011 to November 2014, founding six cases. Data were processed by using the SPSS vs. 20 software.

**Results:** 5 cases are male and 1 is a female. The average age is 52.5 years (30-80). We found as risk factors tumoral conditions in two cases, antecedents of deep venous thrombosis (DVT) in two of them and acute abdominal pathology in one of them. No predisposing factor or previous diseases were established in 2 cases. Prothrombotic conditions as prothrombin gene mutation or anticardiolipin antibodies were not found at any case. Clinical presentation for three cases was abdominal pain, one case of headache, and the rest of them were asymptomatic. Diagnosis was reached by abdominal computerized axial tomography scan (2 cases), abdominal magnetic resonance (4 cases) and vascular ultrasound for DVT (2 cases). Treatment with anticoagulation was initiated in all patients with low molecular weight heparin, and then, with oral anticoagulation. No patients died at the study period. No surgery was needed at any case. All patients were followed up with acceptable health condition.

**Conclusions:** Superior mesenteric venous thrombosis, cerebral venous sinus thrombosis and other extrapulmonary thrombotic conditions are a very unusual group of diseases that are often associated with neoplastic pathology and other pathologies such as antecedents of venous thrombosis, recent surgery, pregnancy or prothrombotic conditions. In our series of cases, two of them have not any predisposing factor. This is a very important circumstance to take account for other studies in the future. Due to non specific symptoms, clinical suspicion in patients with one or more risk factors is fundamental. Imaging studies are essential for the diagnosis and the detection of associated risk factors. In our series, abdominal magnetic resonance imaging was the most profitable test. In all cases the treatment with oral anticoagulation had good results with no recurrence. Further studies with a larger sample are necessary.

## **Incidence and characteristics of plasma cell leukemia in an area of 300,000 inhabitants**

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**Objective:** To describe the clinical and laboratory characteristics of plasma cell leukemia (PCL) during a 10 years period.

**Methods:** Retrospective epidemiological study of patients diagnosed with PCL in a population of 300,000 inhabitants between February 2004 and May 2014. The diagnosis was made when a monoclonal population of plasma cells (PC) was present in peripheral blood with an absolute PC count exceeding 2000/ $\mu$ l and comprising 20% or more of peripheral blood white cells.

**Results:** A total of 17 patients were included, mean age 70 years (49-81) and a female/male ratio of 9/8. We diagnosed 8 cases of primary PCL (pPCL) and 9 cases of secondary PCL (sPCL). The mean age is lower in pPCL (66 vs 73 years). ECOG scale is  $\geq 2$  in 57% of pPCL and in 78% of sPCL cases. The percent of plasma cells in peripheral blood is slightly higher in sPCL group (39% vs 31%) but the percent in bone marrow is higher in pPCL (76% vs 53%). Both hemoglobin (Hb) and platelets mean values were lower in pPCL (7.5 g/L Hb and 65.400 platelets in pPCL and 8.7 g/L Hb and 81.300 platelets in sPCL). Higher levels of beta-2 microglobulin were found in pPCL (8.76 vs 3.76 mg/L) but lactic dehydrogenase (LDH) values were quite similar (2170 vs 2324 U/L). Ferritin levels were higher in sPCL (1274 vs 622 mg/ml). The most common proteins were IgG subtype in both groups. The mean survival in pPCL was 90 days and even shorter in sPCL (84 days). In the pPCL group, 4 patients have been treated with VTD (thalidomide-velcade-dexamethasone), 3 of which with autologous hematopoietic cell transplantation (HCT) in a first time waiting for consolidation with allogeneic HCT in a second time. There are currently 2 patients with maintenance therapy with lenalidomide.

**Conclusions:** The results of our series are consistent with that published. This is a rare and extremely aggressive entity with a very short survival. Our pPCL patients are younger and have a lower ECOG scale value than those with sPCL. They also have higher levels of beta-2 microglobulin and increased frequency of severe anemia with thrombocytopenia. The current treatment in young patients, is aggressive therapy (containing bortezomib) followed by HCT (autologous and allogeneic).

## **Hereditary spherocytosis: a common form of hemolytic anemia, although unexpected when resulting from a de novo mutation**

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**Introduction:** Hereditary spherocytosis is relatively common, with an estimated frequency of 1 in 5000 individuals. Today, we know that is genetically heterogeneous, ranging from mild forms manifesting only in adulthood to severe forms that affect infants catastrophically.

**Case report:** 29 years old man, with no significant past medical history, was referred to internal medicine's consultation for anemia (Hb 11,3 g/dL, normocytic) and splenomegaly (17,8x16,5x5,2 cm) documented by abdominal ultrasound. He referred fatigue and asthenia in the previous year and half, with progressively lesser tolerance to efforts. He denied hematic losses, itching, night sweats, change in color or consistency of

stool, change in urine color or jaundice perception. There was no family history of anemia. Objectively: pale, pale mucous, no cyanosis. No palpable lymphadenopathy at different ganglion chains. There was a palpable mass in the upper left quadrant compatible with increased spleen size. No other changes were found. Laboratory investigation included iron kinetic study, hemolysis markers, reticulocyte index, folic acid and vitamin B12 dosing. The CBC confirmed normocytic anemia (Hb 12.3 g/dL), decreased red blood cells and hematocrit (3,9x10<sup>6</sup>/uL, 30.2% respectively); haptoglobin <8 mg/dL, and reticulocyte count >3%. Hemolytic anemia was found and further investigation was conducted. The peripheral blood smear identified: "red blood cells anisocytosis, poikilocytosis with a predominance of spherocytes, "bite cells", slight polychromatophilic red cells, compatible with hemolytic anemia for intrinsic red blood cells pathology". Further, osmotic fragility at room temperature and increase after 24 h at 37°C. Unequivocally, we were facing a case of hereditary spherocytosis. The genetic study revealed: new mutation for ANK1 gene. Upper abdomen computed tomography showed "marked splenomegaly, spleen with about 19,4 cm of craniocaudal diameter and can be a hereditary spherocytosis picture".

**Discussion:** This case illustrates a mild form of disease, which could go unnoticed particularly because of the absence of family history. So, we emphasize the need of a comprehensive and thorough investigation of anemia, for timely intervention, adjusted to the severity of the disease.

### Syphilis and thrombocytopenia: consequence or coincidence?

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**Introduction:** Thrombocytopenia may be associated with a variety of conditions. At the time of presentation the cause may be unclear and depends on the clinical setting in which it occurs. In otherwise asymptomatic adult, immune thrombocytopenia (ITP) is one of the most common causes.

**Case report:** A 24 years old male patient presented with petechial rash on the upper and lower limbs, trunk, abdomen and oral mucosa and gingival bleeding. He had no relevant pathological history and he was taking herbal medicines for weight loss in the last 7 months. On admission, blood testing revealed absence of platelets with no other abnormalities (normal red and white blood cells counts, peripheral blood smear with no schistocytes and HIV and HCV negative). Admitting severe ITP (primary or drug-induced), the patient started methylprednisolone iv 1.5 mg/kg/day and immunoglobulin iv 1 g/kg/day for 2 days. Subsequently, he was medicated with prednisolone per os 1 mg/kg/day. There was no significant response after 5 days of treatment (platelets count <10.000x10<sup>3</sup> uL) so more laboratory studies were performed. Syphilis infection (Rapid Plasma Reagin and antibody anti-Treponema Pallidum reactive) and a polyclonal gammopathy were identified. Bone marrow aspirate was performed, with no significant alterations. He started doxycycline 100 mg bid

on hospital day 8. The platelet count started to rise after that day: 9th day - 14.000 x10<sup>3</sup> uL, 10th day - 27.000x10<sup>3</sup> uL, 11th day - 37.000x10<sup>3</sup> uL and on the 14th day - 117.000x10<sup>3</sup> uL. He was discharged with the indication to decrease gradually the corticoid dose, to complete doxycycline for 28 days and to discontinue the herbal medicine.

**Discussion:** Infection diseases are a common known cause of thrombocytopenia but association between *Treponema pallidum* infection has not been described in the literature. In this case, was the thrombocytopenia caused by the syphilis infection? Was it primarily immune mediated or drug-induced? Was it multifactorial? It remains unclear, but the important is that the treatment was effective.

### A black diagnosis – clinical case

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**Introduction:** Immune thrombocytopenic purpura (ITP) is an acquired disorder that causes immune destruction of platelets and possibly inhibiting their release by megakaryocytic.

**Case report:** A 20 years old woman was admitted to the emergency department for bruises frame in the lower limbs without traumatism, with one week of evolution. A self-limited gingival bleeding was observed. She also had spiramycine treatment after a dental procedure. Three weeks before she passed a self-limiting respiratory infection. Isolated thrombocytopenia (platelets 13,000 /mm<sup>3</sup>), without reaching other cell lines was also observed. Extensive serology blood tests were negative and no other medication history was documented. She was admitted with a diagnostic hypothesis of ITP and initiated therapy with immunoglobulin 25 g/day for 5 days associated with oral prednisolone 50 mg/day. A rise in platelet count was observed, and at discharge the platelet count was 116,000 /mm<sup>3</sup>.

### When mastocytosis does not itch

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**Introduction:** Mastocytosis is a rare group of disorders characterized by excessive mast cell accumulation in one or multiple tissues, which exact incidence is unknown. Mastocytosis is subdivided into two groups of disorders, cutaneous mastocytosis describes forms of mastocytosis that are limited to the skin and systemic mastocytosis describes forms of mastocytosis in which pathologic mast cells infiltrate multiple extracutaneous organs, with or without skin involvement. Clinical manifestations are variable; skin sings and symptoms, gastrointestinal dysfunction, neuropsychiatric manifestations, musculoskeletal symptoms, osteopenia and osteoporosis.

**Case report:** We present a case of a woman of 58 years with leukocytosis with lymphocytosis, monocytosis and positive antinuclear antibody (ANA) 1/160. Referred early satiety, sporadic vomiting, swelling of the wrists with pain, and swelling ankle later. Relevant personal history, depressive syndrome since age 35 years, pre-malignant intestinal polyps, osteoporosis. Performed echocardiography, endoscopy and colonoscopy, chest radiography, this last detected picture to clarify for computed tomography (CT scan), CT scan which revealed mediastinal lymphadenopathy multiples, retroperitoneal lymph nodes in hepatic hilum. Hepatomegaly and splenomegaly. Histological study of lymph node along small gastric curvature, with paracortical stimulation. Liver biopsy results nonspecific. Bone biopsy and bone marrow examination compatible with mastocytosis (0.3% abnormal mast cells). With high suspicious of mastocytosis performed other laboratory tests: complete blood count, liver function tests (including serum aminotransferases and alkaline phosphatase) and serum tryptase. Therefore presented a major criteria (aggregates of greater than 15 mast cells) and one minor (tryptase higher value to 20 ng/ml) according to the World Health Organization's diagnostic criteria, diagnosis of mastocytosis without skin involvement was confirmed.

**Discussion:** Patients with the symptoms (unexplained flushing or anaphylaxis, unexplained gastrointestinal abnormalities, unexplained hepatomegaly, splenomegaly or lymphadenopathy, unexplained pathologic bone fractures, osteopenia, osteoporosis or osteosclerosis) or laboratory features (unexplained peripheral blood abnormalities, elevated tryptase level), below may be considered for work-up for mastocytosis regardless of the presence of skin lesions, particularly if there is an elevated baseline tryptase level.

### Prevalence and clinical relevance of microcytic anemia in somatically burdened patients in ambulatory practice

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**Objective:** To determine the prevalence, causes of microcytic anemia in somatically burdened patients in the ambulance situation.

**Methods:** A retrospective analysis of the fatal cases of the patients deceased throughout a year in pre-clinical setting (n=2847) was carried out on the 1st stage for the evaluation of the anemia prevalence. On the second stage of the research a screening study was carried out throughout a month: Hb level was determined in all the patients (n=928), who applied for various reasons to one of the outpatient clinics of Moscow. On the 3rd stage the patients with the emergence microcytic anemia (MA) were surveyed to specify the type and causes of the anemia.

**Results:** From 2874 of the deceased patients in 271 (30,6%) cases anemia was present in the clinical or pathological diagnosis. Among them there were 38,1% of males, the average age being 61,6±0,8 years old, 61,9% of females, the average age being 63,1±0,6 years old. The most frequent one was MA, which in

half of the cases combined with cardiovascular diseases (53,6%) and oncology diseases (32%). In case of MA from all the iron metabolism measures - serum iron was fixed more often than other measures (78,3%), the other iron measures were fixed in single cases, which shows the absence of specific (differentiated) approach to the management of the patients with the iron deficiency anemia and functional iron deficiency. On the stage of screening study anemia was revealed in 248 (26,7%) cases from 928 patients. From those 248 cases anemia was previously diagnosed in 92 (37,1%) patients, while in 156 (62,9%) cases anemia was first revealed during the screening study. Among the patients with emergence anemia 115 (73,7%) patients had MA, 39 (25%) ones had anemia normocytic, and in 2 (1,3%) cases it was macrocytic anemia. According to the data of the 3rd stage among MA the iron deficiency anemia was revealed in 66,2% of the cases, the main cause of which in the somatically burdened patients was cancer of various location (41,2%). Functional iron deficiency was diagnosed in 33,8% of the cases, which in one third of cases was diagnosed in the patients with cardiovascular diseases. It was noticed that the anemia severity was growing depending on the severity of the cardiovascular disease.

**Conclusions:** Every 3rd somatically burdened patient has anemia. When Hb screening study was carried out in this category of patients it was found out that only one third of them knew that they had anemia. MA (66,2%) turned out to be the most frequent one. With the help of the laboratory estimation of iron metabolism there is determined the iron deficiency anemia which is mainly associated with oncology diseases and functional iron deficiency connected with cardiovascular diseases, which fact further determines the choice of the drug Hb restoration therapy.

### Monoclonal gammopathy – a fight against time?

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**Introduction:** The light chain deposition disease is characterized by the accumulation of this monoclonal protein in various tissues and organs. These deposits are non-amyloid, do not exhibit a fibrillar structure, do not stain with the Congo red, but do stain with the periodic acid-Schiff (PAS). It may or may not be associated with multiple myeloma. The most frequently affected organs are the kidney, heart and liver.

**Case report:** 69 years old, Caucasian male diagnosed with type 2 diabetes, hypertension and depression, referring asthenia, shortness of breath and weight loss of 12-14 kg in 3 months. The patient presented with fever, cough, asthenia, shortness of breath, lower limbs edema, macroglossia, unstable walking pattern and raised pain sensitivity on both legs. He was diagnosed with bilateral pneumonia and cardiac insufficiency, medicated for those conditions and hospitalized for treatment and further study. The blood analysis showed neutrophilic leukocytosis, normal kidney, liver and thyroid function, normal blood ions, sedimentation rate of 10 mm/h,  $\beta_2$ -microglobulin of 4,69 mg/dL, normal protein electrophoresis, serum and urine immunofixation revealed lambda light chain monoclonal protein and Bence-Jones protein. Further exams didn't reveal any

neurologic, bone or articular lesions. The echocardiogram revealed dilation of both atriums, left ventricle concentric hypertrophy, unspecific thickening of the aortic valve, severe depression of the global systolic function and mild diastolic dysfunction, with estimated ejection fraction of 30%. It is important to refer that the patient had an echocardiogram from 2 months earlier that showed a perfectly normal heart function. The endoscopic study revealed only an atrophic gastritis (rectal biopsy was not executed). During the hospitalization, the patient presented with purpura lesions around both eyes and on both lower limbs. The lower limbs lesions were biopsied as well as the abdominal fat, thinking of amyloidosis. However, these exams were inconclusive and did not stain with the Congo red. The patient died before the authors were able to conclude the investigation and the bone marrow as well as the liver or kidney biopsies was not executed.

**Discussion:** Nonetheless, having the analytic and echocardiographic findings and especially the catastrophic evolution, the light chain deposition disease was the most plausible diagnosis.

### Effectiveness of inferior vena cava filters without anticoagulation therapy for prophylaxis of recurrent pulmonary embolism

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**Objectives:** Indications for inferior vena cava (IVC) filter placement in patients with deep vein thrombosis (DVT) are: 1) absolute contraindication to therapeutic anticoagulation; 2) failure of anticoagulation when there is acute proximal venous thrombosis; 3) life-threatening hemorrhage on anticoagulation. However, carefully controlled trials that demonstrate the ability of IVC filters to decrease recurrence rates or mortality from pulmonary embolism have not been performed. The purpose of our study was to investigate the rate of recurrent pulmonary embolism (PE) and mortality in patients with DVT and IVC filter insertion without anticoagulation therapy and compare it with patients on anticoagulation therapy alone.

**Methods:** We performed a retrospective cohort study of patients with DVT admitted to Soroka University Medical Center between 1/January 2006 and 1/January 2010. Two groups of patients with DVT were compared: patients who received an IVC filter and didn't receive anticoagulation and patients with DVT and similar burden of comorbidity treated with anticoagulation without IVC insertion. We used Charlson's index to compute the burden of comorbid conditions. The primary outcome was incidence of pulmonary embolism. The secondary outcomes were one year all-cause mortality, two year all-cause mortality, recurrent hospitalization rate for thrombotic event in the first year after DVT diagnoses and length of hospital state.

**Results:** In our study 1742 patients were diagnosed with DVT, 93 patients from this population received IVC filters. Patients of the IVC filter group compared with the anticoagulation group had more chronic medical conditions prior to hospitalization, including PVD, CVA, solid and metastatic tumors. The Charlton's score index was significantly higher in patients of the IVC filter group compared with the anticoagulation group [4 (2; 8) vs 3 (0; 6),  $p < 0.001$ ]. The rate of recurrent pulmonary embolism after

matching was not different in both groups of patients (6[6.5] in the IVC filter group vs 3[3.2] in the anticoagulation group,  $p = 0.5$ ). No difference in one year mortality rate was found between the groups (45[48.9] vs 32[34.8],  $p = 0.1$ ).

**Conclusion:** IVC filter without anticoagulation may be an effective alternative for the prevention of recurrent PE in patients with contraindications to anticoagulant therapy.

### Splanchnic vein thrombosis and JAK2 mutation

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**Objectives:** Splanchnic vein thrombosis is associated to myeloproliferative disorders. The diagnosis of etiological factors (V Leiden, coagulation factor II, G20210A mutation, protein C deficiency and myeloproliferative disease) greatly affect prognosis. JAK2 is a cytoplasmic tyrosine kinase that translates signals triggering by hemopoetic growth factors such as erythropoietin in normal and neoplastic cells. The contribution of V617F mutation is frequent in patients with myeloproliferative disorders. We aimed to enhance the correlation between thromboembolic events in deep visceral veins (suprahepatic, portal, mesenteric or splenic) and the appearance of myeloproliferative disorders, in patients with the V617F mutation in JAK 2 tyrosine kinase gene. This mutation is associated with thromboembolic events in latent myeloproliferative disorders.

**Methods:** We studied two patients who were hospitalized because of an occurrence of diffuse abdominal pain of days, progressively deteriorating. The radiological assessment with ultrasound triplex, MRI upper / lower abdomen, revealed splenic, hepatic, upper mesenteric and portal vein thrombosis. Mutation and immunology analysis was performed.

**Results:** None of the patients bring a positive family history of premature thromboembolic events. The laboratory and radiological assessments of patients revealed no solid tumor. One patient had a history of venous sinus thrombosis four years ago, while the second one had free medical history. As part of the investigation of thrombophilia, immunology analysis for protein C and S deficiency, as well as, molecular analysis of prothrombin gene, factor FVa Leiden, antithrombin III (ATIII) and MTHFR proceeded. No mutations were detected. JAK2 mutation analysis for V617F revealed heterozygosity. Bone marrow aspiration and biopsy was performed on both patients and revealed mild megakaryocytic hyperplasia. These findings do not prove the presence of a myeloproliferative disease but bring strong evidence for latent myeloproliferative disorder. Both patients are in anticoagulation treatment and remain monitored with clinical and laboratory follow-up.

**Conclusions:** The presence of JAK2V617F in patients without typical myeloproliferative disorder may be a causative risk factor for thromboembolic events. Patients with JAK2V617F should be continuously monitored and evaluated for the development of a myeloproliferative disease. Control of JAK2V617F should be included systematically in patients with thromboembolic events.

### Abdominal tuberculosis in Madrid: comparative analysis between HIV and non-HIV patients

Abelenda Alonso G., Fernández-Marcote Menor E.M., Cervero Jiménez M., Del Valle Loarte P., Torres Perea R., Delgado Heredia M.J., Agud Aparicio J.L., Jurdado Ruiz-Capillas J.J.

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**Objectives:** HIV infection is the main predisposing factor for TB infection at any location. The purpose of this study is to compare existing clinical differences between HIV and non-HIV patients with abdominal tuberculosis diagnosis in a Spanish second level hospital.

**Methods:** This is a comparative descriptive study of two subsets of patients (HIV and non-HIV) in a retrospective cohort of 20 patients on which clinical and diagnostic data of abdominal tuberculosis have been collected in a period of 28 years.

**Results:** Of the 20 cases reported, 8 patients had positive serology for HIV. 16 were peritoneal TB and 4 TB enteritis. 5 of the 16 cases of peritoneal tuberculosis occurred in HIV patients (31.3%) with 3 suspected solid organ involvement in these patients. In the case of tuberculosis enteritis, 3 of the 4 patients (75%) were HIV. The average age of HIV patients was 33.6 (Md 34; RQ 8.25) and in non-HIV was 52.3 (Md 48; RQ 35). In the HIV group, only 1 of the 8 patients was not Spanish, but in the non-HIV patients 5 of the 12 total was foreign (41.7%). Most HIV patients had a poor immune status: C3 (50%) and C2 (25%) with an average CD4 176.9 (Md 129; RQ 284). There were no differences in the Mantoux (negative in 75% in both groups). The ascitic fluid culture was positive in 6.7% HIV and 50% of non-HIV patients. Laparoscopy was performed in 2 of the 8 HIV patients and in 7 of the 12 non-HIV patients. In 7 of the 8 HIV patients M. tuberculosis was isolated in extraabdominal location while in the non-HIV group was isolated in 50%. The mean time to onset of treatment was 12.3 in HIV patients (Md 9.5; RQ 15) and 17.2 (Md 20; RQ 13) in non-HIV patients. Mean HIV treatment was 9.3 (Md 9.5; RQ 3.75) and in non-HIV 9.1 (Md 10.5; RQ 6). The only 2 relapses of the entire series took place in non-HIV patients so as the only one case of exitus.

**Conclusions:** As significant findings, a distribution of tuberculosis enteritis cases was observed with 75% of patients being HIV; while in the case of peritoneal TB 68.8% of patients were not HIV. We believe this could be explained by differences of pathogenic between one and another presentation. We conclude therefore that if we have a clinic compatible with abdominal tuberculosis in an HIV patient, we must carefully assess the possibility of involvement of the digestive tract as a gateway of the microorganism to the abdominal cavity and eventual submission in the context of disseminated tuberculosis.

### Abdominal tuberculosis in Madrid: epidemiological analysis of 20 cases

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**Objective:** The purpose of this study is to describe the cases of peritoneal tuberculosis in the complete history of a Spanish second level hospital.

**Methods:** A retrospective cohort of 20 patients which were collected epidemiological and clinical data of abdominal tuberculosis in a period of 28 years is presented.

**Results:** The mean age was 44.9 (Md 39; QR 35.5). 90% were men and one third had a foreign nationality. 80% were classified as peritoneal tuberculosis and 20% as enteritis. Comorbidities associated were HIV (40%), HCV (20%), liver cirrhosis (20%), peritoneal dialysis CKD (10%), previous tuberculosis (5%) and exposure to tuberculosis (10%). The time evolution of the clinic was 5.95 weeks. The most common symptom was anorexia (80%). In 40% of cases there were also respiratory symptoms. Mean ADA in ascites was 61.8 (Md 66.1; 49.4 QR). CT scanning was the most requested exploration with peritoneum thickening and ascites being the most frequent findings (69.2%). 12 of the 20 patients were diagnosed by histological sample. Colonoscopy was performed in 6 patients, being found in 50% of cases granulomas. Laparoscopy was performed in 45% with 88.9% of patients having granulomas. The most commonly used test for microbiological diagnosis was ascitic fluid culture which was positive in 53.8% of the 13 patients in whom it was performed. The median time to start treatment was 15 days. The most used initial treatment scheme was INH+RIF+PZD (45%). There was a single case of exitus and a total of 4 patients in whom follow-up at 6 months was lost. The average treatment time was 9.2 months (Md 9.5 QR 6). There were 2 patients with post-treatment relapse (4 and 12 months in each case).

**Conclusions:** We report clinical and epidemiological features of 20 cases of abdominal tuberculosis diagnosed in the 28 year record of our hospital. 16 patients were classified as peritoneal tuberculosis and 4 were diagnosed with tuberculosis enteritis (3 of them, HIV). The predominant diagnostic method was the biopsy, however, the median time from admission to initiation of treatment (Md 14.5; QR 19,75 ) was similar to the overall median (Md 15; QR 18) which could be explained by the long wait until laparoscopy (24.4 days of average). It is significant in our series the high percentage of patients with positive ascitic liquid culture (53.8%). We can conclude that abdominal tuberculosis remains today an important diagnostic challenge in which the tissue sample has proven being important to early diagnosis.

## Is there neutrophilic dysfunction in patients with advanced HCV liver disease treated with new protease inhibitors?

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**Introduction:** In the last year, first IFN-free schemes for chronic HCV hepatitis have revolutionized hepatology in our country. However, many questions still remain regarding safety in patients with advanced cirrhosis. 2 cases of invasive fungal infection in patients with advanced HCV cirrhosis with recent onset of treatment IFN-free schemes are presented. Common denominator was a nonstructural protease NS3/4A inhibitor.

**Case reports:** Case 1: 68 years old woman with chronic liver disease by HCV genotype 1b with portal hypertension Child Pugh B7, F4 fibrosis, cryoglobulinemia type III associated treated with prednisone (0.35 mg/kg) and azathioprine (2 mg/kg). Immunosuppressants were suspended within the first day of treatment with simeprevir + sofosbuvir. At 72h, the patient presented acute on chronic liver failure that was related first to E. coli sepsis, requiring admission into the ICU. After initial improvement, a clinical worsening compatible with septic shock, severe ARF and dyshematopoiesis lead to his death despite the wide antifungal and antimicrobial coverage. Throughout the entire hospitalization, antiviral treatment was maintained. Positive cultures for *Aspergillus fumigatus* and *Candida* spp complex in ascitic and pleural fluid, *C. glabrata* in CVC and urine, *C. albicans* in perineal and *C. parapsilosis* in a pericatheter crop were received. Case 2: 61 years old male with chronic liver disease due to HCV genotype 1a with portal hypertension Child Pugh B9-C10, F4 fibrosis. 72 hours after starting treatment with ombitasvir/paritaprevir/rtv + dasabuvir + RBV, RBV was removed due to suspicion of hemolytic anemia. 10 days later, the patient was admitted into the ICU with acute on chronic liver failure without clear trigger. Antiviral treatment was withdrawn. Despite initial overall improvement, the patient finally passed away with severe sepsis without clear origin, acute liver failure, ARF and dyshematopoiesis. Blood cultures with *C. albicans* and *C. glabrata* were received.

**Discussion:** There's some evidence of increased rate of serious infections in patients treated with first generation protease inhibitor. However, the information about new nonstructural protease inhibitors safety is still poor. Our cases suggest the possibility of an association between these drugs and invasive fungal infection. Treatment introduction of nonstructural protease inhibitors in both patients could be decisive for the development of acute liver failure, severe dyshematopoiesis and systemic fungal infection.

## Epiglottitis – a common disease or a rare form of presentation?

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**Introduction:** Epiglottitis is an acute inflammation in the supraglottic region of the oropharynx with inflammation of

the epiglottis, vallecula, arytenoids, and aryepiglottic folds. It's most commonly caused by bacteria and less commonly by virus and fungi. Differential diagnosis that must be made with laryngeal carcinoma, which shares almost the same symptoms and signs. Epiglottitis can be a life-threatening emergency, leading to airway obstruction and death. With appropriate and timely treatment, the outcome is usually favorable.

**Case report:** An 81 years old female, with congenital deafness, chronic obstructive pulmonary disease, arterial hypertension and pulmonary tuberculosis. Medicated with tiotropium, fluticasone+salmeterol, montelukast and losartan. She presented asthenia and sore throat, denying complaints of fever, weight loss, sputum or dry cough, night sweats, dysphagia, dysphonia, stridor and dyspnea. Neither smoking nor alcohol consumption was noted. Chest X-ray showed bilateral parenchymal infiltrate. Ear-nose-throat examination showed supraglottitis and epiglottitis, and we started empiric treatment with antibiotics and antifungals, with poor response. Human immunodeficiency virus (HIV) serology was negative. We performed a chest CT that revealed calcified paratracheal adenopathies and ground glass bilateral infiltrates. Sputum exam revealed acid-fast bacilli and was confirmed with mycobacterial growth. There were no signs of laryngeal cancer on bronchoscopy. Antibacilar treatment was started and the outcome was favorable.

**Discussion:** Tuberculosis (TB) is one of the most common granulomatous diseases of the larynx, but constitutes less than 1% of all cases of extrapulmonary tuberculosis. Extrapulmonary type is more common in HIV-infected patients. The response of laryngeal TB to antituberculous drugs is usually positive.

## Deceptive presentations mimicking Mycobacterium tuberculosis

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**Introduction:** Tuberculosis in Bangladesh being a major public health problem is suspected commonly in appropriate clinical settings. There are infectious diseases which may present with clinical and laboratory features mimicking *Mycobacterium tuberculosis* infection. In absence of isolation of an organism, such circumstances pose challenges for the physician to decide in prescribing empirical anti-tubercular medications. In this era of evidence based medicine, such decisions are becoming questionable in centers where definite proof of an organism can be obtained. Here we share our experience of dealing few challenging cases mimicking features of tuberculosis.

**Case reports:** From 2013 to 2015, 3 difficult cases were dealt in internal medicine department, BIRDEM General Hospital which were initially suspected as tuberculosis. Case 1 was a Canada immigrant presenting with worsening pneumonia and cold abscess in the arm. Case 2 presented with constitutional symptoms of pulmonary tuberculosis with lung cavity lesion. Case 3 was a patient with seronegative arthritis presenting with non-healing bilateral deltoid abscess and abscess wall histopathology showing epithelioid granulomata. All 3 cases did not respond to conventional antibiotics and 1 case to CAT 1

anti-tubercular treatment. *Blastomyces dermatidis* was isolated from pus of cold abscess and bronchoalveolar lavage of case 1. Sputum culture revealed *Burkholderia pseudomallei* in case 2. Non-tubercular *Mycobacteria* species (rapid growers) resistant to rifampicin, ethambutol was isolated from pus of deltoid abscess in case 3. Case 1 is still on antifungal treatment and subsequent follow-up visits up to 6 months show remarkable improvement. The other 2 cases were also treated accordingly and followed up till completion of treatment and cure.

**Discussion:** Isolation of the organism in any infectious disease remains the gold standard for confirmation of diagnosis. There are infectious diseases that may present with clinical, radiological, histopathological features mimicking *M. tuberculosis*. A delay in proper diagnosis and empirical anti-tubercular treatment worsen the scenario and may even result in death. Appropriate history taking with clinical correlation is crucial for diagnosis. Where laboratory facilities are available, isolation of the causative organism is confirmatory and can be life-saving.

### **Methicillin-resistant *Staphylococcus aureus* in a Portuguese intensive care unit**

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**Objective:** To analyze the incidence and origin of positive methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in an intensive care unit (ICU).

**Methods:** The study was conducted in a Portuguese ICU, from January to December 2014, and included all patients admitted to the ICU. Screening for MRSA was done on admission and then once a week. Positive cultures collected within the first 48h of admission were identified, as well as the origin of those patients. ICU-acquired infections were also analyzed. Colonized patients were treated with topic mupirocin and infected patients received systemic antibiotics.

**Results:** A few patients were found to have community-acquired MRSA. Nevertheless, hospital acquired infection was the most common finding. Pneumonia was the most common site of MRSA infection in this ICU. Previous hospital admissions and antibiotic use were the primary identified risk factors.

**Conclusions:** MRSA infection is a very important cause of mortality in ICU patients. The control of colonization and the adequate treatment of infection are preponderant on survival rates of hospitalized patients, especially when immunocompromised.

### **Systemic infection with methicillin-sensitive *Staphylococcus aureus***

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**Introduction:** To examine the clinical presentation of a systemic methicillin-sensitive *Staphylococcus aureus* (MSSA) infection, on an immunocompetent patient.

**Case report:** Presentation of a patient who was admitted on an Intensive Care Unit (ICU) with the diagnosis of septic shock with multiorgan failure, found to be infected with MSSA on sequential blood cultures. The patient presented with dysphagia, punctiform skin lesions on the extremities, fever and lower back pain. The imagiologic studies revealed bilateral pulmonary lesions, cervical and lumbar spondylodiscitis and a retropharyngeal abscess. Infective endocarditis was ruled out through transesophageal echocardiography. The abscess was surgically drained and the pulmonary and discal lesions responded to a 6-week treatment with intravenous flucloxacillin. Immunological studies were negative for acquired immunodeficiency.

**Discussion:** Systemic MSSA infection is relatively rare in immunocompetent adults. The evolution can be fatal when undiagnosed, due to MSSA deposition in multiple tissues and organs. Endocarditis, discal lesions and multiorgan abscesses should always be excluded in a patient with known or suspected MSSA bacteremia, and treatment must be promptly started.

### **Mediterranean Botonosa fever on the 3rd health zone of Madrid**

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**Background:** The Mediterranean Botonosa fever (MBF) is caused by *Rickettsia conorii*. The MBF is a zoonose, whose vector and reservoir is the dog's tick, the *Rhipicephalus sanguineus*. The evolution of this disease is generally good if it is diagnosed early, of moderate severity and low death rates.

**Objective:** To identify the epidemiological and clinical characteristics of diagnosed MBF patients, within the 3rd health zone of Madrid.

**Methods:** Review, in retrospective, of the MBF diagnosed patients' medical records from year 2000 to 2015 registered on the Príncipe de Asturias University Hospital. Considering as a diagnostic case, patients with compatible clinical records, epidemiological background and indirect positive immunofluorescence for *Rickettsia conorii*.

**Results:** 21 patients have been diagnosed with MBF during the study period. 13 patients meet with the diagnostic criteria, 10 of them presenting fever as the first symptom besides maculopapular rash, 69% of this refers to the trunk. 61.5% showed black marks sign. Among others demonstration less frequent on patients where 38.5% lymphadenopathy, and 46.2% hepatopathy. Regarding the age distribution, 30.8% corresponded to pediatric population with 75% female predominance while in adults the predominance was inversely present in males with 66.7%. 61.5% of patients were in contact with animal or rural areas. In every case, patients were treated with antibiotics, using doxycycline as first line in 83.3% of them. Just in 3 of every 10 cases a monthly serology control was held. None of which exhibited serious complications derived from the MBF.

**Conclusions:** On the revised series, most patients were adult males having been in contact with animals or in rural areas, with fever and exanthema, more than half with black marks, and

higher prevalence of hepatopathy. As we outlined before most cases were treated with doxycycline, with rare serious medical conditions. We must assure suitable a treatment and monitoring.

## **Pseudomembranous colitis is caused by *Clostridium difficile* in an internal medicine ward of a Portuguese district hospital – a 42 months case study**

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**Background:** Pseudomembranous colitis is caused by *Clostridium difficile* and is a major healthcare-associated infection. Its incidence and severity has showed significant increase in recent years.

**Objective:** To determine the risk factors associated with the development of pseudomembranous in patients hospitalized in the internal medicine service between January 2011 and June 2014 with primary or secondary diagnosis of intestinal infection by *C. difficile*.

**Methods:** A retrospective, observational and descriptive-correlation study was conducted based on information collected from medical records of hospitalized patients. The study included 302 patients with diagnosis of infectious diarrhea by *C. difficile*, positive toxin A and B of *C. difficile* or clinical suspicion and colonoscopy with age above 18 years. Statistical analysis was conducted in SPSS 20 for Windows.

**Results:** Patients were selected with hospitalization and medical diagnosis of pseudomembranous colitis caused by *C. difficile*. The 302 patients were hospitalized from the year 2011-2013 and throughout the first semester of 2014. Every year, we registered 54, 97, 99 and 52 cases respectively. The average age of the patients was  $78.4 \pm 12.1$  years, with predominance of the female gender (62.9%). We observed that 31.8% had renal failure, only 9.9% had a history of gastric surgery, 26% used laxatives and 66.3% used a gastric protector; while the 53.3% needed help in their daily activities. 51% of patients were hospitalized 3 months before the diagnosis and 48.8% developed the illness during the hospitalization and was documented prior antibiotic use of 82.5% of patients of which 46.5% were beta-lactams. Diarrhea was present in only 75% of cases, while only 12% had symptoms of abdominal pain and diarrhea. Diagnosis was obtained in 100% by determination of *C. difficile* toxins, in 8.5% of these cultures was identifying 27 ribotyping and in only 5.4% had a colonoscopy. The initial treatment was oral metronidazole in 47.3% of cases, 18.4% used in metronidazole and vancomycin in association, only 3% had therapeutic with intravenous metronidazole; the mean therapeutic time was  $15.4 \pm 10.8$  days. Cases of surgical or cholestyramine treatments were not reported, however, in 81.9% of cases were concomitant use of yeast and antibiotics, which showed no benefit or disadvantage statistically speaking. The duration of hospitalization was in average  $34 \pm 31.4$  days and the mortality rate was of 33.7%.

**Conclusions:** Our study links an increased incidence of pseudomembranous colitis is caused by *C. difficile* in patients who previously used beta-lactams, in patients who were dependent for activities of daily living, and in patients

using gastric protectors, we could also confirm the need for prolonged hospitalization for adequate infection control due to high mortality rate of 33.7% compared to a 0.5 to 3% reported in national and European literature. The authors emphasize the importance of a moderate use of antibiotics with appropriate preventive measures to avoid the development of this infection.

## **Nosocomial infection as a hospital readmission reason**

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**Objectives:** Hospital readmissions have been linked to an increase in health expenses. 30 days after the initial admission is the period most often used to define the hospital readmission. Nosocomial infections are also a public health problem with morbidity, mortality and significant costs. According to the Centers for Disease Control and Prevention (CDC), nosocomial infection is defined as occurring after hospital admission in whom the infection was not present or incubating at the time of admission, that manifests 48 hours or more thereafter; this includes infections acquired in the hospital but appearing after discharge. It was intended to characterize the profile of patients readmitted in 30 days or less, determining the incidence and identifying factors associated with nosocomial infection in patients readmitted in an Internal Medicine Department of a Central Hospital in Portugal.

**Methods:** It was conducted a prospective study with patients admitted to one Internal Medicine Department, in July and August 2014 (summer) and January and February 2015 (winter), whose last hospitalization would have ended 30 days or less before the readmission date; it was excluded patients with elective readmissions. In the investigation was included sociodemographic and intrinsic characteristics of the patient, the hospital stay and the diagnosis or not of nosocomial infection.

**Results:** In a total of 745 patients, 90 were included in the statistical analysis (readmission rate of 12.1%), 52 of them (57.8%) were by nosocomial infection and 47 (52.2%) occurred in the winter. The average age was 79.4 years old, 54.4% were males and only 25.3% lived in nursing home. The mortality rate of readmitted patients was 5.6%, with no significant difference with the mortality rate of the Department. It was found statistically significant relationship between the readmission by nosocomial infection and patient age ( $p=0.029$ ) and degree of dependence on the patient's activities of daily life ( $p=0.001$ ). It wasn't found relationship between the other factors.

**Conclusions:** Although a longer hospitalization is usually associated with more readmissions by nosocomial infection, the same was not observed in our study. The relationship between the season and the number of readmissions by nosocomial infection has also not been proven. It was however noticed that an older age and a higher degree of dependence is associated with greater number of nosocomial infections as a cause of readmission.



## Tuberculosis – surprising numbers in a Portuguese hospital

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**Objectives:** Tuberculosis (TB) is one of the commonest causes of mortality by infectious diseases worldwide, surpassed only by HIV. Despite the multitude of public health programs and campaigns to combat TB, its burden remains high. According to WHO, some Western European countries had incidence rates as low as  $\leq 10/100000$  inhabitants in 2012; the Portuguese Directorate-General of Health claimed a national rate of 21.6/100000, whereas in contrast the Local Health Plan for our municipality stated a higher rate of 45.4/100000 within the same period. We present all the diagnosed cases within our hospital in 2012 (excluding those diagnosed in outpatient care or in the influence area of our institution).

**Methods:** The data was obtained through a retrospective review of clinical documentation pertaining to admissions and discharges during 2012, irrespective of the department to which they were admitted.

**Results:** Fulfilling the above mentioned criteria, we had 102 cases (59% male) with a mean age of 46.1 years (14% aging over 65). 41% were Caucasian, 34% Black, 1% Indian, whilst the remaining did not have their ethnicity on their medical records. 25% were co-infected with HIV (11% had no serology testing available), whilst 19% had other immunosuppressive factors. 70 patients had pulmonary TB, of whom 63% had acid-fast bacilli in their sputum, and 51% had a typical X-ray presentation (apical cavitation); 46 patients had extrapulmonary TB (70% without concomitant pulmonary involvement), the majority of which affected the pleura (21 cases) and lymph nodes (12). Other regions involved were the vertebral column, central nervous system, peritoneum, various gastrointestinal tract organs, bone, skin and adnexa. Only 17% of the diagnoses had no laboratory confirmation, being made solely on the basis of clinical and/or imaging criteria.

**Conclusions:** This data shows us that despite the lower incidence and decreasing trend reported nationally, the population admitted to our hospital presented a much greater rate (considering the total number of hospital admissions in 2012: 30044), which should merit special attention and financing to correct this public health issue in order to minimize its impact on morbidity/mortality. It also indicates that the co-infection rate of TB/HIV is quite high and should not be neglected. Furthermore, it demonstrates that the many and heterogeneous forms of presentation of TB can provide a difficult diagnostic approach and that TB must always be remembered as a differential diagnosis.

## Tuberculosis of the CNS – a case of Mycobacterium tuberculosis brain abscess

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**Introduction:** Despite the decreasing prevalence of tuberculosis in industrialized countries, extrapulmonary presentations

have become more frequent, eventually in the context of HIV infection. Central nervous system (CNS) tuberculosis represents 1% of all cases and 6.3% of extrapulmonary cases, disproportionately afflicting children and HIV+ individuals, and is the most complicated form, being able to cause meningitis, meningoencephalitis, tuberculomas and abscesses. Clinical, laboratory and imaging manifestations may be nonspecific. Brain abscesses are extremely rare, but carry high morbidity and mortality.

**Case report:** 47 years old man, autonomous, HIV+ for 2 years, medicated with antiretrovirals, but with irregular compliance, maintaining a detectable viral load and CD4 T-lymphocyte count  $< 100/\mu\text{L}$ . Went to the ER after falling in the context of strength loss and tingling in the lower limbs. After observation by surgery and orthopedics departments and being treated for a finger dislocation, was finally observed by the internal medicine department. When questioned, mentioned a 2 m fall a week earlier, with head injury but without loss of consciousness or any further symptoms in the following days. Neurological examination revealed decreased visual acuity in the left temporal field, compromised diadochokinesia, dysmetria in left finger-nose and heel-knee tests, ataxia and wide-based gait, without fever or meningismus. MRI revealed 5 cm cortico-subcortical space-occupying lesion in the right temporo-occipital space, compatible with brain abscess, and marked vasogenic edema. This lesion was surgically drained, identifying Mycobacterium tuberculosis in the purulent exudate. Began classical therapy with isoniazid, rifampicin, pyrazinamide and ethambutol, with good clinical response, being discharged after 22 days, with complete recovery of neurological deficits.

**Discussion:** Due to its relative rarity, non-specific symptoms and predominance in resource-starved regions of the world, CNS tuberculosis remains a diagnostic challenge. Given the public health problem that is tuberculosis and the increasing incidence of extrapulmonary forms, the 'eternal clinical copycat' remains a possible differential diagnose, although it is a rare cause of brain abscesses.

## Empirical use of antimicrobial during an interventional program in Gram negative bacilli bacteremia

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**Objective:** The aim of this study is to evaluate the antimicrobials use and the accuracy of the treatment in different bacteremia caused by Gram negative bacilli through an intervention program. **Methods:** We made a prospective interventional study of 1 year duration (2013). We analyze every bacteremia caused by Gram negative bacilli (GNB).

**Results:** We analyzed a total of 60 bacteremia caused by GNB. 6 were polymicrobial isolation. Escherichia coli the most common isolated (32 cases, 53.3%), followed by Klebsiella spp. (10 cases, 16.6%), 6 – Pseudomonas aeruginosa (10%), 4 – Proteus

mirabilis (6.7%), 3 – Citrobacter koseri (5%), 3 – Enterobacter spp. (5%) and 1 – Serratia spp. Multiresistant germs (15%): 6 – Escherichia coli (BLES), 1 – Pseudomonas aeruginosa, 1 – Serratia liquefaciens and 1 – Enterobacter cloacae. Up to 65% (39) were resistant to ampicillin; 25% (15) – to amoxicillin/clavulanate; 6.7% (4) – piperacillin/tazobactam; 11.7% (5) – 3rd generation cephalosporins; 10% (6) – ceftazidim; 11.7% (7) – cefepime; 30% (18) – fluoroquinolones; 8.3% (5) – to aminoglycosides and 1 – intermediate resistance to carbapenems (Pseudomonas aeruginosa). In the first 48 hours patients had: sepsis (40%, 24 cases), severe sepsis (40%, 24 cases) and septic shock (20%, 12 cases). 11.7% received inadequate treatment in the first hours of infection, 100% of targeted therapy was appropriate. Empirical antibiotic treatment: 43.4% (26) carbapenem; 28.3% (17) any cefalosporin; 16.7% (10) penicillin; 8.4% (5) fluoroquinolone; 1.7% (1) aztreonam; and 1 didn't receive empirical treatment prior to isolation. Targeted antimicrobial treatment groups were cephalosporins use in 58.4% (35), followed by carbapenems 28.3% (18). Antimicrobial Intervention was necessary in 25%. Counseling in antimicrobial treatment was performed in 83.3% (50), changing the prescribed treatment in 43.3% being in these cases a narrower spectrum antimicrobial in the 40%. The adaptation to our Empirical Antibiotic Treatment (EAT) guide is only of 60%. The progress of the patients was: death in 10 cases, of which 9 (15%), death was related to bacteremia.

**Conclusions:** The empirical use of antibiotic treatment is adequate but it stills the use of higher-spectrum antimicrobials. The 43.3% of the treatments were changed to a narrower spectrum one. In the literature, a lower threshold is set based in the adaptation of bacterial crops. The adaptation to our Empirical Antibiotic Treatment guide is only of 60%, so we can say that the spectrum of the empirical treatment is worse to the ideal. A greater number of cases data must be analyzed to establish better level of adequacy.

## An unusual case of infected aneurysm

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**Introduction:** Splenic artery aneurysm (SAA) is the third in frequency intraabdominal aneurysm. Infected (mycotic) aneurysms most often present secondary to infective endocarditis. Infected SAAs are rare, but rupture more frequently and bear high mortality.

**Case report:** A 38 years old man presented to our emergency department complaining of acute abdominal pain. On examination he appeared distressed, but his vital signs were unremarkable. His abdomen was tender to the touch and he was lying still to reduce his discomfort. Laboratory results did not reveal a cause for his condition and after surgical consult a CT scan of the abdomen was performed. While waiting for the results, the patient went into shock and was transferred to the operating room. The abdominal CT had revealed a ruptured SAA, which was surgically repaired. Streptococcus mitis was isolated

from tissue cultures, yet all blood cultures were negative. Trans-thoracic and trans-esophageal echocardiograms did not reveal vegetations. He was treated with amoxicillin for 4 weeks and on a 5-month follow-up he has had no complications.

**Discussion:** SAAs can be distinguished between true and pseudoaneurysms depending on the aneurysm wall composition. The former are associated with pregnancy, atherosclerotic disease, autoimmune diseases and trauma. The latter are associated with trauma and pancreatitis. SAAs manifest as incidental findings (80%), abdominal pain (10%) or rupture with shock (2-10%). SAAs demonstrate the so-called "double rupture" phenomenon, where an initial SAA rupture is contained in the lesser sac; when the bleed overflows through the foramen of Winslow, circulatory collapse ensues. Risk factors for rupture include size, pregnancy, and cirrhosis. Infected aneurysms are usually due to S. aureus, S. viridans group, Salmonella spp, Gram negative organisms and are most often secondary to endocarditis. Their natural course is fast, leading to rupture with a high mortality rate. Infected SAAs are exceedingly rare and to our knowledge no other non-endocarditis related cases have been reported. SAAs can be treated with embolization or stenting, although in emergent situations surgical resection is the only option. In patients with risk factors for rupture, splenic aneurysms should be electively repaired to prevent complications. In endocarditis patients developing acute abdominal pain, this condition can prove fatal if not treated urgently.

## Adequate use of antimicrobial therapy in various wards – a cross sectional study in a tertiary hospital

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**Objective:** The rational use of antimicrobial therapy has ever increasing importance, as such our aim was to characterize and evaluate its correct use in the infirmaries of our hospital particularly regarding to renal adjustment, microbiologic specimen collection and directed antimicrobial de-escalation.

**Methods:** We organized a cross sectional study, a day in June 2015. Data was collected by means of our clinical information systems about all patients undergoing antimicrobial therapy in various medical and surgical wards. The following parameters were analyzed: patient demographics, site of infection, antimicrobials being used, current renal clearance, microbiological samples collected, agents isolated and their antibiogram.

**Results:** From a total of 187 patients analyzed 96 (51,3%) were undergoing antimicrobial therapy. They were aged between 20 and 93 years old with a mean of 68 and a median of 72. 52% were male and most (73%) were in medical wards. Urinary (29,2%), respiratory (18,8%) and intra-abdominal (19,8%) infections accounted the majority of infection sites, 4,2% accounted for prophylactic treatment and 5,2% had no identified location. The most prescribed agents were cefuroxime and piperacillin/tazobactam (20,8% each) and there was more than one agent prescribed in 18,8% of patients. The dosage wasn't adjusted to current renal clearance in 11,5% of patients. Microbiological samples were collected before starting therapy in 81,5% of cases

isolating an agent in 43%, the most frequent being *Escherichia coli* (34%). The antimicrobial therapy wasn't de-escalated in 6,3%.

**Conclusions:** Despite the sporadic character implied in a cross sectional study, we recognize a large percentage of admitted patients undergoing antimicrobial therapy at any given time, in which said therapy should have had better planning, regarding prior collection of microbiological samples, and better supervision, regarding timely de-escalation as well as frequent updates of renal adjustment. These results stress the importance of the continuous formation of medical staff, as well as the need of tighter surveillance being performed by antimicrobial stewardship programs.

## Is there any relation between vitamin D deficit on HIV infection characteristics?

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**Objective:** To investigate if vitamin D deficit is related to any characteristic in HIV patients.

**Material and methods:** HIV infected patients' retrospective observational study at Elda General University in follow-up. All HIV patients with a vitamin D available measurement during the follow-up were included in this study. The latest vitamin D levels were the chosen ones. The collected variables were epidemiologic dates, co-morbidity, osteoporosis risk factors, biochemical parameters, vitamin D levels, immunological situation, virological infection control, antiretroviral treatments (ARVT), CHV co-infection, fibrosis grade, VACS index and 5-years time mortality risk. Statistical analysis: SPSS Version 21.0. Comparison of qualitative variable using chi-square statistic, considering significant p value <0.05.

**Results:** A total of 240 patients with an average age of 46.9 y.o. were taken for analyzing (182 men). 12.1% were in jail when the study was carried out. 55% had CHV co-infection. 72.1% had undetectable HIV viral load. 83% were taking ARVT. 83.3% with treatment including tenofovir. 34.6% with efavirenz. 40.8% with protease inhibitors and 10.8% with raltegravir. 230 had vitamin D deficit (95.8%). 27.9% had vitamin D level <10 ng/mL, 48.8% – between 10-20 ng/mL, 19.2% – between 20-30 ng/mL and just 4.2% >30 ng/mL. No significant relationship was observed between vitamin D deficit and gender, tobacco, alcohol, drug-users, co-morbidities, CHV and BHV, evolution time, CD4 levels, osteoporosis risk factors, VACS index and 5 years mortality risk. Significant relationship was found between vitamin D low levels and incarcerated population (p=0.0002) and seasonality, being this deficit higher in lower sun exposition months.

**Conclusions:** Most HIV patients have low or very low vitamin D levels with slightly higher prevalence in comparison to other countries' publications. ARVT treatment and good virological control are related with vitamin D deficiency but not infection time. Although the number of incarcerated patients at the time of the study was low, being in jail seems to have relation with vitamin D deficit. More long-term studies are needed in order to evaluate the real impact that hypovitaminosis and its treatment have in our patients' evolution.

## Hemophagocytic syndrome as the presenting manifestation of visceral leishmaniasis: a study of three cases

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**Objectives:** Leishmaniasis is a chronic parasitic infection due with skin and/or visceral manifestation. Visceral leishmaniasis is a severe form in which the parasites have migrated to the vital organs. We aimed to investigate the clinicopathologic features, bone marrow examination, and prognosis of hemophagocytosis. Methods: The clinical and pathologic findings of 3 cases of hemophagocytosis as a manifestation of visceral leishmaniasis were reviewed.

**Results:** The age of patients, 3 males, ranged from 20 to 60 years old (median 37 years). The main complaints were fever, asthenia and weight loss in the three cases. The body examination showed: temperature (n=3), hepatosplenomegaly (n=2), isolated splenomegaly (n=1). Laboratory findings included, in the three cases, pancytopenia, inflammatory syndrome with high CRP and polyclonal increase in gamma globulins. The serum ferritin level increased in two patients. A hypertriglyceridemia and a cholestasis were found in the three cases whereas cytolysis was found only in 2 cases. Therefore, a diagnosis of disseminated intravascular coagulation syndrome (DIC) was considered in the 3 cases. Besides, bone marrow examination revealed active hemophagocytosis. Surprisingly, many *Leishmania* amastigotes were observed within marrow macrophages in 2 cases. Nevertheless, *Leishmania* infection was confirmed, in the 3 cases, by positive serology. Moreover, patients were negative for other viral, bacterial and parasitological infections. Furthermore, a response to anti-*Leishmania* treatment was seen in the three cases with improvement of clinical condition.

**Conclusions:** Visceral leishmaniasis associated with macrophage activation syndrome was described mainly in children. However, it can also occur in adults.

## Raoultella spp. infection: clinical and microbiological findings of an emerging agent

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**Objectives:** *Raoultella* human infections have a low prevalence; nevertheless *Raoultella* spp. pathogenicity has been well documented. The purpose of this study is to characterize clinical and laboratory features of patients with *Raoultella* spp. infection.

**Methods:** We enrolled all *Raoultella* spp. infection cases occurring over a 5-year-period in a major teaching hospital center. For microorganism identification VITEK-2 system was used

from 2010 to mid-2012 and Maldi-tof since mid-2012 to 2014. **Results:** Raoultella spp. was detected in 57 isolates deemed responsible for clinical infection. *R. planticola* was isolated from culture specimens in 32 patients. The majority of patients were female (62.5%), mean age was 68.9±15 years. The infection was community acquired in the 68.8% of patients. The most prevalent diagnoses were cystitis (50%), bacteremia (9.4%) and pneumonia (9.4%). Immunodeficiency was present in 18 patients (56.3%). Among these, 55.6% were diabetic and 27.8% solid organ transplant recipients. Antibiofilms showed widespread susceptibility except ampicillin. The most used antimicrobial agent was amoxicillin/clavulanate (53.1%). 5 patients (15.6%) died during the course of admission. *R. ornithinolytica* was isolated from culture specimens in 25 patients. 60% of patients were male, mean age was 66.1±16.1 years. The infection was community acquired in the 64% of patients. The most prevalent diagnoses were cystitis (36%) and pneumonia (24%). Immunodeficiency was present in 16 patients (64%). Among these, 37.5% were diabetic and 18.8% solid organ transplant recipients. Antibiofilms showed widespread susceptibility to cefotaxime, ciprofloxacin and gentamicin. The most used antimicrobial agent was piperacillin/tazobactam (24%). 2 patients (8%) died during the course of admission. No cases of *R. electrica* or *R. terrigena* were detected.

**Conclusions:** Our study highlights the importance of Raoultella spp. infections among diabetic patients and solid organ transplant recipients. Clinical features were diverse, cystitis being the most frequent presentation. In vitro susceptibility was always within the spectrum of the used antibiotic and in many cases there was a potential for de-escalation of therapy. *R. planticola* mortality was higher than *R. ornithinolytica*, although the difference was not statistically significant ( $p=0.38$ ). Further studies are needed to advance the understanding of the risk factors and virulence of this emerging agent.

## Descriptive study of arbovirosis (Dengue and Chikungunya disease) in travelers returning to Cantabria (Northern Spain) from Caribbean region and Southeastern Asia, from 1990 to 2014

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**Objectives:** Infections caused by arboviruses are becoming more common in Europe because of the increased intercontinental migratory population movements. Dengue disease (DD) is caused by an arbovirus of genus Flavivirus (with 4 serotypes) and it is transmitted by mosquito *Aedes aegypti*. Chikungunya disease (CD) is caused by an arbovirus of genus Alphavirus, which is transmitted to humans by infected mosquitoes. There is no specific treatment for DD and CD, being focused on relieving the symptoms. DD and CD are the most frequent arboviral

infections found in our continent. We aimed to characterize the cohort of patients diagnosed with DD and CF, and analyze risk factors of severe infection to be admitted in hospital.

**Methods:** Descriptive cohort of patients diagnosed with DD and CD in all the Hospitals of the region of Cantabria, from the 1st January, 1990 through 30th of September, 2014.

**Results:** 8 cases of arboviral infections were recorded, 4 DD and 4 CD. 75% of patients with DD were men, and 75% of CD were diagnosed in women. Patients diagnosed with CD proceeded from Dominican Republic (75%) and Haiti, while DD was diagnosed in patients from Dominican Republic (50%), Haiti (25%) and Thailand (25%). Median age at diagnosis was 38.5±14.5 years. None of them had associated comorbidities. Mean Charlson Index was 1±1. Median time from the onset of the symptoms to the diagnosis was 11.5±6 days. Diagnosis of DD and CF were performed at 11.5±6 days from the starting of symptoms. Related symptoms in patients diagnosed with arboviral infections were: fever (87.5%), arthralgia (75%), asthenia (71.4%), myalgia (50%) and exanthema (25%). Mild thrombopenia was recorded in 2 patients, with median platelet count 1.41x10<sup>6</sup>±1.46x10<sup>4</sup> cel/mL. Hemorrhagic syndrome was not found. 1 patient had anemia (mean hemoglobin 11.9±1.2 g/dL) and 3 patients (37.5%) had hepatitis (50% of them in CF). Platelet transfusions were needed in 2 patients: 50% in CF. Serologic tests for DD and CF were performed in all patients: IgM was positive in 37.5% patients (66.7% CF), IgG in 50% patients (50% in CF), and PCR was positive in 1 patient with DD. 2 patients needed to be admitted in hospital (50% DD), during 10±7.2 days, mainly due to persistence of fever and severe thrombopenia. None patient needed admission in Intensive Care Unit and there was not any death during the in-hospital stay. Risk factors for in-hospital admission were: asthenia (RR 7,  $p=0.29$ ), duration of symptoms >5 days (1.26,  $p=0.04$ ), hepatitis (2.26,  $p=0.35$ ), count of platelets <90000 (8.99,  $p=0.17$ ) and transfusion of hemoderivates (8.90,  $p=0.03$ ).

**Conclusions:** In our series, we found that both arbovirosis have similar symptoms at the onset of diagnosis, and the in-hospital admissions were low (25%), mainly related to thrombocytopenia, needed of platelet transfusions, severe asthenia, onset of symptoms >5 days and mild hepatitis. These cases remind clinicians to consider DD and CF in all travelers presenting with febrile illness and arthralgia, who are returning from Central America and Southeast Asia. The presence of mosquito vectors for DD and CD together with viraemic patients could potentially lead to autochthonous transmission of these arbovirosis in our continent.

## Current epidemiology of HIV-infected patients admitted to the intensive care unit

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**Objectives:** Since the introduction of effective antiretroviral therapy, epidemiology of Human Immunodeficiency virus (HIV) infection has changed in many areas, including patients who require admission to the intensive care unit (ICU). The aim of our

study was to evaluate the current epidemiology of HIV-infected patients admitted to the ICU in a university hospital.

**Methods:** We conduct a retrospective observational study. All HIV-infected patients admitted to any ICU at the Hospital Clinic of Barcelona from January 1, 2012 to December 31, 2013 were included. Data was obtained from medical records, and are expressed as mean (standard deviation) or percentage.

**Results:** 54 patients were included, 85.2% male, with a mean age of 47.7 (12.4) years. Among the patients 40.7% had been addicted to intravenous drugs, 44.4% were co-infected with hepatitis C virus (HCV) and 11.2% had diabetes mellitus. The pre-admission Barthel was 100 in 90.7%. At admission, HIV-infection was known for 13.4 (9.3) years on average, 66.7% of the patients were receiving antiretroviral treatment and 40.7% had suffered previously an opportunistic infection. Last CD4 cell count was 198.7 (237.4) cells/mm<sup>3</sup>, and 59.2% of the patients had less than 200 CD4/mm<sup>3</sup>, whereas the mean plasmatic viral load was 75,932.35 (231,733.3) copies/mL, being undetectable in 52.2% of the patients. Regarding the reasons for admission, only 17.6% were acquired immunodeficiency syndrome (AIDS) related (because of severe immunosuppression). During hospitalization, 59.3% of the patients maintained or initiated treatment in the ICU. Mechanical ventilation was required in 43.4% of the patients, whereas 40.7% presented renal failure, but only 3.7% required renal replacement therapy. ICU and Hospital length of stay were 9.1 days (13.7) and 21.2 (19.2), respectively. In-ICU and in-hospital mortality were 16.7% and 27.8%, respectively. Among ICU survivors, 82.2% had a Barthel Index  $\geq$ 80, rising to 84.6% at hospital discharge.

**Conclusions:** Currently, the main causes of ICU admission of HIV-infected patients are not related to AIDS. HCV co-infection is very common, and in-ICU mortality is similar to other non-HIV infected patients. Furthermore, among survivors, performance status at hospital discharge is good.

## Computerized axial tomography scan versus fibrobronchoscopy as prognostic complementary tests for tuberculosis

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**Objectives:** Tuberculosis (TB) remains being a worldwide public health problem. Patients admitted to an Internal Medicine Department of all Spanish hospitals may provide a suitable background for the analysis of two diagnostic procedures as the computerized axial tomography scan (CT) and fibrobronchoscopy (FB), concerning their prognostic value in TB clinical approach.

**Methods:** National data from the minimum data set (MDS) registry of patients discharged from the Services of Internal Medicine (MI) after admission to the hospitals of the National Health System (NHS) for TB (CIE 9-MC) were analyzed between 2005 and 2011. This information considers demographic features

(age and gender), admission and discharge dates, discharge circumstances (discharge to home, transfer to another medical centre, voluntary discharge or decease), major diagnosis and up to 12 secondary diagnoses for hospital ward admission, and finally, up to 20 validated diagnostic tests. Both multivariate and bivariate analysis were accomplished ( $p < 0,005$ ) in order to detect differences on demographic and clinical data distribution, including employment of CT or FB on complementary tests.

**Results:** A number of 25.367 patients with TB as major diagnosis on discharge were identified, of whom 69,6% were male. The average age was  $47 \pm 19,4$  years old. 25% of patients reached a Charlson index upper than 2. CT was performed on 7216 patients (28%), whether FB was carried out on 552 of them (2%). Hospital admissions in which chest CT was used show a longer average stay (23,1 days on average vs 16,9;  $p < 0,001$ ). Employment of chest CT rendered decreased in-hospital mortality (4% vs 6%;  $p < 0,001$ ) as well as FB, which application was associated with lower mortality (3% vs 5%;  $p < 0,001$ ). Chest CT means a protective factor against mortality after logistic regression analysis and adjusting for age, gender (female) and Charlson index (OR 0,59; IC: 0,53-0,70;  $p < 0,001$ ). In the cases in which FB was undertaken, no differences were found related with increased survival after a multivariate analysis (OR 0,59; IC: 0,34-1,03;  $p = 0,06$ ).

**Conclusions:** Chest CT was associated with decreased in-hospital mortality. At this moment, we are still pondering the reasons why this procedure improves TB hospitalization prognosis, but we do state that this technique involves greater accuracy on TB clinical approach. Besides, chest CT may allow an earlier detection of endobronchial and pleural complications, which would require specific and forward medical management as well as treatment. Further studies are demanded so as to evaluate the risk versus benefit ratio of FB implementation during TB admission.

## Tuberculosis and non-communicable chronic diseases on patients admitted into Spanish internal medicine departments from 2005 to 2011

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**Objectives:** Tuberculosis (TB) remains being a worldwide public health problem. In this study we ponder whether the comorbidities and non-communicable chronic diseases (NCCD) may have an influence on TB prognosis. Admissions into an Internal medicine department represent a desirable framework to analyze this effect.

**Methods:** National data from the minimum data set (MDS) registry of all patients discharged from the Services of Internal Medicine (MI) after admission to the hospitals of the National Health System (NHS) were analyzed between 2005 and 2011. This information meant demographic features (age and gender), admission and discharge dates, discharge circumstances

(discharge to home, transfer to another medical centre, voluntary discharge or decease), major diagnosis and up to 12 secondary diagnoses for hospital ward admission, and finally, up to 20 validated diagnostic tests. All patients with both diagnoses at discharge moment, TB and NCCD were included. NCCD encompassed chronic obstructive pulmonary disease (COPD), heart failure (HF), diabetes mellitus (DM), chronic respiratory failure (CRF), chronic renal failure (CNF), chronic liver failure (CLF) and dementia. Both multivariate and bivariate analysis were accomplished ( $p < 0.005$ ) in order to detect differences on demographic and clinical data. Charlson index was accomplished, adjusting for age, as comorbidity measurement. The differences on demographic and clinical data distribution among patients with or without TB were examined, taking into account the presence or absence of NCCD in both, by means of multivariate and bivariate analysis ( $p < 0.005$ ).

**Results:** A number of 25.367 patients with TB as major diagnosis on discharge were identified, of whom 25% of patients reached a Charlson index  $> 2$ . NCCD as COPD (8.6% vs 4.5%;  $p < 0.001$ ), DM (7.7% vs 4.8%;  $p < 0.001$ ), dementia (20.4% vs 4.9%;  $p < 0.001$ ), CNF (14.9% vs 4.7%;  $p < 0.001$ ), CLF (9.4% vs 4.7%;  $p < 0.001$ ) and HF (17.6% vs 4.6%) were associated with major in-hospital mortality compared with patients who suffered from TB but not from these NCCD. After logistic regression analysis, we observed that CLF (OR 2.03 CI: 1.67-2.46;  $p < 0.001$ ), HF (OR 1.67; CI: 1.36-2.06), dementia (OR 2.01; CI: 1.42-2.82;  $p = 0.002$ ) and CNF (OR 1.57; CI: 1.27-1.95;  $p = 0.006$ ) were the NCCD resulting with an increased in-hospital mortality due to TB. No differences were found related with neither DM nor COPD on multivariate analysis.

**Conclusions:** Admitted patients into Internal medicine departments of Spain with TB as main diagnosis, did also present with relevant comorbidities in 25% of studied cases. We observed in these patients that concurrent comorbidities as HF, CLF, dementia and CNF are NCCD related with independently increased in-hospital mortality. Further complete prospective studies are demanded so as to evaluate the prognostic role of these NCCD related with accompanying TB risk versus benefit ratio of FB implementation during TB admission.

## An uncommon diagnosis for a common symptom

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**Introduction:** Brucellosis is a systemic disease and may affect any organ or system. Rare presentations might include lower back pain.

**Case report:** We report the case of a 33 years old Caucasian man, who was admitted to the emergency room with a history of high intensity lower back pain ongoing for 2 months and refractory to analgesic treatment. It was accompanied by a non-intentional weight loss (20 kg, 23.4% of body weight), and fever with profuse night sweats. Physical examination revealed pain on palpation of the lumbar spine as the sole finding. There was an unremarkable medical history without chronic medication. The

patient worked as a meat cutter and had a animal farm. Upon further diagnostic test, blood work and radiographs appeared normal. A CT scan of the lumbosacral spine showed alterations that could be associated with sacroiliitis, inflammatory arthritis, or ankylosing spondylitis. Pain control was difficult. Blood cultures were positive for *Brucella* spp. Therefore, antibiotic treatment with rifampicin (900 mg id) and doxycycline (100 mg bid) was initiated for 9 weeks with good clinical response.

**Discussion:** Brucellosis – although increasingly less frequent – continues to be an uncommon cause of back pain. A complete medical history including the epidemiological clues is crucial for a correct diagnosis and implementation of effective therapy. Adhesion to therapy is very important in those cases to prevent recurrences as the localized forms of brucellosis are predominantly chronic, with long evolution and marked by frequent recurrence.

## Chickenpox is not always gentle: pneumonia with acute respiratory distress syndrome as a rare complication of Varicella zoster virus infection

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**Introduction:** Chickenpox is an infection caused by Varicella zoster virus (VZV) with a peak of incidence between 1 and 6 year old children. It results in a characteristic maculopapulo-vesicular disseminated skin rash. It is usually benign but in immunocompromised individuals can lead to clinical complications.

**Case report:** Male, 47 years old, 20 pack-year smoker, alcohol consumption of 100 g/day and a previous history of pulmonary tuberculosis 10 years in the past. He presented to the ER with cough and mucous sputum for the last 7 days, fever for 3 days and abdominal pain and pruriginous skin rash that started in the thorax but hastily disseminated to the entire body. At admission the patient presented pain and dyspnea, polypnea, fever, dispersed bronchi bilaterally at chest auscultation and dispersed vesicular lesions in the skin and oral mucosa with hematic content, pustules and papules. A thoracic CT scan showed peribronchovascular parenchymatous densifications with ground-glass areas suggesting an infectious process with endobronchial dissemination. Blood tests showed cytolytic hepatitis and rhabdomyolysis. Due to the fast clinical decay, with acute respiratory distress syndrome (ARDS) criteria, the patient was transferred to the ICU where he started mechanical ventilation, hemodialysis for acute kidney injury and aminergic support for the septic shock. Despite these measures and treatment with acyclovir, ceftriaxone and azithromycin, the patient needed to be started on ECMO which he continued for 20 days. A bronchofibroscope revealed scattered ulcerated lesions, septic workup from admission was sterile for bacteria, fungi and Mycobacteria, serology studies for HBV, HCV and HIV were negative, PCR for VZV was also negative, immunoglobulin and immunologic study were normal, and no relevant immunosupresion factors could be identified. Blood

tests showed severe kidney, liver and hematological failure. The patient had a favorable response at day 35 of admission and was transferred to the medical wards. At hospital discharge he had no respiratory failure, had improved kidney function without hemodialysis.

**Discussion:** This was a case of VZV pneumonia, with severe ARDS in a young immunocompetent patient, with an uncommon severity, with no history of diseased contacts, and an unusual skin rash. In conclusion, chickenpox is an infection with a clinical diagnosis and should not be forgotten in the adult. Because of its potential medical complications it should have an adequate clinical surveillance.

## HIV treatment adherence: associated neurological delirium of taboo to HIV

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**Introduction:** The aim is to alert health workers about a great factor of therapeutic failure that stills happens, even though great advances and research. It is also important to know how to discriminate it from own neuro-psychological complications.

**Case report:** A 38 years old male, infected with HIV in 1992, when he was 16, due to shearing needles, basic scholarship. He used to work as a farmer. Medical background: HCV infection, dependent of drugs, after having a car accident and inform about his disease he was rejected familiarly and socially. He decided to move of residency, losing his trace, denying his condition and not having treatment. He developed AIDS 10 years later and returned to be helped by his family and friends. He kept himself denying, rejecting to accept his disease and treatment, referring some kind of delirium. At the end of his life, he had multiple pulmonary comorbidities, mainly of pulmonary origin. Having some help by his family and a stable partner, accepted medication and started highly active antiretroviral therapy (HAART). He passed away in 2015, after several hospitalisations as a result of a hardly treatable nosocomial pneumonia multi-resistant with pleural effusion and empyema.

**Discussion:** New treatments have allowed to speak about HIV-like a chronic illness, with reduction of associated morbidity and mortality, but even though treatment is accessible, patients many times do not follow it. In his case we highlight other important point about one of the most frequent complications as neuro-cognitive disorders. Current therapies against HIV have not provoked some expected changes in relation to neuro-cognitive disorders associated to HIV and nowadays these conditions still remain. Early and quick detection of neuro-psychological problems has become a priority in the treatment of the disease. Therapeutic adherence is still a significant problem after 35 years of its release. Psychosocial stereotype factors are the most influent, without discarding related cognitive impairment that takes to a reduction in quality of life and other factors that might aggravate the situation, carrying the patient evitable complications.

## Listeria monocytogenes meningitis in an immunocompetent adult: a case report

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**Introduction:** *Listeria monocytogenes* (*L. monocytogenes*) is an uncommon cause of bacterial meningitis in immunocompetent adults. The meningitis caused by *L. monocytogenes* differs from other types of bacterial meningitis, especially in treatment and prognosis. *Listeria* has a predilection for the brain parenchyma, especially the brain stem, and the meninges. Mental status changes are common. Seizures, both focal and generalized, occur in at least 25% of patients. It does occur in immunocompetent adults, although this is extremely rare, and, unless recognized and treated, *Listeria* infections can result in significant morbidity and mortality, so that's why early recognition and treatment are so important and are the aims of the report of this clinical case.

**Case report:** We describe a clinical case of a 78 years old male that was admitted to our hospital, having had fever (up to 39.5°C), confusion and disorientation for some days prior to admission. He had no history of recent travel and sick contacts. As past medical history, he had an interstitial lung disease (silicosis), arterial hypertension and dyslipidemia. On physical examination, the patient was confused, showed an ataxic march, there was no neck stiffness and the remainder systemic examination was unremarkable. Results of the initial laboratory studies showed only an elevated C-reactive protein and the rest of serum biochemistry values were normal. A brain computed magnetic resonance demonstrated no parenchymal abnormality. A lumbar puncture was performed and the analysis of his cerebrospinal fluid showed leukocytosis with lymphocyte predominance, high protein concentration, and low glucose. The cultures of blood yielded a *L. monocytogenes* susceptible to ampicillin and gentamicin and a final diagnosis of *L. monocytogenes* meningitis was made. The patient started treatment with above-mentioned antibiotics. On the 11th hospital day, he was fully conscious and well oriented, his march was normal and the fever subsided. The patient was then discharged home and, on follow-up, he remains in good clinical condition.

**Discussion:** *L. monocytogenes* has become an important cause of community-acquired acute meningitis in developed countries. Because of the high case mortality rate, it is important that *L. monocytogenes* should be considered among the possible causes of community-acquired bacterial meningitis in any patient, even an immunocompetent adult, and those who fails to respond to empirical antibiotic therapy.

## Pneumocystis jirovecii pneumonia in a patient without HIV infection

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**Introduction:** *Pneumocystis jirovecii* pneumonia (*P. jirovecii*) can occur in immunocompromised patients without HIV

infection. Risk factors, clinical features, treatment outcomes, and factors related to mortality in these patients may be useful for physicians who care for these patients. Although the association of *Pneumocystis carinii* pneumonia with connective tissue disease (CTD) has been noted for a long time, there are few series reported.

**Case report:** We describe a clinical case of a 59 years old male that was admitted to our hospital, having had fever (up to 38.5°C) and shortness of breath at rest for three weeks prior to admission. As past medical history, he had rheumatoid arthritis under daily glucocorticoid therapy and cytotoxic drugs weekly (methotrexate). Physical exam reveals an anxious man with blood pressure 130/70 mmHg, normal pulse, and respiratory rate 24. Lungs are clear on percussion. No accessory muscles are being used. No cyanosis is present. Febrile (38°C), and remainder systemic examination was unremarkable. Results of the initial laboratory studies showed elevated inflammatory systemic markers, but the rest of serum biochemistry values were normal. In the first day after admission, the patient exacerbates his dyspnea having marked hypoxemia and the image of the thorax showed diffuse interstitial infiltrates. Subsequently, he had an evolution to acute respiratory distress syndrome needing mechanical ventilation. Induced sputum and bronchoalveolar lavage fluid were performed and showed infection by *P. jirovecii* and the patient started select antibiotherapy. On the 14th hospital day, he was asymptomatic, the fever and dyspnea subsided and the patient was then discharged home. On follow-up, he remains in good clinical condition.

**Discussion:** *P. jirovecii* may complicate a variety of immunocompromised states especially autoimmune diseases and hematologic malignancy. When patients with CTD who are receiving immunosuppressive therapy develop fever, dry cough, dyspnea, and chest radiography shows diffuse interstitial infiltrate, the diagnosis of *P. jirovecii* pneumonia should be highly suspected. Induced sputum or bronchoalveolar lavage fluid (BAL) must be quickly performed to confirm diagnosis. Patients who receive corticosteroids and/or cytotoxic drugs should receive primary *P. jirovecii* prophylaxis. The mortality rate is high especially in severe cases that need mechanical ventilation. Intensive care and close monitoring are needed for these patients.

### **Fever and abdominal pain: mesenteric adenitis as a manifestation to *Haemophilus influenzae* infection. A case report**

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**Case report:** We report a case of mesenteric adenitis secondary to *Haemophilus influenzae* infection. A 51 years old woman with history of hypothyroidism in substitution therapy was admitted because of malaise, abdominal pain, high fever, nausea without vomiting for 12 hours of evolution. Lower right abdominal pain with positive Blumberg sign was observed by routine physical examination. Results of first laboratory test showed:

leukocytosis and elevation of acute-phase reactants. Differential diagnosis was made with patient clinic, previous history and laboratory test, between appendicitis, rupture of ovarian cyst, torsion of ovary, tumor, cyst or ovarian mass. She was valued by gynecology discarded gynecological surgical acute abdomen. Abdominal ultrasound is performed with findings of liquid free peritoneal and edematous loops of intestine and colon. Abdominal CT could not discard acute appendicitis. Exploratory laparoscopy was requested with intraoperative findings of multiple mesenteric lymph nodes of inflammatory aspect, and thickened with inflammation of ileum, performing appendectomy. Pathological anatomy results described fibrotic and necrotic inflammatory material. *Haemophilus influenzae* was isolated in exudate sample and blood cultures. Final diagnostic was ileitis terminal and mesenteric adenitis 2nd to infection by *Haemophilus influenzae*. Amoxicillin-clavulanic acid was started for 14 days with good clinical evolution.

**Discussion:** Mesenteric adenitis may manifest as an acute abdominal syndrome. It represents main differential diagnosis of acute appendicitis. The most frequent infection causes is Adenovirus, also found *Campilobacter*, *Salmonella* spp., *Yersinia enterocolitica*, *Shigella* spp, *Bartonella* spp, *Mycobacterium* spp, and Epstein-Barr virus among others. *Haemophilus influenzae* is a pleomorphic coccobacillus Gram-negative, characterized by its presentation as a respiratory infection, meningitis, skin, and joint. Its presentation as abdominal disease as it was that of patient case is uncommon. Cases with mucosa lesion of terminal ileum and colon, producing nodal growth and necrotic ulcers have been described very difficult to distinguish acute appendicitis. Conclusions: Mesenteric adenitis is a poorly defined disease of nonspecific etiology, part of differential diagnosis of acute appendicitis. It's characterized by abdominal pain. Presence of high fever and systemic involvement suggests bacterial or viral etiology.

### **Prospective study of *Staphylococcus aureus* bacteremia in a university hospital**

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**Objective:** To describe characteristics of *Staphylococcus aureus* bacteremia (SAB) from a prospective continuous registry in a teaching hospital.

**Methods:** A total of 246 episodes of SAB in 232 patients between August 2010 and April 2015 were included. An episode of SAB was defined when *S. aureus* was isolated from one or more peripheral blood culture samples. Epidemiological, clinical, and microbiological data were prospectively registered. Categorical data are described as frequency (percentage) and quantitative variables as mean (standard deviation).

**Results:** mean age of patients was 74.6 (14.7) years and 164 (67%) were male. Cardiac disease (190, [77%]), chronic kidney disease (76 [31%]), solid neoplasm (66 [29%]) and chronic lung disease (49 [20%]) were the leading comorbidities. The mean



score in Charlson index was 3.7 (2.4). 64 (26%) patients were on treatment with immunosuppressant or corticosteroid therapy. 100 (41%) SAB episodes were community-acquired, 78 (32%) were nosocomial-acquired and 68 (27%) were health-care related. Common risk factors were: previous hospital admission in the last month (162, 66%), presence of urinary catheter (102, 42%), prior (3 months) antibiotic treatment (79, 32%), presence of central vascular catheter (21, 9%), permanent intravascular device in (43, 18%), previous surgery (42, 17%). At presentation of SAB, 61 (25%) patients had septic shock and mean Pitt score was 2.2 (2.3). The most frequent foci of SAB were: unknown in 67 (27%), respiratory in 45 (18%), catheter-associated in 38 (15%), endovascular other than catheter in 34 (14%) and skin and soft tissue in 28 (12%). Thirty-one percent of the isolated strains (75 cases) were resistant to methicillin (MRSA), and 147 of the SAB episodes (60%) received appropriate empirical therapy according to the final microbiological results. During 30-day follow up, 44 episodes (18%) of persistent bacteremia (persistence of *S. aureus* in blood cultures after appropriate antibiotic treatment was initiated) and 70 deaths (27%) were recorded.

**Conclusions:** We show a relevant prevalence of community-acquired SAB (particularly among elderly people). Similar results have been described by other authors, including mortality rates from 15 to 25%. We also find a higher prevalence of MRSA than that found in series from Northern Europe (<1%), France (17.4%) or United Kingdom (14%); but less than Portugal or Romania (46%).

## Tuberculous meningitis: two sides of the same disease

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**Introduction:** Tuberculosis is an infection caused by *Mycobacterium tuberculosis*. It is the second most common infectious cause of death in adults worldwide. It can affect every tissue of the human body, including the central nervous system (CNS). The dominant form of CNS disease is meningitis (MTB). Early diagnosis is critical because the clinical outcome depends upon the stage at which therapy is initiated, and even despite effective treatment it has a high fatality ratio.

**Case reports:** Case one: female patient, 72 years, with hypertension, was admitted to neurology department with headache, photophobia and decreased strength in the legs bilaterally with two weeks evolution. A lumbar puncture (LP) was performed and the examination of cerebrospinal fluid (CSF) showed 247 polymorphonucleated (PMN) cells, protein of 112 mg/dL and glucose of 42 mg/dL. Quadruple antibiologic and corticoid therapy was initiated. The search for *M. tuberculosis* in the CSF with polymerase chain reaction technique was positive. The brain magnetic resonance image (MRI) showed hyperintense periventricular foci. Despite the therapy, the clinical status worsens, with progressive implication of the III, VII and VIII cranial nerves, pituitary gland and cauda equine. The patient entered a stupor state and died, after 140 days of therapy. Case two: female patient, 40 years, with

hypertension, was admitted to neurology department with fever, headache, myalgia and confusion with 5 days evolution. The patient presented disorientated, with papillary edema and no nuchal rigidity. The CSF examination showed 310 PMN cells, protein of 1 mg/dL and glucose of 53 mg/dL. The Gram stain showed Gram positive diplococcus and the patient started therapy with ceftriaxone and corticoid. After 10 days the patient reinstituted fever. The LP was repeated, and the examination of the CSF showed 125 lymphocytes, protein of 114 mg/dL and glucose of 50 mg/dL. Considering that the CSF analysis was highly suspicious of MTB, and after excluding other causes, quadruple antibiologic therapy was initiated. The CSF search for *M. tuberculosis* was negative. The brain MRI after gadolinium enhancement showed hyperintense meningeal signal in the temporo-insular region. The patient clinical status improved and she was discharged after 15 days. To the date, she finished the one year course of therapy and is clinically without sequelae.

**Discussion:** These two cases show how the same disease can have different distinct courses, despite the early onset of antibiologic therapy.

## Rhodococcus equi: a rare necrotizing pneumonia in immunodeficient patients

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**Introduction:** *Rhodococcus equi* infection in humans is unusual and not well-known. We describe in a patient the clinical, radiological and laboratory characteristic of this rare pathogen, as well as its treatment and evolution.

**Case report:** A 48 year-old patient was admitted in emergency service complaining about high fever, constitutional syndrome and loss of weight of 5 months-evolution. He was seropositive for HIV (since 1987) and had a chronic VHC hepatopathy. He did not take any chronic treatment. In April 2014, he was diagnosed of a high-grade lymphoma which could not be treated because of social problems. On the physical examination there were several submandibular and axilar soft, mobile and non painful lymph nodes. Laboratory studies: CD4 lymphocyte count was 65/mm<sup>3</sup> (21%), CD8 144 (44%) and CD4/CD8 0,47. Thorax radiography revealed a necrotizing multilobar pneumonia and the computed tomography scan showed several consolidations in different pulmonary lobes with necrosis areas and cavitation zones, as well as generalized lymphatic nodes. Further studies included a positron emission tomography (PET-TC) which demonstrated hipermetabolic supra and infradiaphragmatic adenopathies compatible with the lymphoma and higher hypermetabolism of the pulmonary lesions. The sputum cultures (initially negative) and posterior bronchial alveolar lavage (BAL) results established a definitive diagnosis: a *Rhodococcus equi* infection. According to the antibiogram report, he was treated with intravenous

erthapenem, azithromycin and levofloxacin during one month approximately (until the sputum culture turned negative) followed by long term oral treatment with satisfactory evolution. He also started antiretroviral therapy (ART) and received treatment for the lymphoma. In our patient, as usually in this entity, the diagnosis was made in an important cellular immunosuppression stage. The chest radiography showed a multilobar necrotizing pneumonia. The sputum cultures and BAL established the microbiological diagnosis. The evolution with appropriate combined antimicrobial treatment was satisfactory.

**Discussion:** This report describes the diagnosis and evolution of a necrotizing pneumonia caused by *Rhodococcus equi* in a man with advanced HIV infection. It is important to consider a wide range of possible entities involved in immunodeficient patients with necrotizing pneumonia. This is why obtaining respiratory samples turn out to be so helpful in certain diagnosis.

## Unusual infectious endocarditis

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**Introduction:** Whipple's disease is a rare disease of difficult diagnosis due to the diversity of its signs especially when the classical digestive and articular symptoms are absent. We report a case whose diagnosis was established on the specimen of mitral valve replaced due to a severe prolapse and complete rupture of cusps.

**Case report:** 52 years old male patient with a history of post-smoking chronic obstructive bronchitis, a chronic alcoholism presented with severe acute heart failure due to severe mitral regurgitation without clinical evidence of infective endocarditis. The echocardiography showed a complete prolapse and probable cusps rupture which required urgent valve replacement with the installation of a mechanical valve. During the intervention, it was noted an unusual valvular thickening and vegetations compatible with endocarditis. Then, the patient has had a conventional treatment with amoxicillin + gentamycin + fluconazole. After discharging the patient, results of the surgical specimen confirmed a *Tropheryma whipplei* infection (positive polymerase chain reaction (PCR)), which required the patient's return for further investigations and specific treatment. There was no gastrointestinal, articular or neurological involvement. Histology, PCR on duodenal biopsies were negative as well as PCR on blood and saliva. The patient was released under prolonged treatment with hydroxychloroquine + cyclines without trimethoprim-sulfamethoxazole due to absence of neurological involvement. After a few months the patient stopped the treatment by himself and remains in complete remission. Folic acid and vitamin B12 deficiencies were confirmed and supplemented.

**Discussion:** *Tropheryma whipplei* endocarditis is exceptional and can progress without classical signs of endocarditis. PCR is the most sensitive technique since histology is often negative. The treatment is long and requires patient compliance which is not always the case.

## Immunocompromised patients and quantiferon. A complex relationship

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**Introduction:** Immunocompromised patients (IP) gets more often everyday on daily clinical practice: solid cancer on chemotherapy, hematological malignancy, immunosuppressant drugs, inflammatory bowel and connective tissue disease. QuantiFERON-TB (QTF) got into scene as an alternative to purified protein derivative skin test (PPD) on tuberculosis (TBC) screening programmes in IP. Despite its higher specificity and promising results at the very beginning, more than 10% of QTF results demonstrate false negative.

**Case report:** 47 years old male, ex-smoker with Crohn disease. Regular treatment with anti-TNF drugs and cholestyramine (previous PPD-, CXR normal). 10 days development feverish condition, without a known outbreak, admitted to unknown origin fever (UOF) further studies (anodyne physical examination, CXR normal). A few days later, the patient started with dyspnea symptomatology and hepatosplenomegaly. CXR displayed micro-nodular pattern and with perturbed microbiology studies (acid-fast bacilli-AFB >50/field, nucleic acid amplification+ *Mycobacterium tuberculosis*, adenosine deaminase 88 U/l), a computerized tomography seemed to be required (nodular lesion at right upper lobe with diffuse massive bilateral micro-nodular pattern. Manifold and multilevel mediastinal lymph nodes). QTF undetermined at that time. Miliary TBC was then confirmed. Serology: negative for cytomegalovirus, human immunodeficiency virus, B+C hepatitis virus and syphilis. During the tuberculostatic treatment (rifampicin + isoniazid (INH) + pyrazinamide (PZA) + ethambutol (EMB)), the patient suffered from a severe cholestasis liver dysfunction (total bilirubin 4.6 times the upper limit of normal (TULN), direct bilirubin 38 TULN, GGT 20 TULN), obliging to stop full therapy. Liver biopsy demonstrates tuberculosis etiology chronic granulomatous hepatitis, AFB+. AntiTBC treatment was then progressively reintroduced (levofloxacin + INH + EMB + PZA). The patient has evolved favorably but under bone marrow dissemination suspicion, QTF has turned negative.

**Discussion:** Despite of new diagnosis procedures, as QTF, is imperative to keep a heightened level of TBC cause suspicion at an UOF condition, even more if it occurs in an IP. TBC still needs to be discarding by more methods. We consider necessary to optimize the screening and prevention TBC protocols in IP, taking in count, the results that evidence the possibility of false negative results using actual procedures and the increase of the IP prevalence.

## The impact of clinical suspicion level in early diagnosis: case report

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**Introduction:** Normally the late diagnosis and therapeutic of spondylodiscitis results on a high morbidity. Diagnosis is complicated by the coexistent joint degenerative pathology and

the incipient or absent radiological signs in the initial phase.

**Case report:** 59 years old female, hospitalized with a diagnosis of pneumonia, empirically treated with ceftriaxone and clarithromycin. Previously treated with etoricoxib and metamizol by fever and back pain, interpreted as a resulting from osteoarticular pathology. Presented interscapular pain with mechanical characteristics, with 15 days of development, worsened and compromising the overall condition about 3 days before admission. Also reported muscle pain, severe asthenia, intense dyspnea and fever of 39°C. Poor general condition, pain on palpation of the spinous processes of the dorsal region and crackles at the level of the right pulmonary base to pulmonary auscultation. Analytically with C reactive protein of 304 mg/dL, leukocytosis 10600 mg/dL, neutrophilia of 84.2%, thrombocytopenia 85000 mg/dL and a hypoxemic respiratory failure. By the clinical extreme pain, findings on physical examination and suspected spondylodiscitis, the patient realized a spinal MRI, which revealed suggestive signs of spondylodiscitis. It was isolated a multisensitive drugs *Staphylococcus aureus* in blood culture. The antibiotic strategy was changed to flucloxacillin. The patient was discharged with oral antibiotic therapy scheme with a favorable clinical, analytical and imaging evolution.

**Discussion:** The interest of this case consists in the alternative diagnosis, cataloged initially as pneumonia with exuberant systemic inflammatory response. The diagnosis was supported by a clinical presentation, more specific and sensitive imaging method, enabling timely treatment, resulting in reduced functional sequelae.

### **Study of *Mycobacterium lentiflavum*'s isolates in a tertiary hospital in Spain. An emerging pathogen?**

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**Objectives:** *Mycobacterium lentiflavum* (ML) is a slow growing non-tuberculous mycobacteria (NTM), first identified in 1996. ML disease in children with cervical lymphadenitis have been reported and rarer in adults with lung disease. We analyze patients with ML isolates in our Hospital.

**Methods:** The analysis includes ML isolates in our hospital from 2009 to 2013. The samples were processed in liquid and solid medium by conventional methods and were identified with hybridization techniques and susceptibility testing. Demographic, clinical, radiological, predisposing factors, treatment and outcome were analyzed. Colonization and infection were defined according with American Thoracic Society criteria.

**Results:** NTM were isolated in 206 patients: 54 *Mycobacterium avium* complex (26.4%), 49 *Mycobacterium gordonae* (24%), 44 ML (21.5%) and 59 other NTMs. ML was isolated from respiratory samples in 42 adults and from lymphoid tissue in 2 children with lymphadenitis. All of these were sensitive to clarithromycin/cycloserine; 10 were unknown. 35 patients had comorbidities which affected to local pulmonary immunity (18 COPD with/without bronchiectasis, 12 bronchiectasis) or

systemic immunity (3 rheumatoid arthritis, 1 gastric cancer and 1 chronic lymphocytic leukemia). 30 patients had abnormal chest radiographic (11 bronchiectasis, 9 unilateral infiltrates, 4 pulmonary nodules, 4 atelectasis and 2 "ground glass"). 41 cases from all samples were considered ML colonization. Of these, 11 (26%) died in next 3 years for non-neoplastic causes and 16 (38%) had not been performed control cultures. There were 3 cases of ML infection: 1 adult with bronchiectasis who received treatment with clarithromycin for 7 months with clinical and radiological improvement and negativization sputum culture and 2 children with cervical lymphadenitis were being treated with clarithromycin and ciprofloxacin for 7 months but they only had improvement after surgical excision at second month of treatment.

**Conclusions:** ML isolates are increasing in our environment and is the 3rd frequency MNT currently. Although infection was caused in adults in only one case, the high mortality rate in the medium term of these patients suggests that we should pay more attention to ML isolates. Most isolates show multidrug resistance to antituberculous agents with full sensitivity to cycloserine and clarithromycin.

### ***Clostridium* diarrhea relapse – reports of two successful cases with a different approach to the antibiotic therapy**

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**Introduction:** The authors describe two cases of *Clostridium difficile* diarrhea relapsing on standard therapy. The objective is to discuss a new approach in the elderly, known to be more susceptible to this disease.

**Case reports:** The first case is of a woman, 89 years old, with a history of hypertension and dyslipidemia. She was admitted in our ward for diarrhea. The study revealed *C. difficile* toxin on fecal analysis and pseudomembranous colitis on colonoscopy. She completed 3 cycles of antibiotic (metronidazole and vancomycin) owing to relapses with improvement in-between. At one month after the last cycle there was a third relapse and she was started on vancomycin and rifampicin for 14 days followed by vancomycin 125 mg twice a week for 4 weeks in the outpatient setting with no following relapses. The second case is of a woman, 92 years old, with a history of atrial fibrillation, hypertension and interstitial lung disease. She was admitted in our ward for community-acquired *C. difficile* diarrhea. The CT-study revealed an exuberant pericolic inflammatory process. She completed three cycles of antibiotic (metronidazole and vancomycin) also owing to relapses, with improvement in-between. Again, complete remission only came when the final standard course of vancomycin was followed by 125 mg twice a week for 4 weeks cycle, completed in the outpatient setting.

**Discussion:** *Clostridium difficile* is the most common cause of nosocomial diarrhea in developed countries. Over the past decade the incidence (new and relapsed cases) and mortality have increased significantly in the hospital and also in the outpatients. In 2013 the American College of Gastroenterology issued revised recommendations for diagnosis and treatment

of such situations with emphasis on relapses in the elderly population suggested vancomycin standard 14 days therapy followed by 4 weeks of 125 mg twice a week (Scott Curry, personal communication). These two cases underline not only the aggravating reality of *C. difficile* diarrhea, as a nosocomial and community-acquired entity, but also demonstrates the importance of considering new approaches on the antibiotic therapy to be used in the several relapsing scenarios, an ever-growing problem in current healthcare, especially in fragile patients as is the cases with the elderly population.

## Erythema nodosum – a manifestation of tuberculosis primary infection

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**Introduction:** Tuberculosis (TB) may present atypically, requiring a high level of suspicion. Erythema nodosum (EN) can arise in primary forms of TB, due to a hypersensitivity reaction to a specific protein which occurs in a patient with or without evidence of active disease.

**Case report:** Female patient, 29 years old, hospitalized for fever and pain in the lower limbs with 15 days of evolution. This symptomatology was preceded by productive cough. Cutaneous lesions in the lower limbs compatible with EN in the initial physical examination. Epidemiologically stands out contact with TB patient about 18 months before. In analyses – elevation of inflammatory parameters. Chest x-ray revealed suspicious lesions of TB. In thoracic CT scan was observed the presence of "tree-in-bud" pattern. The direct examination of alcohol acid resistant bacilli in the sputum was positive. It was admitted the diagnosis of TB and the patient started antituberculosis therapy. Subsequently, the PCR detection method was also positive for *Mycobacterium tuberculosis*. The patient had a favorable evolution with complete remission of fever and part of the EN. About three months later, thoracic CT scan showed infiltrated in the right lower lobe. Clinically – without signs or symptoms and complete remission of EN.

**Discussion:** Alert to an atypical presentation of tuberculosis and the value of a detailed anamnesis that in most cases directs the clinician to the correct diagnose.

## Voluminous *Parvimonas micra* cervical abscess

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**Introduction:** The cervical abscesses are, in the majority of cases, a result of oropharyngeal and odontogenic infectious disease, being anaerobic bacteria an important causative agent. *Parvimonas micra*, known as *Peptostreptococcus micros*, part of the oral flora, are often associated with periodontitis. We report

a case with a voluminous cervical abscess to *Parvimonas micra*, with insufficient response to empiric therapy.

**Case report:** A 35 years old woman, with no relevant medical history was admitted for investigation and treatment of swelling of the parotid region and lower left hemiface, with 3 weeks of evolution, with painful fluctuation and only partial improvement under therapy with amoxicillin/clavulanate. Physical examination revealed multiple caries. TC of the neck documented "Voluminous collection in the ascending limb of the lower jaw (4x6 cm), with extension to pterygoid fossa, zygomatic arch and angle of the jaw". RM-CNS showed "hyper-intense area osteo-dural in the left middle fossa, adjacent to a focal lesion compatible with a brain abscess (23x14.5 mm). Further, surrounding edema, conditional deletion of regional cortical sulci was apparent". Facial abscess was drained and empiric therapy with metronidazole, ceftriaxone and corticosteroids was started. 6 molars were extracted from patient. After identification of *Parvimonas micra* in the pus drained, therapy was adjusted to penicillin 24 MIU/day. With the drainage of the abscess and adjustment of therapy to central nervous system levels, clinical improvement, resolution of the facial abscess and reduction of temporal abscess was observed.

## Part of the cure, part of the disease

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**Introduction:** Systemic lupus erythematosus (SLE) is an autoimmune disorder that affects multiple organs. In some cases, treatment with aggressive immunosuppressive agents is necessary, which is sometimes associated with infectious complications.

**Case report:** We present the case of a 28 year old male, who was diagnosed with SLE 3 months before. At the time of diagnosis, he presented with malar rash, pleural effusion, class IV lupus nephritis with nephrotic range proteinuria, autoimmune anemia, thrombocytopenia, leucopenia and positive ANA (1/640) and DsDNA 493 U/L. He was started on hydroxychloroquine, prednisolone and mofetil micophenolate, and remained in a tight follow up. After 1 month, there was a marked improvement in his renal function, but he remained anemic, despite normalization of markers of hemolysis, and evidence of decreased illness activity. On a routine appointment, he complained of progressive and incapacitating asthenia and exertional dyspnea, anorexia and weight loss (about 11 kg), dysphagia and oral pain. He denied fever, arthralgias or increased edema. The hemoglobin was 7,5 mg/dL, with normal bilirubin, LDH and haptoglobin. The complement was normal and DsDNA was low. He was admitted for further investigation. The esophagoduodenoscopy revealed candida esophagitis on the upper third of the esophagus, and mucosal erosions on the antrum and duodenal bulb. The colonoscopy revealed multiple erosions on the rectum, sigmoid and ascending colon. The bacteriologic exam of the stool was negative. Serologies were negative except for cytomegalovirus, with high antigenemia and positive PCR. The ulcer biopsy confirmed the diagnosis of CMV colitis, and the patient was started on ganciclovir, with a good clinical and analytical response, and negative virologic

exams. He was discharged with prophylactic dose of valganciclovir, and mofetil micofenolate was discontinued. He remains in follow up one year later, with no other complications and adequate control of the disease with prednisone 7,5 mg per day and hydroxicloroquine 400 mg per day.

**Discussion:** With this case, we aim to illustrate the diagnostic difficulties between a disease flare and a complication of the immunosuppressive treatment, as well as the need for a high suspicion index for infectious complications in patients undergoing these therapies.

### **Clinical features, short term mortality and prognostic risk factors of septic patients admitted to internal medicine units: an Italian multicenter prospective study**

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**Objectives:** Over the past few years a number of different studies have reported an increasing incidence of sepsis. However, only a few studies provided data on the epidemiology and management of sepsis within internal medicine departments. Aim of the study: to assess the clinical and epidemiological features, short term mortality and prognostic risk factors of a large cohort of septic patients treated in internal medicine units.

**Methods:** 31 internal medicine units from 14 different Italian regions participated in the study. Within each participating unit, all admitted patients were actively screened for the presence of sepsis.

**Results:** 533 patients were included (50% Gram positive bacteria, 46.8% for Gram negative bacteria); 78 patients (14.6%, 95% CI 11.9, 18.0%) died during hospitalization; mortality rate was 5.5% (95% CI 3.1, 9.6%) in patients with non-severe sepsis, and 20.1% (95% CI 16.2, 28.8%) in patients with severe sepsis or septic shock. Severe sepsis or septic shock (OR 4.41 95% CI 1.93, 10.05), immune system weakening (OR 2.10, 95% CI 1.12, 3.94), presence of active solid cancer (OR 2.14, 95% CI 1.16, 3.94) and age (OR 1.03 per year, 95% CI 1.01, 1.06) were significantly associated with an increased mortality risk, whereas blood culture positive for *E. coli* was significantly associated with a reduced mortality risk (OR 0.46, 95% CI 0.24, 0.88).

**Conclusions:** In-hospital mortality of our population appeared in line with the results of recent studies conducted in the ICU setting. Other larger prospective studies are warranted to confirm our preliminary findings.

### **Brain abscesses: uncommon presentation of infective endocarditis**

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**Introduction:** Infective endocarditis clinical presentation is characterized by highly diverse and quite nonspecific symptoms.

Microabscesses in brain and meninges occur commonly in *S. aureus* endocarditis but they are infrequent.

**Case report:** 75 years old female with a past medical history of chronic liver disease, apparently of non-alcoholic steatohepatitis etiology, type 2 DM and hypertension. She was admitted with one week of fever, chills and prostration. On the past 48h she developed gait instability with left deviation, associated with tremor and postural instability of left inferior limb. On physical examination the patient was febrile, with attention deficit, ataxia and proprioceptive defect of left inferior limb. A new systolic murmur was heard in all the precordium. Laboratory workup revealed a normal hemogram and renal function, but an isolated elevated C reactive protein (2,5 mg/dL). Her serological tests were negative for HIV and hepatotropic viruses. Her blood cultures revealed a methicillin-sensitive *Staphylococcus aureus*. Head CT and MRI revealed a lesion in the left post central gyrus, 12x14x28 mm, associated with peripheral vasogenic edema, consistent with brain abscess. TT and TE echocardiogram documented mitral vegetations, severe aortic stenosis, mild to moderate mitral regurgitation and mild pulmonary hypertension (PSAP 40 mmHg). A full body CT scan excluded secondary focalizations. The surgical drainage of the abscess was discussed, but given the size of the lesion, the conservative approach was favored and the patient was put on eight weeks of antibioticotherapy. On the fourth week of treatment a reassessment was made by head CT, revealing overlapping features. During hospitalization the patient's clinical situation deteriorated, progressing to non-oliguric acute renal injury. After exclusion of obstructive pathology, the following hypotheses were considered: vasculitis/glomerulonephritis in context of infective endocarditis versus interstitial nephritis induced by antibiotherapy (flucloxacilin). The patient's condition deteriorated and she was transferred to the ICU, where she was given organ support therapy. The patient passed away in the ICU.

**Discussion:** Brain microabscesses in *S. aureus* endocarditis constitute a rare presentation of this disease. Given its complex and highly variable symptoms, extra-cardiac symptoms were fundamental in the process of clinical thinking.

### **Crust (Norwegian) scabies – consequences of late diagnosis in a medical ward**

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**Introduction:** The aims of this work are to understand the pathology of Crust scabies and analyze the consequences of late diagnosis.

**Case report:** 83 years old patient living in a long-term care facility was admitted to an internal medicine ward with the diagnosis of urinary sepsis, for which he was appropriately treated and recovered without incidences. At admission he presented with chronic crust lesions in both hands and front upper thorax that on account of chronicity were not initially addressed. After the first week of treatment the lesions became more intense with white crusts that were spreading and were unresponsive to hygiene measures. At about the same time two nurses and one

nurse assistant working in the hospital ward complained of red spot itching lesions in the hands and were diagnosed with Crust Scabies. The focus of disease was traced back to the patient with the uncommon crust lesions. All patients affected were successfully treated with topical scabidical agent. The patients long-term care facility was informed and eradication posed a challenge on account of this being a highly contagious form of scabies and the need for organization of time sensitive hygiene measures in a large number of staff and residents.

**Discussion:** Earlier diagnosis of disease would enable adequate isolation management and subsequent prevention of disease spreading. Awareness on common features, transmission pathway and typical infestation of common infectious contagious agents with the purpose of making earlier diagnosis may prevent disease spreading. In this case the burden of disease in admitted patients, healthcare workers in both facilities and their families cannot be undermined. Furthermore, accessible and available treatment is a key feature in therapeutic success.

## **Fusobacterium necrophorum. Beyond Lemierre's syndrome**

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**Introduction:** *Fusobacterium necrophorum* is an anaerobic Gram-negative bacteria usually present in the oral cavity. It is the most common pathogen causing Lemierre's syndrome or septic thrombophlebitis of the internal jugular vein. Exceptionally has been described as an agent of other clinical manifestations, such as empyema or liver abscess.

**Case reports:** Case 1: A 35 years old male was admitted with left flank pain, cough with expectoration and fever during 5 days. He had been diagnosed with gastroesophageal reflux by pH monitoring and he was smoker of 10 cigarettes a day. The temperature was 38.3°C, the mouth was septic and breath sounds were decreased in the lower left hemithorax. Analyses highlighted leukocytosis (18230/mm<sup>3</sup>), thrombocytosis (601000/mm<sup>3</sup>), anemia (Hb 12.5 g/dL) and elevated acute phase reactants (ESR 95 mm/h and C-reactive protein 22.8 mg/dL). Chest x-ray showed a loculated left pleural effusion. Pleural fluid showed 3150 cells (95% PMN), with a pH of 6.7, and in the pleural fluid culture grew *Fusobacterium necrophorum* sensitive to penicillin. Ceftriaxone and clindamycin were prescribed and a chest tube was placed. Due to the absence of response to the drainage, pleural decortication was practiced, confirming later the complete pulmonary reexpansion. Case 2: A 77 years old male was admitted to the hospital because he had fever and abdominal pain in epigastrium and right upper quadrant during the last week. He had been diagnosed of hypertension, DM type 2 treated with metformin, and rectal adenocarcinoma that was treated by abdominoperineal resection, chemotherapy and radiotherapy 16 years earlier. On examination the temperature was 37.9°C, and was appreciated a 4 cm hepatomegaly. In analysis there were leukocytosis (14250/mm<sup>3</sup>), elevated liver enzymes (ALT 98 U/L, GGT 189 U/L, AP 440 U/L) and ESR (49 mm/h). Ultrasound and abdominal CT showed multiple hypodense

liver lesions suggestive of abscesses. In blood cultures grew *Fusobacterium necrophorum* sensitive to penicillin. Amoxicillin-clavulanate was prescribed intravenously for 2 weeks and then orally. Outcome was favorable with resolution of the previously described alterations.

**Discussion:** *Fusobacterium necrophorum* is a relatively common cause of visceral abscesses in animals, however in humans is an uncommon clinical presentation beyond Lemierre's syndrome. The origin of the infection is probably oropharyngeal with hematogenous spread, although it has not been demonstrated. Unlike Lemierre's syndrome, which can be fatal, atypical manifestations described in the literature typically have a favorable outcome with antimicrobial therapy and drainage of collections if necessary.

## **Community-acquired pneumonia in the very elderly description in an internal medicine ward**

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**Objectives:** Community-acquired pneumonia (CAP) is defined as acute infection in patients without recent hospitalization (<90 days) or contact with health care facilities. The incidence increases with age and is higher in male gender (MG). With high prevalence worldwide, it is the leading infectious cause of death, with high costs for health system. The authors intend to characterize the patients hospitalized with the diagnosis of CAP and compare the very elderly group (VE) with other patients (NVE).

**Methods:** Observational retrospective study based on the collection of clinical data of patients admitted in an internal medicine ward, during 12 months, with the diagnosis of PAC. In the VE are included patients with ≥80 years and in the NVE with <80 years.

**Results:** Total sample includes 91 patients, 49 of them in the VE (53.8%). Comparing the groups it appears that in VE: 1) Mean age is 89±4.6 years (vs 67.9, p<0.001); MG is more frequent (61.2 vs 40.5%, p=0.049); 36.3% are totally dependent in daily life activities (46.9 vs 23.8%, p=0.029); 2) mean number of comorbidities is 3.8±1.6 (vs 3.2±1.7, p=0.071), with higher prevalence of hypertension (37.4 vs 27.5%, p=0.382), heart failure (33 vs 18.7%, p=0.06) and chronic kidney disease (28.6 vs 12.1%, p=0.010); 3) hospital stay is longer (24.1±7.8 vs 8.9±5.9, p=0.11); 4) mean CURB65 is 2.5 (vs 1.6, p=0.067), PSI is higher (142.5±28.2 vs 105.7±29, p<0.001) and PaO<sub>2</sub>/FiO<sub>2</sub> lower (267.6±85.6 vs 304±94.1, p=0.064); 5) At admission, present lower hemoglobin (11.8 vs 13.1 g/dL, p=0.028), leukocytes (10.967 vs 13.351x10<sup>9</sup>/L, p=0.028) and C-reactive protein levels (11.9 vs 12.4 mg/dL, p=0.79) and higher creatinine (1.5 vs 1.1 mg/dL, p=0.011) and urea (76.9 vs 46.3 mg/dL, p=0.005); at discharge, maintain higher creatinine (1.1 vs 0.9 mg/dL, p=0.011) and urea (72.9 vs 47.8 mg/dL, p=0.005). Analyzing the total sample: 6) patients with higher serum lactate >2 mmol/L have longer hospital stay (14.8±10.7 vs 9.6±6.4 days, p=0.037) and higher number of comorbidities (4.5±1.5 vs 3.4±1.7, p=0.018) 7) There

is 4 deaths: 75% were in the VE; 50% are MG; mean hospital stay is of 27.5±12.7 days (vs 9.4±5.6 days, in whole sample); in 50%, serum lactate was >2 mmol/L (p=0.041).

**Conclusion:** The VE have higher degree of dependence, number of comorbidities, hospital stay, severity index and mortality. However, the results showed lower mortality then expected.

## Portugal Legionnaires' outbreak – relationship between radiological findings and hypoxemia

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**Background:** Legionnaires' disease (LD) is the pneumonia caused by *Legionella pneumophila*. It presents with classic pneumonia symptoms along with gastrointestinal manifestations. *Legionella* infection almost always produces an abnormal chest radiologic finding. Although there is no characteristic finding and all types of infiltrates have been reported, the most common pattern is a unilobar infiltrate that progresses to consolidation. Previous studies suggest that imagiological pattern does not correlate with hypoxemia or dyspnea. Despite the lush findings, LD usually has favorable outcome and good prognosis.

**Objective:** The author's aimed to study the radiological pattern present on admission, as well as their relationship with hypoxemia.

**Methods:** Patients admitted during the Portugal Legionnaires' outbreak (October 12th to December 4th), who were diagnosed with Legionnaires' disease (positive urinary *Legionella* antigen test) and that performed arterial blood gas on room air (fraction of inspired oxygen of 21%), were retrospectively analyzed. Variables: hypoxemia, radiological pattern, consolidation right upper lobe (RUL), right middle lobe, right lower lobe (RLL), left upper lobe or left lower lobe.

**Results:** The study included 123 patients; 47.2% presented hypoxemia (partial pressure of oxygen <70 mmHg). As documented in literature the unilobar pattern was the most prevalent (73.2%). The RLL was the most frequently affected (34.1%), followed by RUL (30.9%). Statistical analysis confirmed that hypoxemia is significantly associated with radiological pattern ( $\chi^2(3)=19.7$ ;  $p<0,001$ ;  $n=123$ ). Multilobar pattern is significantly associated with hypoxemia (odds ratio 8,574;  $p<0,001$ ;  $n=113$ ), when compared with unilobar pattern. Consolidation of RLL and consolidation of RUL proved to be significant predictor variables in the regression model (Wald (I)=13.368,  $p<0.001$ ; Wald (I)=7.599,  $p=0,006$ ; respectively).

**Conclusions:** Despite the diversified radiological findings of Legionnaires' disease, this study appears to demonstrate that hypoxemia is influenced by imaging pattern. Namely, consolidation of RLL and RUL can be strong predictors of hypoxemia in this disease.

## TB or not TB: that is the question

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**Introduction:** Tuberculosis (TB) is a major global health problem. The most common manifestation is pulmonary, but

the extrapulmonary form represents 20% in immunocompetent patients, 35% of which corresponds to ganglionic form.

**Case report:** 78 years old patient, without relevant medical history, with a 1 year complain of asthenia, anorexia and weight loss (22% of total body weight). From the investigation prior to current admission we point out an elevated sedimentation rate (126 mm<sup>3</sup>/h) and C reactive protein (12,5 mg/dL), anemia of chronic disease and negative HIV. CT scan of the thorax, abdomen and pelvis showed a gastric body neoplastic lesion and adenopathies (regional and mediastinal). She was submitted to gastric endoscopy that revealed a proliferative and ulcerated lesion, whose biopsy was positive for granulomatous chronic inflammatory process, necrosis and multinucleated giant cells, but negative for neoplasia. In addition she underwent eco-endoscopy in which multiple adenopathies with metastatic features were identified, leading to surgery in order to perform gastrectomy. Due to lack of intraoperative evidence of neoplasia it was only excised a lymph node, histologically compatible with suppurative granulomatous lymphadenitis, with no neoplastic tissue and negative mycobacteriologic examination. In the current admission we obtained a positive Mantoux reaction (18 mm) and IGRA (Interferon Gamma Release Assay) 1,04 IU/ml but negative features (acid-fast bacilli and polymerase chain reaction (CRP) for *Mycobacterium tuberculosis*) at bronchoscopy. The excised lymph node was revised and we found numerous Langhans multinucleated giant cells. Ganglionic TB with gastric involvement was then assumed and tuberculostatic treatment was started. After positive CRP for *Mycobacterium tuberculosis* at the excised lymph node the diagnosis was, at last, confirmed. **Discussion:** TB is a complex disease with several presentation forms and a vast list of differential diagnosis, hence the importance of considering it in the initial approach. This case shows the benefits of a holistic management in Internal Medicine, especially when facing a challenging disease like TB.

## Tuberculous tonsillitis in a patient treated with an anti-TNF agent

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**Introduction:** The increasingly use of TNF antagonists has improved the management of several immunomediated diseases. However, it has also led to a higher incidence of infections. Active tuberculosis is a known adverse effect of TNF antagonists. Patients treated with TNF antagonists have a relatively larger proportion of disseminated and extra-pulmonary tuberculosis. Occasionally, tuberculosis can be found in the head/ neck (laryngitis, tonsillitis or pharyngitis). Tuberculous tonsillitis is a relatively rare presentation of extra-pulmonary tuberculosis. It commonly presents with sore throat and cervical lymphadenopathy. This presentation, as well as abnormal tonsillar findings, such as ulcerations, masses and white patches, makes it difficult to differentiate it from other infections or even a malignant tumor.

**Case report:** The authors report the case of a 33 years old woman, with previous diagnosis of left optic neuropathy

and bilateral retinal vaso-occlusive vasculitis, associated with positive HLA-B51, suggestive of Behçet's syndrome. She was immunosuppressed with adalimumab (40 mg every 2 weeks for the last 6 months), cyclosporine (150 mg twice a day) and prednisolone (10 mg once a day). Before initiating the treatment with adalimumab, she was carefully evaluated in order to exclude latent or active tuberculosis: suggestive symptoms and signs were negative, chest x-ray was normal, Interferon-Gamma Release Assay (IGRA) and two step tuberculin skin test were both negative. She was admitted to the hospital complaining of odynophagia for the last 2 weeks, and showed a hypertrophied and ulcerated left tonsil as well as cervical adenopathy. A tonsil biopsy revealed a granulomatous inflammatory process. The Ziehl-Neelsen stained positive for acid-fast bacilli. The chest x-ray revealed a miliary pattern. As the patient had no respiratory secretions, gastric juice was collected, which came positive for Mycobacterium tuberculosis complex DNA. A diagnosis of tonsillar and pulmonary tuberculosis was established. Treatment with isoniazid, rifampicin, ethambutol and pyrazinamide was initiated with success.

**Discussion:** This case report reinforces the low threshold for tuberculosis diagnosis in unusual locations in patients treated with anti-TNF therapy.

## Seeing (is) what matters – a clinical case

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**Introduction:** Mediterranean spotted fever typically presents with fever, malaise and skin rash; however, it may exhibit uncommon symptoms like ocular involvement – there are reports of mild to moderate retinitis in a minority of patients; severe retinitis or associated uveitis are exceedingly rare. The authors present a case of exuberant retinitis as the primary manifestation of Mediterranean spotted fever.

**Case report:** 35 years old male, health resource manager, residing in Portugal. No relevant medical history, medication or substance intake. Vacation in rural area 1 week prior to symptom onset. Previously asymptomatic, develops throat pain, fever (39.5°C), malaise and headache. Treated with clarithromycin, followed by amoxicillin-clavulanate, during which he develops generalized maculo-papular rash, involving palms and soles but not the face. Antibiotic was switched to cefazolin with remission. 5 days later, he develops blurry vision and conjunctival hyperemia. Ophthalmology ER observation: right eye (RE) visual acuity 2/10, panuveitis, retinitis, intraretinal hemorrhage; left eye (LE) acuity 4/10, panuveitis, perimacular retinitis, vitritis. General ER observation: skin lesions described above; no other relevant findings. Admitted to internal medicine ward for investigation, evaluated daily by ophthalmologist. 50% loss of eyesight in 24 hours, (RE 1/10, LE 2/10), with worsening of retinitis lesions – according to neuro-ophthalmology, nonspecific pattern compatible with either neoplastic, autoimmune (Behçet's) or infectious disease (bacterial, viral or fungal). Due to predictable progression to amaurosis, a prednisone pulse was administered and empirical treatment was started with doxycycline, acyclovir

and fluconazole. Laboratory findings: negative serologies for Toxoplasma, Treponema, Cytomegalovirus, Epstein-Barr, Human Immunodeficiency virus, HBs antigen, anti-HBc and anti-HCV antibodies. Serology for Rickettsia spp strongly positive (1/512 titer), Coxiella IgM positive (high Rickettsia titer cross-reaction). Patient was diagnosed with Rickettsial retinitis. Significant recovery of visual acuity after 3 weeks of doxycycline and prednisolone (RE and LE 10/10, 8 months later).

**Discussion:** The importance of a careful anamnesis cannot be overstated, and must include detailed epidemiological background. This case represents a very rare presentation of Mediterranean spotted fever, accurately diagnosed thanks in part to a proper patient interview.

## A curious case of fever of unknown origin

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**Introduction:** Fever of unknown origin (FUO) in adults is defined as persistent high body temperature that lasts for more than 3 weeks with no obvious source despite appropriate investigation. The 4 subgroups of the diagnosis of FUO are infections, malignancies, autoimmune diseases and miscellaneous. A thorough history, physical examination and standard laboratory testing remain the basis of the evaluation of the patient with FUO. Newer diagnostic modalities including updated serology, viral cultures computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scan have important role in the assessment FUO.

**Case report:** The authors describe a clinical case of a 30 years old otherwise healthy female, suffering of low back pain for the past month, high grade fever, continuously taking painkillers with no effect. In April 2015 the patient went to an Internal medicine appointment with the same complaints (low back pain, irradiating to the right leg and intermittent fever mostly at night time) and was admitted to the inpatient department for further investigation. Once examining the patient, a painful lump on lower back was detected and a soft tissue ultrasound and a CT scan of the vertebral column was requested. The CT scan revealed lumbar fat densification at the level of L5 vertebra, 37x20 mm with no muscular involvement. For a better understanding of such pathological structure, the patient underwent a lumbar MRI showing thickening of the soft subcutaneous tissues extending from L2-S1 in the midline, extending from a superficial level to subcutaneous tissue, suggesting a generalized infectious subcutaneous process with multiple, small-sized abscesses in its core. The patient was tested for microbiological and autoimmune diseases which were all negative. During the hospital stay the patient started levofloxacin with substantial improvement of her pain as well as temperature control. She has now completed 2 months of antibiotic, remaining asymptomatic since then.

**Discussion:** It is important to realize FUO may represent uncommon manifestation of common disease such as low back pain. This case draws our attention to the importance of



investigation of persistent symptoms such as fever that appear on a daily basis in our practice. No port of entry was identified. Low back pain can be caused by a harmless pathological process, if not properly diagnosed and left untreated it might constitute a life-threatening condition upon dissemination.

## Relying on intuition

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**Introduction:** Visceral leishmaniasis, also known as kala-azar or "black fever", is a non-contagious zoonosis caused by the protozoan *Leishmania* and transmitted by the mosquitoes *Lutzomyia longipalpis* and *Phlebotomus*. Although not very frequent in Europe, one should be aware of this disease because of its systemic repercussion and high mortality rate when untreated.

**Case report:** We present a case report of a girl admitted with fever, pancytopenia and splenomegaly, who had been to a summer camp, close to a river, two years earlier, complaining of asthenia since then. Our aim is to show a case of illness diagnosed in a less common way, inferred by late immunity and response to therapy. The exhaustive study included blood analysis, with several viral and bacterial serologies, blood and urine cultures, full-body CT scan and myelogram. The response to the therapy instituted, liposomal amphotericin B, was evaluated by fever resolution and improvement of pancytopenia and splenomegaly. During the hospital stay, the patient maintained sustained fever, that yielded only temporarily to antipyretics, and pancytopenia worsening, requiring blood transfusion. It was first instituted antibiotic therapy with clarithromycin, posteriorly altered to piperacillin-tazobactam and metronidazole, without clinical and analytical improvement. Given the past history of stay in a holiday camp close to a river, there was a high suspicion of leishmaniasis. The blood analysis revealed iron metabolism in favor of an inflammatory/chronic disease, the serologies were all negative except IgG anti-*Leishmania*, and the myelogram did not show *Leishmania* amastigotes. We initiated therapy with liposomal amphotericin B, with resultant sustained apyrexia, from the fourth day on, and favorable evolution of pancytopenia and splenomegaly.

**Discussion:** This case report shows an indirect way of diagnosing visceral leishmaniasis, through late immunity and therapeutic response. The most common is to find the parasite in spinal examination, which was not possible in this patient. Despite negative or inconclusive analytic results, one should always rely on intuition and act accordingly.

## What antibiograms taught me last year?

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**Introduction:** In the last couple of years we watched a rise in antibiotic resistance with repercussion in patients' evolution.

In an attempt to establish a probability score between culture results and patient evolution the authors analyzed the results corresponding to the year of 2014.

**Objective:** Create a correlation of probability that allows us to anticipate the evolution of an infection according to antibiotic resistance of the isolated microorganism.

**Methods:** 1) Analyze and characterize the antibiogram of patients admitted in an internal medicine ward with positive cultures; 2) Location of the acquisition of the infection (hospital vs community); 3) Patient evolution. Pearson correlation was used with all data and significant data was worked up with a linear regression.

**Results:** In community acquired infection the greater the antibiotic resistance the greater the mortality. It was more evident with cefotaxime, levofloxacin and oxaciline. Although related with an increased mortality it had no relation with the duration of hospital stay. In hospital acquired infections the hospital stay was smaller in elderly patients. The mortality rate was significantly higher in patients with longer hospital stays (each day represented an increase of 7%) and in those with amoxicillin and clavulanic acid.

**Conclusions:** The relation between hospitalization time and mortality rate suggests that quick antibiogram results and prompt institution of antibiotic has a positive influence in patient prognosis. The sensibility of different antibiotic and resistances doesn't influence the prognosis although amoxicillin and clavulanic acid, levofloxacin and oxacilin in particular are a sign of bad prognosis (amoxicillin and clavulanic acid is the most used antibiotic in the infirmary where this study was made).

## Comparison of HBsAg seroprevalence between two districts and two eras in Istanbul

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**Objective:** Hepatitis B virus has been a major pathogen in the etiology of chronic hepatitis. The prevalence of hepatitis B is higher in developing countries in comparison to the developed countries. Prior studies held earlier in different regions of our country have revealed a prevalence of HBsAg about 3-12%. This ratio may change according to the study group chosen. In this study, we wanted to evaluate the further results of routine newborn vaccination hepatitis B virus after 1998. Besides we wanted to compare a socioeconomically higher district with a relatively high immunization rate with a poorer one with low rates in the same city.

**Methods:** This study was carried out retrospectively in 2 different regions and 3 centers of Istanbul between years of 1994-2002 and 2003-2009. One of the districts was more developed compared to the other one with lower internal migration from rural areas. HBsAg positivity of out-patient clinic patients with various problems was evaluated. HBsAg was studied with ELISA. In 1994-2002 years, 3972 women and 2349 men (total 5721 subjects) were included in the study. Between 2003 and 2009, 1751 female, 12207 male (total 13958 subjects) were included. All age groups, ranging from 0-80 years were included as a part of study.

**Results:** At the end of the study (years of 1994-2002) 282 of the subjects (4.9%) (2.5% male, 2.4% female) were found to be positive for HBsAg. Between 2003 and 2009, we also analyzed the difference between, two socioeconomically different areas. While we found 4.3% (women 0.4%, men 3.8%) HBsAg seroprevalence in more developed region, we found 17% HBsAg seroprevalence in the internal migration area. In detailed examination, while male ratio was very high (11.2%), female ratio was found to be at a reasonable level (5.7%). All of those men were internal immigrants who weren't vaccinated against hepatitis B.

**Conclusions:** High HBsAg rate of people without hepatitis B vaccination shows the importance of vaccination. In regions with regular vaccination programme, HBsAg rate decreases gradually. Newer immunization programmes held in our country for the newborns include also hepatitis B vaccination. Thus we think HBsAg prevalence will significantly fall in the following years and newer studies are showing promising results.

### It's not only about opportunistic infections

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**Introduction:** Opportunistic infections in immunocompromised patients are a major challenge in every clinical setting. Occasionally, infections may be multifactorial, commonly including endemic diseases as well.

**Case report:** A 79 years old woman with a recent diagnosis of myelodysplastic syndrome, low-grade B-non-Hodgkin lymphoma and autoimmune hemolytic anemia, presented due to prolonged fever. Her standard medical treatment included 16 mg of methylprednisolone and cyclosporine, and she had previously received a weekly regimen of moxifloxacin prior to admission, without improvement. Physical examination and imaging studies revealed a severe lower respiratory tract infection, warranting a bronchoscopy. Cytomegalovirus (CMV) copies in the bronchoalveolar fluid were 4.375/ml, so the diagnosis of CMV pneumonia was established. However, during investigation, a Wright reaction proved also positive, with a titer of 1:10240. Even though the patient consumed strictly pasteurized products and the only transmission route could have been transfusion, the possibility of acute brucellosis could not be excluded. Apart from ganciclovir, a 6-week regimen of doxycycline and gentamicin was initiated, with a subsequent decrease in the titer of Wright reaction. The patient remained afebrile on the fifth day of treatment. Notably, *Brucella melitensis* was not cultured in blood and marrow cultures, but Wright reaction turned negative upon the end of treatment.

**Discussion:** The annual incidence of Brucellosis in women aged over 65 years in Greece is estimated to 2.05 per 100.000 people in Greece (2005-2011). Rarely, the disease has been described in patients with hematological or other malignancies, either concomitantly with the diagnosis of the malignancy or in the setting of febrile neutropenia. Concerning the hematological malignancies, a crucial predisposing factor is the decrease of T- cell immunity, due to the disease itself or to its treatment. In patients with immunosuppression and/or pancytopenia,

opportunistic infections are the usual, but not the unique cause of prolonged fever. In endemic countries, investigation for Brucellosis should not be omitted.

### Risk factors for recurrent *Clostridium difficile* infection

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**Objectives:** *Clostridium difficile* infection (CDI) represents 20-30% of cases of antibiotic-associated diarrhea and the most frequent cause of infectious diarrhea in healthcare institutions. The aim of this study is to analyze the clinical features of patients with CDI and to find which risk factors are associated with its recurrence.

**Methods:** 105 cases of CDI were analyzed in Hospital Universitario de Canarias from January 2011 to March 2014. Major epidemiological, clinical and laboratory data were collected. We analyzed the differences among patients with and without recurrence.

**Results:** The mean age was 61.6 years. 82.6% had received antibiotics and 47,6% had a recently admission. At the moment of diagnosis, 45.7% had fever, 25.7% had hypotension, 61.8% presented leukocytosis and 26.5% showed increased creatinine. CRP was >60 mg/L in 59.8% and 26.5% had elevated creatinine levels. Pseudomembranous colitis was the clinical presentation in 37.3%. Recurrences occurred in 9.5% of cases and was associated with increased levels of creatinine and CRP ( $p=0.036$  and  $p=0.034$ , respectively). Moreover, hypotension was more frequent in patients with recurrence ( $p=0.001$ ). Pseudomembranous colitis patients had recurrence more frequently ( $p=0.01$ ). The onset of recurrence implied an increase in the length of stay (23 to 99.5 days;  $p=0.001$ ).

**Conclusions:** CDI had recurrence in 9% of cases and involved delay in hospital discharge. The risk factors for its appearance were acute renal injury, arterial hypotension and elevated CRP levels. Pseudomembranous colitis was also associated with a high risk of recurrence.

### Differential diagnosis of low back pain: brucellosis

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**Introduction:** Brucellosis is an infectious disease caused by bacteria of the genus *Brucella*, which can be transmitted to humans through direct contact with secretions from infected animals and by eating dairy products unpasteurized. The clinical manifestations are nonspecific, with a high prevalence of osteoarticular complaints.

**Case report:** An 87 years old patient, female gender, previously autonomous, with prior contact with sheep for several years, with known pathological history of degenerative osteoarticular pathology, hypertension, normocytic and normochromic anemia. Usually treated with indapamide, omeprazole, vinpocetine, betahistine and ibuprofen in SOS. She was admitted to the Orthopedics after falling, resulting in sacroccocygeal trauma, with intense back pain radiating to the right leg and with inability to walk. Internal Medicine collaboration was requested on suspicion of spondylodiscitis due to Brucella. The patient was hemodynamically stable, without fever and with a normal physical examination. Analytically: normochromic and normocytic anemia with 11.0 g/dL of hemoglobin; without leukocytosis or neutrophilia; renal function without change; C-reactive protein 2.02 g/dL; sedimentation rate of 110 mm/h, Rose Bengal positive, Wright reaction 1/320, blood culture coccobacilli Gram negative, suggestive of Brucella which however did not grow in culture. MRI of the lumbar spine: changes of the vertebral bodies from L1 to L4 suggestive of granulomatous spondylodiscitis, small abscess of the psoas muscle on the right in L2 plan, degenerative changes of L3-L4 and L5-S1 and a probable hemangioma in L4. The patient underwent directed antibiotic therapy, with gradual clinical improvement and, with negative blood cultures at discharge. She also presented with intense pain with need for fentanyl in high doses.

**Discussion:** Given the high prevalence of secondary osteoarticular changes to brucellosis, it must be considered as a differential diagnosis in cases of arthralgia.

## **Epstein-Barr virus. An old enemy but new diagnostic guidelines and finally effective strategies using microRNAs**

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EBV remains undoubtedly the public enemy number one in terms of multi-pathogenic potential. But beyond the clinical and diagnostic aspects well-known in infectious pathology, there is recently a different approach more focused on clinical manifestations according to the immune conflict related to the virus and likely to trigger disorders such as autoimmune diseases or lymphoma, to mention only the most frequent and better identified. A more dynamic understanding of the kinetics of antibodies as part of the good old immunofluorescence, an accurate measurement of viral load and judicious identification of interactions with the MHC will identify with precision the etiopathogenic impact of EBV in multiple chronic diseases. Furthermore the introduction to a therapeutic aim of microRNAs via nanobiotechnologies and according to the principles of hormesis and molecular dynamic *ab initio* represents a real revolution in the context of the long term regulation of this virus, which is so involved in all kinds of human pathology. The description of some clinical cases will help to illustrate this novel approach both diagnostic and therapeutic, only enable at present time to loose many patients from chronic pathological conditions, which may sometimes evolve dramatically.

## **Clinical implications of changing bacterial flora of infected diabetic foot ulcers – 12 years experience in a large referral center**

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**Objectives:** Appropriate empirical antimicrobial treatment for infected diabetic foot ulcer is challenging due to emerging bacterial resistance. This clinical problem is specifically more challenging when choosing empirical oral antibiotic treatment for ambulatory patients, as oral antimicrobial agents are suspected to carry higher resistance profiles. Whether this resistance is due to changed bacterial flora is not known. This study aims to determine whether the species and antibiotic sensitivities of bacterial pathogens currently associated with diabetic foot infections has changed in the last decade.

**Methods:** Aerobic and anaerobic bacteria cultures were obtained from 95 type 2 diabetes mellitus outpatients with infected foot ulcers of moderate severity. The type, relative proportions and antibiotic susceptibility of isolated bacteria were compared to our previous findings in 2000.

**Results:** Gram negative bacteria were predominant consisting of 51.4% of all isolations, followed by Gram positive bacteria (38%) and anaerobic bacteria (9.8%). 58 patients (61%) had multi bacterial infection. The most common pathogen of all isolations was *Staphylococcus aureus* – 32 (14.8%), followed by *Enterococcus faecalis* – 24 (11.2%), and *Pseudomonas aeruginosa* – 20 (9.3%). 40.6% of all *Staphylococcus aureus* were methicillin resistant (MRSA). 38.4% of all Gram negative bacteria were resistant to ciprofloxacin, and 62.6% were resistant to ampicillin-clavulanic acid. The prevalence of Gram negative bacteria was significantly increased compared to 2000 data: 51.4% and 34.6% respectively ( $p < 0.001$ ). In addition, resistance of *Staphylococcus aureus* and *Pseudomonas aeruginosa* to commonly prescribed antibiotics namely methicillin and ciprofloxacin was increased significantly: 40.6% staphylococcal resistance to methicillin versus 22.9% and 52% resistance of *Pseudomonas* to ciprofloxacin versus 23.2% in 2013 and 2006 respectively.

**Conclusions:** The bacterial flora underlying diabetic foot infections has considerably changed in the last decade shifting towards ciprofloxacin and ampicillin-clavulanate resistant Gram negative bacteria and MRSA. These data should be taken into consideration when a decision regarding empirical antibiotic treatment is made in these patients.

## **Extrapulmonary tuberculosis. A challenging clinical case**

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**Introduction:** The differential diagnosis of lymphadenopathy still represents a medical challenge for the multitude of associated clinical conditions, in most cases with very similar presentation and high morbidity and mortality, so it is primordial its prompt and accurate diagnosis.

**Case report:** 43 years old female complained of persistent abdominal pain for 6 months. Abdominal ultrasound showed multiple mesenteric and aortic lymphadenopathies and a gestational sac consistent with 6 weeks pregnancy. The laboratory tests showed a microcytic anemia (hemoglobin 10.6 g/dL), raised erythrocyte sedimentation rate (92 mm<sup>3</sup>/h), negative culture tests. The histology of the excised abdominal ganglion revealed a non-necrotizing granulomatous lymphadenitis with giant multinucleated Langhans cells. The remaining evaluation, restricted by pregnancy, was inconclusive, including normal Interferon Gamma Release Assay and angiotensin converting enzyme, bone marrow smear showing only a reactive pattern and magnetic resonance imaging that ruled out pulmonary and other lymph node involvement. The patient was later diagnosed with embryonic malformation and conducted a medical termination of pregnancy. After this, clinical reassessment showed a new supraclavicular mass, mild fever and night sweats. She was subjected to a supraclavicular lymph node biopsy whose histology revealed necrotizing granulomatous lymphadenitis with positive acid-alcohol resistant bacillus (AARB) concentration and positive culture for *Mycobacterium tuberculosis*. Chest computerized tomography revealed multiple splenic and pulmonary nodes. The bronchoalveolar lavage fluid showed no evidence of AARB. The diagnosis of disseminated ganglionic tuberculosis was made and the specific therapy was promptly initiated with clinical remission of symptoms.

**Discussion:** Though rare in most western countries, tuberculosis is still a frequent and important diagnosis to be considered in our country when approaching a patient with lymphadenopathy. Extrapulmonary tuberculosis represents 20% of all cases of tuberculosis worldwide in immunocompetent patients and about 50% of immunocompromised patients, 35% of which representing ganglionic tuberculosis. It often mimics several other diseases that appear with lymphadenopathy and since it is a potentially curable disease, its diagnosis is crucial.

### Acute necrotizing retinitis: a retrospective analysis at University hospital in Madrid

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**Objectives:** Necrotizing retinitis is a rare syndrome. It's classic form, acute retinal necrosis (ARN) and progressive outer retinal necrosis (PORN) that affects immunocompetent and immunocompromised patients respectively. The aim of this study was to describe the cases of necrotizing retinitis diagnosed at our institution.

**Material and methods:** Retrospective review of the period 2006-2013 from medical records in patients diagnosed with ARN and PORN. We analyzed demographic, clinical presentation, microbiological diagnosis, treatment and patient outcomes.

**Results:** 7 patients, 5 males were detected. Average age 51.2 years. 6 were diagnosed of ARN and 1 of PORN in a patient with AIDS in which also retinitis was the presentation HIV infection. Incidence 3.5 cases per 1 million population/year. The clinical

presentation was in all of them the loss of visual acuity (VA). 2 were attributed to Varicella zoster virus; 1 of them existed in the recent history of Varicella with confirmatory serology and the other was determined by PCR of aqueous humor. In 2 other cases, the serology was positive for VHS. In 3 cases, no etiologic studies were performed. 5 were treated with acyclovir iv by 14 days, followed by oral acyclovir for 6 weeks. The evolution of the fundus of the eye was favorable in all of them except 1 that presented a week inflammatory lesions, so acyclovir was replaced by foscarnet for 2 weeks thereafter favorable evolution. 2 were treated from the beginning with foscarnet (1 HIV patient). HIV-infected patients started antiretroviral therapy (atrilpa) within 2 weeks of treatment with foscarnet, achieving undetectable HIV at 4 weeks and continued to receive, orally, fancyclovir and prograneclovir up the CD4 count was >100, which occurred at 12 months. All presented retinal detachment (RD). Only 2 received very early treatment, had good evolution and didn't develop RD.

**Conclusions:** Although the ARN and PORN have a low incidence, severity of both entities requires a high index of suspicion and early treatment to improve visual prognosis. The appearance of RD worse prognosis. HIV serology and PCR study of aqueous humor should be included in all patients.

### Prevalence of dyslipidemia in HIV-infected patients in La Mancha Centro Hospital

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**Objectives:** Studies have consistently shown high prevalence of dyslipidemia among patients infected with Human immunodeficiency virus (HIV); with and without antiretroviral treatment (ART). There has been a cardiovascular increased morbidity and mortality in these patients. The aim of this study to estimate the prevalence of dyslipidemia in HIV-infected patients in our hospital at diagnostic time.

**Material and methods:** We conducted a descriptive study of 96 patients followed at internal medicine infected with HIV. Laboratory parameters included: total cholesterol, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), tryglicerides (TG), at the initial visit. The statistical analysis was realized by the package SPSS 18.

**Results:** 96 patients were included; mean age 39.9 years; 77% male and 23% female. The mean total cholesterol level was 173 mg/dL, HDL-C 47.5 mg/dL, LDL-C 98.9 mg/dL and TG 154.7 mg/dL. Analyzed by sex: male – mean total cholesterol level 171.9 mg/dL, LDL-C 99.4 mg/dL, HDL-C 44.9 mg/dL, TG 137.8 mg/dL. Female – mean total cholesterol 180.5 mg/dL, LDL-C 97.5 mg/dL, HDL-C 57.3 mg/dL, TG 108.5 mg/dL. According to NECP guidelines, we defined hypercholesterolemia, as levels above 200 mg/dL cholesterol, and hypertriglyceridemia as TG levels greater than 150 mg/dL. Prevalence of hypercholesterolemia in these patients was 28.1%, hypertriglyceridemia – 36.5% and 14.6% for mixed dyslipidemia. Analyzing this data separately in groups of men and women, the results were: prevalence in men – hypercholesterolemia 28.4%, hypertriglyceridemia 23%, mixed dyslipidemia 14.9%. Prevalence in women – total cholesterol 27.3%, hypertriglyceridemia 31.8% and mixed dyslipidemia 13.6%.

**Conclusions:** Mean age in HIV-infected patient at baseline was 39.9 years. Prevalence of dyslipidemia in HIV-infected patients is high: hypercholesterolemia 28.1% and hypertriglyceridemia 36.5%, these results are consistent with data published, reported high prevalence of dyslipidemia in HIV-infected patients without ART.

## Cat-scratch disease in a Portuguese hospital

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**Objectives:** The infection with *Bartonella henselae* (BH) is usually a benign self-limited infection which in some cases can progress to systemic infection. The cat is considered the main reservoir for BH, especially those less than 6 months old that infect humans through bite or scratch. In order to better understand BH infection, the authors carried out a review of all serology for *Bartonella henselae* held at St. Andrew's Hospital (Leiria), between 01/01/2009 and 31/12/2013.

**Methods:** Retrospective review of patient clinical records with positive serology *Bartonella henselae*. Defined as a case: a single titer less than 1/320 and/or IgM +, seroconversion or significant increase of titres, clear evidence of scratch or cat bite and/or contact with cat and exclusion of other diseases. The following data were collected and analyzed: sex, age, epidemiological context, signs and symptoms, laboratory data and antibiotic treatment.

**Results:** During the studied period, 31 cases were detected (16 female and 15 male). The prevalence of BH was higher in people under 15 years old. There was a seasonal incidence, with peaks in October and November. Febrile illness (83.8%) was the most prevalent form of presentation, followed by enlargement of lymph nodes (16.2%). The most reported symptoms were fever and asthenia. On physical examination axillary lymphadenopathy was the most common finding. With regard to laboratory tests highlight the increased erythrocyte sedimentation rate (ESR), leukocytosis and positive PCR. After treatment all patients were discharged from the query or improved admission.

**Conclusions:** In general the analysis of the sample is overlapping the majority of published studies. There was predominance in young people, regardless of gender. The febrile illness was the most common form of presentation and the lymph nodes most affected were in descending order, axillary, cervical, submandibular and inguinal. There were 3 cases (9.6%) with liver involvement, which meets the bibliography with regard to atypical presentations of the disease. In all cases the BH infection had a benign clinical course without evidence of sequelae.

## Abdominal pain and fever: primary peritonitis by *Streptococcus pyogenes*

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**Introduction:** To describe a case of primary peritonitis by *Streptococcus pyogenes* complicated by septic shock. Primary

or spontaneous peritonitis is called to the one in which obvious cause was not objective, is monomicrobial etiology and its finding in people without comorbidities is very rare. Primary peritonitis by *S. pyogenes* is more common in young women and can evolve to streptococcal toxic shock (STSS) with secondary multiorgan failure syndrome.

**Case report:** A 38 years old woman, sexually active, was admitted by abdominal pain of sudden onset and fever since 12 hours ago. Physical examination showed hypotension (80/40 mmHg), 150 bpm, 38°C, saturation O<sub>2</sub> 98%, and signs of peritoneal irritation. Laboratory blood test presented: procalcitonin 5,66 ng/ml, leukocytosis (23400/L), coagulopathy and metabolic acidosis, with negative pregnancy test. In ultrasound and abdominal CT scan showed liquid free peritoneal. Differential diagnosis was made with patient clinic, previous history and laboratory test, between secondary peritonitis, endometriosis and pelvic inflammatory disease. Urgent abdominal laparotomy was performed with findings of diffuse purulent peritonitis, plastron in pelvis minor with dilation and hyperemia of fallopian tubes. Prophylactic appendectomy and bilateral salpingectomy were performed. She admitted to intensive care unit with a diagnosis of septic shock, she required vasoactive drugs to maintain blood pressure and urine output. Empirical antibiotic therapy was started with piperacillin-tazobactam and metronidazole. *Streptococcus pyogenes* was isolated on liquid abdominal culture and antibiotic was changed by penicillin G and clindamycin, with good clinical evolution and leukocytosis and acute phase reactants decreased. Final diagnosis: primary peritonitis complicated by *Streptococcus pyogenes*.

**Discussion:** Possibility of primary peritonitis by *S. pyogenes* should consider to young patients, especially women, without previous pathology, with acute peritonitis without apparent cause and image tests without relevant findings. It is early start with antibiotic treatment of wide spectrum is very important due to aggressive evolution (septic shock or SSTS) until cultures results. In case of *S. pyogenes* infection, therapy of choice consists of clindamycin and penicillin, reserving laparotomy for cases with unfavorable evolution.

## Encrusting cystitis by *Corynebacterium urealyticum* infection. A case report

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**Introduction:** Encrusting cystitis is defined as a rare entity characterized by inflammation ulcerated bladder with calcium deposits in its wall, precipitated by a number of predisposing factors: previous bladder damage, urinary tract infection by specific germs (*Corynebacterium urealyticum*), bladder alkaline pH and immunosuppression. We report a case of encrusting cystitis by *Corynebacterium urealyticum* infection.

**Case report:** A 71 years old man with history of hypertension, nephrolithiasis, adenocarcinoma of prostate (treated by radical prostatectomy and external radiotherapy) with tumor recurrence (bone and lung metastasis). Carrier of artificial urinary sphincter, and repeated urinary infections. He was

admitted because of voiding syndrome, malaise and fever. No abnormality was observed by routine physical examination. Results of first laboratory test showed: creatinine 3.4 mg/dL, hemoglobin 7.4 g/dL, leukocytosis, alkaline urine with pH 7.2 and pyuria. Differential diagnosis was made with patient clinic, previous history and laboratory test between tumor progression, new tumor, urinary infection and obstructive syndrome by nephrolithiasis. Renal ultrasound showed moderate bilateral hydronephrosis. Cystoscopy showed bladder inflammation and calcifications embedded in bladder wall. Body-CT showed bilateral hydronephrosis persistence and multiple bladder calcifications. Bone gammagraphy showed no tumor progression. Pathological anatomy results described partially calcified fibrotic and necrotic material. Final diagnostic was encrusting cystitis, given the findings of urine alkaline pH, encrusting bladder calcifications and isolation of *Corynebacterium urealyticum* in urine culture. Vancomycin was started (adjusted to renal function) for 14 days. Surgery was performed to remove calcified plaques with good clinical evolution and disease resolution.

**Discussion:** Infection urinary tract by *C. urealyticum* (urinary opportunistic pathogen) is an infection under-diagnosed due to need a cultivation of long duration for its isolation, favored by urinary manipulation and own features of patient. It should be considered in patient with obstructive uropathy in presence of alkaline urine, crystals of struvite or sterile pyuria. Its treatment of choice is glycopeptide due to its multidrug resistance, being important for the prevention of complications such as encrusting cystitis or pyelitis secondary to its urease-producing capacity.

### Posaconazole as antifungal therapy in osteomyelitis and recurrent septic arthritis by *Candida tropicalis*

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**Introduction:** *Candida* is an uncommon cause of septic arthritis in relation to states of immunosuppression. We report a case of recurrent septic arthritis and osteomyelitis of knee by *Candida tropicalis*, importance of presumption diagnosis and an adequate therapy with an early onset and long duration.

**Case report:** A 78 years old man with history of diffuse B large cell lymphoma, colorectal cancer, carrier of colostomy. He was admitted to complicated Baker's cyst with *Candida tropicalis* isolation, so he received treatment with caspofungin, continued with fluconazole to complete 6 weeks of treatment. A month later, he returned for fever up, and sign of left knee arthritis, arthrocentesis showed results of purulent fluid, 178000 leukocytes and 93% of polymorphonuclear, carrying out urgent surgical cleaning and starting treatment with ceftazidime and vancomycin. *Staphylococcus epidermidis* was isolated in cultures. In arthrocentesis control, worsening was observed and *C. tropicalis* was isolated so adding to caspofungin, surgical cleaning performed. Study of sensitivity of *C. tropicalis* showed sensitive to echinocandins and azoles (CMI to fluconazole of 4 mg/L), continuing with voriconazole to the discharged. In

review we evidenced a marked decrease of reactants in acute phase and transaminase elevation, suspecting toxic hepatitis by voriconazole and suspending treatment (he completed 4 weeks only). Days after, he had recurrence of symptoms, arthrocentesis showed isolation of *C. tropicalis*, liposomal amphotericin B and 5-fluocytosine treatment was started. MRI of articulation showed bone erosions and signs of arthritis, it was compatible with osteomyelitis. Secondary to comorbidity, bone involvement and chronicity of process, conservative treatment with a long broad-spectrum antifungal like posaconazole for 8 weeks, with good clinical evolution and without new episodes of septic arthritis. Final diagnosis: Recurrent septic arthritis and osteomyelitis by *Candida tropicalis*.

**Discussion:** *Candida* septic arthritis should be considered in context of monoarthritis knee in patients with hematologic malignancy and risk factors. The diagnosis is established by culture of the infected site. Adequate drainage is essential for the treatment associated with anti-fungals for 6 weeks. In this case, posaconazole is used as a therapeutic alternative with good results in treatment of recurrent osteomyelitis *Candida* and with poor response to other antifungal regimens.

### *Corynebacterium striatum* prosthetic aortic valve endocarditis – a case report and literature review

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**Introduction:** *Corynebacterium* species are Gram-positive bacilli that are commensal organisms of skin and mucosal membranes; when isolated in cultures, are generally assumed as a contaminant. Still, it's been proven to cause various infections, among them, infectious endocarditis (IE). Our aim is to report a clinical case, followed by a review of the literature.

**Case report:** 85 years old woman, whose medical history included valvular heart disease (aortic valve replacement with a biologic prosthesis), hypertension, obstructive sleep apnea and chronic renal disease, was admitted with fever. She had an unremarkable examination, with an already known systolic murmur and no IE stigmata. C-reactive protein was elevated and later, *Corynebacterium striatum* was isolated in 6 separate sets of blood cultures, taken at 3 different times. Transesophageal echocardiogram revealed an image suggesting vegetation of the prosthetic aortic valve with a periprosthetic abscess and vancomycin, gentamicin and rifampin were instituted. Cardiovascular surgery was advised against due to the patient's comorbidities. Subsequent blood cultures were negative. Following 16 days of medical treatment, she developed a myocardial infarction with a third-degree atrioventricular block and echocardiogram revealed an abscess fistula to the left ventricle, with its severely function compromised. Her condition rapidly deteriorated and died one day later.

**Discussion:** The literature review revealed 15 reported cases of IE due to *C. striatum* in native valves and 3 in prosthetic valves in the last 25 years. Only 2 of those in aortic position and 1 case were successfully treated with antibiotics alone. In our case, the surgery was not performed, so empirical therapy to IE in a

prosthetic valve was chosen. However, combined medical and surgical therapy may help the outcome. Our case highlights the importance of early recognition, antibiotics selection and optimal surgical timing in a extensively unknown but very aggressive IE pathogen.

**Conclusions:** *C. striatum* is a rare cause of valvular damage, posing as a diagnostic challenge. If repeated blood cultures are positive, they shouldn't be overlooked and a high suspicion for IE should be considered especially in high-risk patients.

## A case of acute enteritis due to typhoid fever in a Portuguese hospital

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**Introduction:** Typhoid fever is a severe systemic illness characterized by fever and abdominal pain. *Salmonella enterica* serotype Typhi is the organism responsible. This condition affects an elevated number of people living in impoverished areas and is acquired through the ingestion of contaminated water and food. In developed countries the disease is usually "imported". We intend to report an "imported" case of typhoid fever with a problematic course. Information on the clinical course and management of the patient with typhoid fever seen at Hospital de São José in April 2015 was extracted from his case record.

**Case report:** A 37 years old Indian man was admitted to our ward with a 5-day history of sustained fever accompanied by diarrhea on the last day. On examination, the patient was febrile, tachycardic, normotensive and eupneic, with diffuse abdominal tenderness and a 3-cm hepatomegaly. Hemoglobin was 13.0 g/dL, WBC count  $4.8 \times 10^9/L$  with 80.8% neutrophils and 12.1% lymphocytes, platelet count  $110 \times 10^9/L$ . Abnormal biochemical values were: AST 135 U/L, ALT 57 U/L, GGT 88 U/L, LDH 1024 U/L, sodium 126 mEq/L, potassium, 3.1 mEq/L, CRP 210.9 mg/L and CK 1795 U/L. Blood culture grew *Salmonella typhi*. Treatment with intravenous ciprofloxacin (800 mg in 2 divided doses) was initiated but switched to intravenous ampicillin (12 g in 6 divided doses), according to antibiotic sensitivity testing. He maintained high fever and developed severe haematochezia. Concurrently, there was a drop in hemoglobin, WBC count and platelets levels, with a rise in liver enzyme levels. Colonoscopy and biopsies revealed ileal enteritis. His clinical condition abruptly deteriorated with severe diffuse abdominal pain accompanied with involuntary abdominal wall rigidity. Peritonitis secondary to intestinal perforation was confirmed by abdominal CT. He underwent small bowel resection with anastomosis. Twenty four hours later, he underwent additional resection with ileostomy due to anastomotic dehiscence. He became afebrile after a 14-day course of piperacillin-tazobactam and was discharged on day 32.

**Discussion:** Typhoid fever should be considered a differential diagnosis in patients from endemic areas presenting with fever and abdominal pain. Empirical antibiotic therapy should be chosen according local resistance patterns. Therapy should be instituted as soon as possible to prevent high-mortality complications of typhoid fever, such as intestinal perforation.

## Tuberculosis, a re-emerging disease in internal medicine departments

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**Objective:** Tuberculosis is still a relevant disease owing to its resurgence in some special populations.

**Methods:** A collaborative retrospective study from 2006 to 2013 aiming at analyzing the clinical features of tuberculosis in patients admitted to the internal medicine departments in Tunisia and Spain was conducted.

**Results:** A total of 48 patients were included. Mean age was 45 years old and sex ratio F/M=2. 21% of the patients were under long-term corticosteroid and/or immunosuppressants for systemic diseases. A concomitant systemic disease was found in 19% of the patients. Fever was the most common clinical sign; it was present in 85.3% of patients and was followed by sweats (54.1% patients), weight loss (43% patients) and general malaise in 39%. Long term fever was described in 78.3% of patients. The disease was revealed by polylymphadenopathies in 26.8% of cases, granulomatous anterior uveitis in 6.3%, panuveitis in 3.2%, cytopenias in 11 % and erythema nodosum in 6.3% of cases. Mantoux test was positive in 54% of cases. Koch's bacillus was found in 23.2% and 24.2% in sputum and urine, respectively. The diagnosis was histologically confirmed by the presence of caseous necrosis granuloma in lymph node biopsy in 15 cases, biopsy of the lacrimal gland in 2 case, biopsy of the bladder in one case, iris biopsy in one case and a colonic biopsy in 1 other case. Extra pulmonary tuberculosis was identified in 78.4% of cases and pulmonary tuberculosis in 21.6% of cases. Adverse effects of anti-TB drugs were found in 24% with an average delay of symptoms of 31 days.

**Conclusions:** Tuberculosis in internal medicine is characterized by the prevalence of extra-pulmonary forms with an early onset favored by the use of immunosuppressive drugs in the context of any other systemic disease. TB treatment could increase morbidity because of the relatively frequent occurrence of side effects.

## Enterovirus-induced acute respiratory distress syndrome in an immunocompetent adult with concomitant immune thrombocytopenia

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**Introduction:** Enteroviruses are a group of highly contagious, non-enveloped, positive stranded RNA viruses. They are commonly associated with respiratory tract infections in infants and children, but can also affect adults. There have been documented cases of Enterovirus-induced acute respiratory distress syndrome (ARDS) in adults with chronic lung disease or immunocompromise, but only a few cases in otherwise healthy adults. We present a case of Enterovirus-induced ARDS

in an immunocompetent adult with concomitant immune thrombocytopenia (ITP).

**Case report:** A 19 year old man presented to his general practitioner with sore throat, malaise and fever. After 2 weeks he had not improved and routine blood tests revealed a platelet count of 15 with normal hemoglobin and white cell count. The man was admitted to hospital at which point he had a clear chest, his oxygen saturations were 99% on air and chest X-ray was normal. He was treated as presumed viral-induced thrombocytopenia with intravenous immunoglobulin and antibiotic cover with tazobactam/piperacillin. He continued to spike high temperatures and on day 2 of admission his oxygen saturations fell to 86% on air. Chest X-ray showed bilateral infiltrates suggestive of ARDS. He was transferred to the intensive care unit (ICU) where he received high flow oxygen. Serology confirmed Enterovirus IgM positive. HIV serology was negative. The decision was made with the patient to withhold antiviral therapy (ganciclovir) due to the risk of further thrombocytopenia. We did not prescribe steroids for the thrombocytopenia due to the ongoing infection. The patient left ICU on day 8 and was discharged on day 13. He received only one platelet transfusion as cover for insertion of an arterial line.

**Discussion:** Acute respiratory distress syndrome is a rare but recognized complication of enterovirus infection in immunocompetent adults. Enterovirus infection is also associated with ITP, although this is more common in infants and young children. In managing a 19 year old man who developed both these complications due to Enterovirus infection, we found that he improved with little intervention other than high flow oxygen, immunoglobulin and cover with IV antibiotics. In this case the contraindications to use of antivirals for severe Enterovirus infection causing ARDS and the use of steroids for viral ITP did not prevent a good outcome.

### **Case report: infective endocarditis of an implantable cardiac electronic device caused by *Enterococcus durans***

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**Introduction:** A serious complication of implantable cardiac electronic devices (ICED) is infective endocarditis. Coagulase negative Staphylococci (CoNS) are the most commonly isolated microorganisms (10-68%), followed by *Staphylococcus aureus* (24-59%) and Gram-negative bacilli (1-17%). *Enterococcus* spp. are responsible for 5-6% of ICED infections, *Streptococcus* spp. for 4-6%, while fungi are uncommon pathogens (0.5-2%). *Enterococcus durans* is rarely reported in human clinical infections and is estimated to be responsible for <1% of all Enterococcal infective endocarditis.

**Case report:** A 77 years old female with a history of an implanted cardiac defibrillator was admitted to our hospital due to fever and isolation of *Enterococcus durans* in 3 of 3 blood cultures. Patient's medical history was remarkable for metallic aortic and mitral cardiac valves, due to rheumatoid stenosis of the valves

(history of rheumatic fever in childhood). Two years ago she was successfully treated for infective endocarditis, caused by vancomycin resistant *Enterococcus* (VRE). Thereafter, a cardiac defibrillator was implanted, due to episodes of ventricular tachycardia. Atrial fibrillation, hypothyroidism, chronic kidney disease and heterozygous beta thalassemia were also reported. A transthoracic echocardiography was performed, with no signs of endocarditis. Patient underwent a transeosophageal echocardiography, which revealed oscillating intracardiac vegetation on the implanted cardiac defibrillator. A diagnosis of infective endocarditis was manifested. Based on the results of antimicrobial susceptibility antibiotic treatment with a combination of ampicillin (12 g daily) and gentamicin (dose customized to patients GFR) was administered. Blood cultures drawn one week after initiation of antibiotics were negative. Intracardiac masses on the implanted cardiac defibrillator disappeared in the second transesophageal echocardiography after two weeks of therapy. The cardiac defibrillator was explanted 2 weeks after integration of antimicrobial therapy. Administration of antibiotics was continued for a total of 6 weeks. Patient was followed for a period of 8 weeks, being afebrile, while blood cultures were negative.

**Discussion:** In this report we present a case of infective endocarditis caused by *Enterococcus durans* in a patient with a permanent cardiac defibrillator. It's the first reported case of infectious endocarditis of an ICED caused by *Enterococcus durans*.

### **Role of CD64 expression on neutrophils in the diagnosis of sepsis and the prediction of mortality in adult patients with community-acquired infections presenting with fever**

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**Objectives:** The aim of the present study was to evaluate the role of CD64 on neutrophils in patients with community acquired infections presenting with fever, as a possible marker to aid diagnostic procedures and to evaluate its efficacy in predicting mortality.

**Methods:** A total of 32 patients (19 males, 13 females) presenting with fever >38°C at the emergency room (ER) of the department of internal medicine of the Patras University Hospital, were enrolled in the study during a period of 12 months. Serum for neutrophil CD64 antigen expression were obtained from the patients on admission (day 1) and on days 3, 7 or discharge/death. The determination of CD64 expression on neutrophils was operated through dual-color cytometry flow analysis in whole blood samples. Results were expressed as arbitrary units (mean fluorescence intensity [MFI]). Additionally, the patients were evaluated using the Simplified Acute Physiology Score (SAPS-II), the Sequential Organ Failure Assessment (SOFA) and the Mortality in Emergency Department Sepsis (MEDS) score on the same days while all the indicated clinical, laboratory



and imaging procedures as required for fever's differential diagnosis were followed. A questionnaire regarding demographic characteristics, comorbidities, medications used and patients' survival was also filled. All statistical analyses were performed using SPSS v.21.

**Results:** Higher mean CD64 expression on neutrophils was significantly correlated to fever 48 hours and 7 days prior measurement ( $p=0.01$ ). CD64 neutrophil expression was higher in patients presenting with abdominal infections. CD64 neutrophil expression was higher in patients who developed SIRS and sepsis at all-time points. Significantly higher expression was seen in patients who had severe sepsis at day 7 of measurement. Additionally the mean CD64 expression on day 1 was higher in non survivors compared to survivors while prior antibiotic treatment was correlated to decreased expression of CD64 on neutrophils ( $p=0,016$ ).

**Conclusion:** CD64 appear to be an early indicator for survival and a useful diagnostic marker for the infection progression of patients presenting in ER departments with fever.

## Ova and parasites in stools: clinical features and review of a series of 32 cases

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**Objective:** Review the results of parasitological stool studies in a period of 14 years.

**Methods:** Parasitological stool studies were analyzed in Cabueñes Hospital (Gijón, Spain) between January 2009 and December 2014. Patients were collected from an electronic database. All patients with positive tests were reviewed. For the analytical study SPSS 20.0 was used.

**Results:** A total of 2063 samples were analyzed, 32 of which with positive results. We identified 17 men (53%) and 15 women (47%), mean age 49.6 years (SD 19, range 24-85). Of these patients, 29 (91%) had Spanish nationality, and 3 (9%) foreign nationality (Mali, Senegal and Sahara). The stool samples were requested on an outpatient basis in 25 (78%) cases and in hospitalized patients in 7 (22%) cases. The most common reason for consultation was diarrhea in 18 (56%) patients, abdominal pain in 11 (34%), rectal bleeding in 6 (19%), vomiting in 6 (19%), weight loss in 4 (12%), pruritus in 4 (12%) and asthenia in 3 (9%). In additional studies, in the blood count, anemia was found in 4 (12%) cases and eosinophilia in another 4 (12%) cases with an eosinophilia average of 27.5% (range 13-57%). Colonoscopy was performed in 20 (62%), abdominal ultrasound in 14 (47%) and computerized axial tomography in 3 (9%) patients. The outcome was favorable in 20 (62%) patients with resolution of the disease (disappearance of the clinic and /or negativization sample) and unknown in 12 (36%). No patient suffered complications and 3 (9%) died, none from related causes. Microbiology Service reported the

following results: 9 (28%) cases with *Giardia lamblia*, 9 (28%) *Entamoeba coli*, 6 (19%) *Blastocystis hominis*, 2 (6%) *Taenia* spp, 2 (6%) *Enterovirus vermicularis*, 1 (3%) *Uncinaria*, 1 (3%) *Cryptosporidium parvum*, 1 (3%) *Hymenolepis nana*, *Entamoeba coli* and *Blastocystis hominis* and 1 (3%) with *Iodamoeba butchilii* and *Giardia lamblia*. Metronidazole was used in 10 (30%) patients, albendazole in 3 (9%) and praziquantel in 3 (9%). In 16 (50%) patients treatment was not required.

**Conclusions:** Our results are consistent with that described in the medical literature; protozoal infections are more frequent than helminth. The incidence of these infections is low, thanks to the measures of public health and vector control in our country. The main symptom is diarrhea and evolution is good even when half of the patients do not required treatment.

## *Clostridium difficile* binary toxin producer in a tertiary hospital

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**Objectives:** *Clostridium difficile*'s binary toxin (CDT) it is associated with a worse prognosis in recurrent or persistent *Clostridium difficile* infection (CDI). The aim of this study is to analyze the clinical and epidemiological features of all CDI cases and to investigate the relationship between severity of symptoms and presence of CDT.

**Methods:** Prospective study. All CDI cases from January 2012 to June 2013 detected by GDH antigen and toxin (Techlab C. Diff Quick Chek Complete®, Alere) and PCR method for detection of toxigenic *Clostridium* gene (Xpert C. *difficile*, Cepheid) were included. Statistical analysis was performed with SPSS 19.0.

**Results:** 35 cases were diagnosed in 34 patients (18 were women) aged between 18 and 95 years old (mean 66 y.o.). In 13 patients (39%) the binary toxin gene was presented (group 1), in the others it wasn't detected (group 2). The use of antibiotics previously in group 1: 13 cases (100%), group 2: 19 cases (90.5%), proton-pump inhibitors use 12 cases (92.3%) vs 20 cases (95.2%); neoplasia 5 cases (38.5%) vs 12 cases (57.1%); personal history of colonic disease 4 cases (30.8%) vs 3 cases (14.3%) and steroid treatment 4 cases (30.8%) vs 9 cases (42.9%) were predisposing factors for both groups. B-Lactam antibiotic 10 cases, (29.4%) and cephalosporins 9 cases (26.5%) were the most frequently related to CDI in both groups. Community-acquired disease was in 8 cases (4 in each group). Severe CDI appeared in 3 binary toxin positive cases (23.1%) and in 1 of negative binary toxin (4.8%). There wasn't any complications in any group. It had been one recurrence and a related death was presented in group 1 (7.7%), any case in group 2. Treatment: 18 cases metronidazole (52.9%), group 1: 7 (53.8%), group 2: 11 (52.4%) in comparison to vancomycin 16 (47.1%), group 1: 6 (46.2%), group 2: 10 (47.6%).

**Conclusions:** CDI incidence is increasing in the last few years. This may be due to several circumstances such as an abusive use of antibiotics in general population and the improvement of sensitivity in diagnostic test for CDI. Binary toxin production is running as an independent factor for the severe CDI onset and also in recurrences or deaths. In our series there is a higher incidence of severe illness in group 1 compared to group 2 due to the presence of binary toxin gene. Recurrences and cases of death are related to CDI as it is described in the literature, these cases appeared only in those with positive binary toxin gene. The data at our disposal is undersized so studies with a larger sample size are needed. In our series there was no differences between any prescribed treatment, also there wasn't any treatment failure.

### Optimize the diagnosis of Clostridium difficile infection, comparison between pre-intervention and post-intervention

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**Objectives:** The aim of this study is to compare Clostridium difficile infection (CDI) after the introduction of some improvement performances in a tertiary referral hospital. Also to get to know better the incidence of CDI improving the identification of CDI cases in a tertiary referral hospital.

**Methods:** Descriptive study with pre intervention and post intervention. The intervention consisted in the implementation of some doings aimed to early diagnosis, involving nurses in sampling as well as the introduction of more sensitive diagnostic tests (GDH / PCR gene against toxigenic C. difficile toxin). The pre-intervention period was from January 2011 and December 2012. The post-intervention study was from January 2013 to December 2013. Statistical analysis was performed SPSS v20.

**Results:** Pre-intervention study (n=18), 6 (33%) were diagnosed by GDH and positive Clostridium difficile PCR. 39% were women. Mean age was 60 years old (range 25-86 y.o). CDI was the reason for admission in 55.6% of cases. All of them had a predisposing factor. 17 (94.4%) had received antibiotic treatment previously, quinolones (n=5, 29.4%), carbapenems (n=5, 29.4%), beta-lactams (n=3, 17.6%), cotrimoxazole (n=3, 17.6%) and cephalosporins (n=1, 5.9%). In 6 cases (32.3%) it was outpatient acquired infection (5 nosohusial infections, 1 community-acquired infection). The treatment used was metronidazole (77.8%) and vancomycin (22.2%). Post-intervention study n=16, 11 (68.8%) were diagnosed by GDH and positive Clostridium difficile PCR. 62.5% were women. Mean age was 68.5 years old (19-95 y.o). CDI was the reason for admission in 25% of cases. All of them had a predisposing factor, n=15 (93.8%) had received antibiotics treatment previously, beta-lactams (n=7, 43.8%), cephalosporins (n=5, 31.3%), carbapenems, cotrimoxazole and daptomycin (n=1, 6.3% each). In 2 cases (12.5%) it was outpatient acquired

infection (non-community-acquired infection). The treatment used was vancomycin (n=11, 68.8%) and metronidazole (n=5, 31.3%).

**Conclusions:** CDI is underdiagnosed due to several causes such as lack of request for the determination in the stool by professionals because of the frustration generated by the low sensitivity of previous diagnostic tests. Determining toxigenic GDH gene and Clostridium difficile PCR has increased considerably CDI cases. In our series there was a considerable increase of CDI cases after the intervention (more sensitive tests (CD PCR and GDH) and the involvement of nurses to sampling earlier). Antibiotics involved in CDI establishment changed after the intervention, mainly because of the establishment of a new empirical antibiotic therapy guide in Jerez Hospital. In the pre-intervention period metronidazole was the antibiotic predominantly used versus vancomycin, used in the post-intervention period. The intervention sessions showed to the doctors more effectiveness with vancomycin against CDI. CDI is underdiagnosed; a simple intervention can significantly increase the diagnosis.

### Empirical antimicrobial treatment in mobile applications era

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**Objectives:** New technologies are being implemented in our daily lives and also in health issues. Proper empirical antimicrobial treatment is essential; hence the use of complex empirical treatment guides is increasing. It is desirable to have an easy tool that simplifies this task in inexperienced staff. That is why we have created a simply and intuitive app.

**Methods:** The idea to develop an app useful for medical staff came because it was needed to update local guides in Empirical Antibiotic Treatment (EAT). From March 2013 to October 2014 we have designed several algorithms in infectious disease as a decision tree to establish the most appropriate EAT. Those algorithms have been processed to be included in a mobile phone application whose design allows it to be consulted intuitively and nimbly.

**Results:** We got an app for Android devices and IOS systems to help medical staff to choose the most appropriate EAT. The variables took into account in the design and development of the algorithms were both clinical (signs and symptoms) for each pathology and additional tests. There are both multivariate and dichotomous variables. After several steps one get to an end table where the risk of multi-resistant germs, that may be involved independently in each disease, and an accurate EAT is proposed. In less than 3 months more than 750 downloads were made in our medical area.

**Conclusions:** The creation of this mobile app can be very useful because the use of mobile devices is increasing. The EAT app users can dynamically select all the possible variables and easily will get the most accurate treatment.

## Imported strongyloidiasis: epidemiological, clinical and laboratory characteristics in a regional hospital setting in Granollers, Barcelona

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**Objectives:** Strongyloidiasis is caused by infection with *Strongyloides stercoralis* (SS). Manifestations of infection can range from asymptomatic eosinophilia in immunocompetent hosts to disseminated disease with septic shock in immunocompromised hosts. It is endemic in tropical and subtropical regions, but due to travel movements and immigration it can also be seen in developed countries. The most common manifestations are gastrointestinal, cutaneous, or pulmonary symptoms that can persist for years; some patients simply present eosinophilia in the absence of symptoms. The aim of this study was to evaluate the clinical, laboratory and epidemiological features of strongyloidiasis in a regional hospital setting in Spain.

**Methods:** Review of strongyloidiasis cases followed-up at the Internal Medicine Department of our centre during 2014.

**Results:** 8 patients were diagnosed with strongyloidiasis during this year, equally male and female, with an average age of 32 years. All were immigrants, 6 of them from Bolivia, 1 from Ecuador and 1 from Dominican Republic, and had been living in Spain for a mean of 8 years. None of the patients reported a recent travel. Reason of consultation was: eosinophilia in 3 cases; eosinophilia and symptoms in 4 cases; screening in 1 case. 6 patients presented comorbidities; 2 of them being immunocompromised: 1 had a C3 stage HIV infection; 1 was on long-term immunosuppressive treatment; 4 had Chagas disease; 1 presented other concomitant forms of parasitic infection. The most common manifestations were gastrointestinal (n=6) and cutaneous (n=3), whilst none presented with respiratory symptoms. Eosinophilia and elevated IgE were present in 7 cases. Stool tests were performed in all patients (4 of them were positive) and serology in 6 (5 of them positive). All patients received treatment with ivermectine and 1 patient with ivermectine + mebendazole. After treatment, symptoms were solved in all patients. Eosinophilia persisted in one patient despite of therapy.

**Conclusion:** 1) Strongyloidiasis in non-endemic areas is probably underestimated. 2) Early detection is necessary in patients with high eosinophilic count or elevated IgE levels, even when no symptoms are present. 3) In negative stool culture, serology test should be considered.

## Severe malaria criteria: descriptive study of 57 patients who required admission to intensive care unit in Barcelona

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**Objective:** To know the prevalence and characteristics of severe malaria criteria in patients with severe malaria that required admission to an intensive care unit in a non-endemic country.

**Methods:** We performed a retrospective observational study, including all patients with severe malaria that required admission to an ICU in Hospital Clínic of Barcelona from September 2003 to January 2015. Epidemiological, clinical and laboratory data was collected from the medical chart. WHO criteria for severe malaria were used. Data are expressed in median (range).

**Results:** 57 patients were included, 37 men, with median age of 37 years (range 14-69). All of them had travelled to endemic areas. Hyperparasitemia (>2,5% of red blood cells parasited in blood smear) at diagnosis was present in 37 (65%) patients, with a median parasitemia of 4.6%. Altered level of consciousness was present in 16 patients (28%), seizures in 5 (8%), prostration in 24 (42%), respiratory failure in 18 (32%), shock in 15 (26%), hyperbilirubinemia (>2,5 mg/dL) in 36 (63%), spontaneous hemorrhage in 5 (5%), metabolic acidosis in 14 (25%) and hemoglobinuria in 10 (18%). 20 patients (35%) presented serum creatinine >1,2 mg/dL, but only in 6 (11%) it was over 3 mg/dL. Normocytic anemia was present in 36 patients (63%) but it was not severe (Hb <5 g/dL or hematocrit <15%) in any of the patients. 19 patients (33%) presented lactate levels >20 mg/dL, but only in three of them (5%) was >45 mg/dL in the first 24 hours. Serum glucose was <60 mg/dL in 10 patients (17.5%).

**Conclusions:** Hyperparasitemia and hyperbilirubinemia are the most common severity criteria that present patients with severe malaria admitted to ICU in a non-endemic country. Although less frequent, organ dysfunction is present in more than 1/3 of patients, being neurological impairment, respiratory failure and shock the more prevalent.

## Adrenal crisis in a patient with scurfolosis

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**Introduction:** Addison's disease is in the majority of the cases associated with an autoimmune disease (70-90%) or an infectious disease (7-20%).

**Case report:** A woman, 61 years, with a previous history of HIV infection (C3), diagnosed in 2010 sub ART, now with T- CD4+ lymphocyte 200 cells/uL (18%) and undetectable viral load; non-Hodgkin diffuse large B-cell lymphoma of the left parotid gland (2011) with controlled of disease after R-CHOP and scurfolosis (a month before admission) started on HRZE. On admission: she was prostrated, nauseated, febrile (39°C), hypotensive (83/45 mmHg) and hypoxic with a partial respiratory failure: pO<sub>2</sub> 57 mmHg, pCO<sub>2</sub> 38 mmHg. Analysis revealed Hb 9.9 g/dL, 3040 leukocytes/uL with 76% neutrophils, platelets 115 000/uL, CRP 14.4 mg/dL, creatinine 1.1 mg/dL, with a normal ionogram, AST/ALT: 1303/339 U/L, GGT 848 U/L, total bilirubin 1.6 mg/dL and LDH 922 U/L. She underwent resuscitation with fluid challenge and was transferred to the Infectious Disease Department with a

provisional diagnosis of pneumocystosis, being started on co-trimoxazol after bronchoalveolar lavage which did not reveal any infectious causes. Her clinical evolution, although the inflammatory and respiratory parameters improved, was characterized by a marked hypotension, unresponsive to fluids and bradycardia together with hyponatremia (Na+ 126 mEq/L), hyperkalemia (K+ 5.8 mEq/L), hypoglycemia and a normal renal function. Suspecting adrenal insufficiency, Synacthen® test was performed (ACTH 108 -> 43.6 pg/ml and cortisol 23.4 -> 35.9 ug/dl), such as renin assay (1291 pg/ml) and aldosterone (52.3 pg/ml), confirming the diagnosis. The abdominal CT showed no structural changes of the adrenal glands. The evaluation of thyroid function revealed decreased FT4 and TSH, normalized with therapy with levothyroxine. Autoimmune component was excluded. Patient started treatment with hydrocortisone and ion exchange resin without response, which improved only after initiation of fludrocortisone. Diagnosis of primary adrenal insufficiency was assumed with tuberculosis as the most likely etiology.

**Discussion:** Giving the high comorbidity and mortality it seems crucial to be aware of adrenal gland dysfunction in certain clinical settings.

## Diabetic neuropathy and osteomyelitis

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**Introduction:** Diabetic peripheral neuropathy and its consequences – chronic wound infections and osteomyelitis – are becoming more frequent, as diabetic prevalence is increasing. Prevention and treatment of these events are essential in order to improve quality of life and prevent early disability.

**Case report:** A 55 years old man with poorly controlled diabetes mellitus type 1 and end-stage kidney disease on dialysis through central venous access was sent to our hospital with the diagnosis of an uncontrolled methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia. He also had history of peripheral neuropathy and stage 4 retinopathy. He had a 6-day development of low-grade fever, headaches and vomits, associated with 2-month right-foot discomfort and walking difficulties. He was on its sixth day of intravenous cefazolin and gentamicin, prescribed at his hemodialysis center. Upon admission he was hemodynamically stable, with low-grade fever, normal cardiopulmonary auscultation and absence of inflammatory signs on the central venous catheter. He presented a non-dolorous ulcerated lesion on the plantar surface of his right foot, with inflammatory signs and fluctuation. Bilateral ankle-brachial index was >1. His analytical study showed hemoglobin 11,7 g/dL, 14,3x10<sup>9</sup> leukocytosis and C-reactive protein of 367,2 mg/l. Ciprofloxacin and vancomycin were empirically introduced. *Serratia fonticola* and MSSA strains, both susceptible to ciprofloxacin, were isolated from the foot abscess. Blood cultures were negative. Echocardiogram revealed no endocarditis. Osteomyelitis of tarsus and calcaneus associated with bone destruction and radiographic signs of cellulitis of subjacent tissues were found on the plain radiography. The patient was subsequently submitted to

right transtibial amputation and he is currently integrated in a muscular rehabilitation program.

**Discussion:** Chronic osteomyelitis through contiguous soft tissue infection can develop as consequence of negligent care of peripheral neuropathy. Symptoms are often subtle and difficult to recognize. Image studies, such as radiography, and blood and wound cultures are essential for diagnosis and targeting antibiotic treatment. Antibiotic route and duration remains controversial. However the association with bone and soft tissue necrosis indicates an amputation, since it is related with limb disability and recurrence of infection.

## Rare manifestation of miliary tuberculosis

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**Introduction:** Tuberculosis (TB) is an infectious disease entailing enormous mortality and morbidity. Miliary TB is a potentially fatal form of TB that results from massive lymphohematogenous dissemination of *Mycobacterium tuberculosis* bacilli. Diagnosis of miliary TB is a challenge that can perplex even the most experienced clinicians. There are nonspecific clinical symptoms, and patients may present with asthenia, fever of unknown origin, or dysfunction of one or more organ systems. Pneumothorax is common in cavitary tuberculosis; however it is rare in miliary tuberculosis. The authors report a case of miliary tuberculosis that presented initially with pneumothorax.

**Case report:** An 83 years old woman, with history of vascular epilepsy, presented in the emergency department with fever and shortness of breath with sudden onset. On examination, she had drowsiness, cyanosis, tachycardia, hypotension (blood pressure 90/50 mmHg), tachypnea (respiratory rate of 40 per min) and exuberant subcutaneous emphysema. Pulmonary auscultation revealed decrease in breath sounds over the left hemithorax. Percussion with hyperresonant note on the left hemithorax. Heart sounds were normal. Chest radiograph revealed exuberant right pneumothorax. Intercostal drainage chest tube (connected to under-water seal) was inserted in 5th intercostal space in mid axillary line, with immediate relief of dyspnoea. After pulmonary expansion, bilateral miliary pattern was evident. Sputum direct smear was repeatedly negative for acid-fast bacilli. Mantoux test was negative. Computed tomography scan of the thorax revealed micronodular pattern, bilateral, with centrilobular distribution and extent to the apical areas. Bronchofibroscopy was made and bronchoalveolar lavage fluid revealed granulomatous inflammation. The culture was positive for *Mycobacterium tuberculosis* complex (as well as blood cultures). Hepatic biopsy revealed non-necrotizing granulomatous hepatitis. Initiated treatment with antituberculosis agents. Final diagnosis: miliary tuberculosis with hepatic, pulmonary and pleural dissemination.

**Discussion:** Miliary TB has a spectrum of manifestations that still perplex the most experienced clinicians and are a diagnostic challenge. The myriad clinical manifestations, atypical radiographic findings, and difficulties in establishing TB as the etiological diagnosis are the main challenges in the diagnosis of miliary TB.

## Chlamydia trachomatis proctitis in homosexual HIV-infected patient

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**Case report:** Male 33 years, homosexual, HIV-infected and on antiretroviral therapy several years. In the last two months before evolutionary controlling viral load and CD4 it was undetectable above 1000 cells/ml. He was admitted for a prolonged box constipation, abdominal and anal pain, urgency and low stools with mucus and sometimes bloody content. Laboratory tests were not relevant except serology for Chlamydia trachomatis 1/32 and anal smears positive for Chlamydia trachomatis. Diagnostic tests included the sigmoidoscopy that showed a large solitary rectal ulcer from the anal margin to 8 cm proximally, which occupied 60% of the circumference. The ulcer had a background mammillated and friable. Diagnosing Chlamydia trachomatis proctitis in HIV-infected patient was given. He was treated with oral doxycycline (100 mg/12 hours) with significant clinical improvement after a few days. In the evolution he developed a thrombosed hemorrhoid requiring thrombectomy, without other incidents. Discharged from hospital with home treatment until completing 3 weeks of oral doxycycline. A month after completing the antimicrobial treatment, a control sigmoidoscopy was performed appreciating a significant improvement of the ulcer with a significant decrease in the length of it and its appearance.

**Discussion:** We emphasize the rarity of this case by the etiology (Chlamydia trachomatis) and presentation (proctitis) may induce diagnostic and therapeutic. But above all, it can serve as a paradigmatic example to draw attention to medical and social community on the increase in our region STI in the group of young homosexuals who do not implement the recommended prevention measures.

## Etiology of fever of intermediate duration in a tertiary care hospital, 2008-2014

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**Objectives:** Fever of intermediate duration (FID) has recently been proposed as a separate entity with well-defined etiological features. The aim of this study is to describe the etiology of this condition among patients attended in a Quick Diagnosis Unit (QDU) and to highlight differences with an extensively studied entity, fever of unknown origin (FUO).

**Methods:** FID is defined as fever >38°C, lasting 7 to 28 days, that remains undiagnosed after performing a basic evaluation (patient's history, physical examination, hemogram, serum creatinine, urine analysis, and chest radiograph). QDU is an internal medicine outpatient clinic for patients with suspected serious disease who need to undergo preferential diagnostic tests. A retrospective study of the cases of FID attended in

QDU between 2008 and 2014 was carried out. The main epidemiological, microbiological and clinical variables were collected and analyzed.

**Results:** Globally, 350 patients were referred to QDU with fever as chief complaint: 95 of them fulfilled the criteria of FID. 56 (58.9%) were male and the mean age was 47.1±18.3 years. An etiologic diagnosis was obtained in 83 patients (87.4%), whereas in 12 cases (12.6%) fever resolved without determining the cause, despite completion of the diagnostic workup. The most frequent etiology was an infectious disease (73 cases, 76.8%). The microbiological identification of the etiologic agent was available in around half of cases: viral infections in 22 (30.1%) patients (Cytomegalovirus 9, Erythrovirus B19 7, Human immunodeficiency virus 5, Epstein-Barr virus 2); bacterial infections in 12 (remarkably, 4 cases of endocarditis by gram positive cocci and 2 cases of Boutonneuse fever); a Mycobacterial and a mycotic infection. 4 patients (4.3%) were diagnosed with an autoimmune disease. 2 patients (2.1%) were diagnosed with lymphoma and 4 patients (4.3%) with other conditions (thyroiditis, hyperthyroidism, post-streptococcal reactive arthritis and sarcoidosis).

**Conclusions:** In our setting the most frequent cause of FID is an infectious disease. We found a notably lower proportion of tumoral and inflammatory etiologies compared with FUO series. This is paramount to establish an appropriate diagnostic and therapeutic approach for this condition.

## Acute Q fever with intensive care management

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**Introduction:** Q fever is an uncommon zoonosis caused by Coxiella burnetii (CB), a small Gram negative Cocobacillus with obligatory intracellular cycle. The infections results of the inhalation of CB spores, present in excreta, milk and parturition fluids of infected animals. The acute disease has a wide range of presentations, including lung, liver and neurological involvement, and sometimes as an indeterminate febrile syndrome. Severe endocarditis by CB is the hallmark of the chronic disease.

**Case report:** 66 years old, Caucasian male, without relevant clinical background, was admitted in the urgency department with fever, cough, dyspnea, epigastric abdominal pain, nausea and vomiting with four days of evolution. He presented polypnea, painful hepatomegaly, and widespread rhonchi and crackles at auscultation. Thoracic X-ray showed slight perihilar bronchovascular intensification. Gasometry and laboratory findings exhibited global respiratory insufficiency, elevation of acute phase reactants and elevation of hepatic enzymes together with coagulation compromise. The empiric antibiotic therapy for community acquired pneumonia proved unsuccessful. The patient's clinical status worsened with the transfer to the intensive care unit. After exclusion of other clinical entities, the serological diagnosis of Q fever was made, the patient

began doxycycline treatment with progressive resolution of the clinical situation.

**Discussion:** Q fever diagnosis is difficult due to the diversity of possible presentations. The association of atypical pneumonia and hepatic cytolysis should raise suspicion of this infectious disease, especially when contact with animals is present.

## Tuberculosis with anti TNF-alpha treatment

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**Objectives:** The treatment of chronic inflammatory diseases has entered a new era since the advent of biotherapies. Despite their undeniable efficiency, the use of these molecules exposes to many adverse effects. Given the immunosuppressive action of biotherapies, an increase of infectious complications is expected, including tuberculosis. We report two new observations of tuberculosis in patients treated with anti-TNF alpha. **Methods:** This is a retrospective study including patients receiving anti-TNF alpha between 2004 and 2015. The records of patients who developed tuberculosis were reviewed.

**Results:** Among 25 patients treated with anti TNF-alpha, two cases of tuberculosis were noted. **Observation 1:** A 23 years old patient with juvenile idiopathic arthritis resistant to methotrexate was treated with etanercept. In the pre-therapeutic assessment research, latent tuberculosis was negative. 12 months after the initiation of the treatment, the patient developed a cervical lymph node and tuberculosis was confirmed by anatomopathologic examination. An anti-tuberculosis treatment was conducted for 8 months with a clinical improvement. The etanercept was resumed after the healing of tuberculosis without signs of reactivation. The patient is still symptom free after 18 months. **Observation 2:** A 45 years old patient with Crohn's disease associated with ankylosing spondylitis in its axial form was treated with infliximab. 18 months later, the patient developed pulmonary tuberculosis confirmed by bacteriological examination. The patient had been treated with anti tuberculosis treatment for 6 months. After the cure of tuberculosis and giving the outbreaks of Crohn's disease, treatment with adalimumab was started. A recurrence of pulmonary tuberculosis 24 months after the start of adalimumab was noted. The anti-tuberculosis treatment was resumed and adalimumab was stopped. A clinical improvement was noted and the patient is still symptom free for tuberculosis after 12 months.

**Conclusions:** The incidence of tuberculosis in patients treated with biotherapy is increasing; the absence of latent tuberculosis in pre-therapeutic assessment suggests the role of these molecules in the induction of tuberculosis. The occurrence of infectious complications during treatment with biological therapy should not restrict the indications of these molecules but should encourage close monitoring of patients to diagnose and treat these complications in time.

## An infectious cause of asystole in a young woman

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**Introduction:** Streptococcus pneumoniae is a bacterial pathogen that affects children and adults with underlying disease. This microorganism colonizes the upper respiratory tract and can cause otitis media, pneumonia, bacteremia and meningitis. The risk for pneumococcal infection is higher in immunosuppressed patients (e.g., congenital immunodeficiency, HIV infection, leukemia, Hodgkin's disease, malignancy, organ or bone marrow transplantation and under treatment with alkylating agents or systemic corticosteroids). We report a case of a young woman with a prior history of non-Hodgkin's lymphoma and colon adenocarcinoma, who was diagnosed with septicemia and septic shock due to Str. pneumoniae.

**Case report:** A 39-year old Caucasian woman, with an extensive history of treated non-Hodgkin's lymphoma four years ago, recent left hemicolectomy due to adenocarcinoma, epilepsy, open foramen ovale and ischemic stroke 8 years ago, presented in the emergency room with fever up to 39°C since 2 days, tachypnea and generalized weakness. On physical examination she had tachypnea and crackles in her right upper lobe. She was diagnosed with septic shock and severe metabolic and lactic acidosis (pH=7.125, pO<sub>2</sub>=65 mmHg, pCO<sub>2</sub>=16.1 mmHg, HCO<sub>3</sub>=5.2 mmol/L, lactic acid 12.5 mmol/l), disseminated intravascular coagulation, elevated LDH 986 U/L, severe hypogammaglobulinaemia and acute renal failure. The ECG showed LBBB (previously known) and her chest X-ray revealed right upper lobe pneumonia. The patient was treated with high flow oxygen mask, intensive hydration, calcium gluconate and NaHCO<sub>3</sub> iv, piperacillin/tazobactam 4.5 g iv, amikacin 1g iv and vancomycin 1 g iv. She responded clinically, temporarily though, since an hour after her admission, she had a cardiac arrest (asystole), she revived after 7 minutes of CPR and underwent PEA an hour later with no successful outcome this time. The blood cultures isolated Str. pneumoniae sensitive to vancomycin.

**Discussion:** Streptococcal infection should always be considered in the differential diagnosis of fever in immunosuppressed patients. Despite appropriate antimicrobial therapy and intensive medical care, the overall case-fatality rate is 15-20% among adults, higher in immunosuppressed ones. It is important to note that half of these deaths could be prevented through the use of vaccine.

## Clostridium septicum bacteremia in a diabetic patient presenting with abdominal pain

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**Introduction:** Clostridium septicum is a bacterial pathogen commonly associated with necrotizing skin or soft tissue infections, which can present with nonspecific or atypical symptoms. An association exists between colon carcinoma and Cl. septicum infection, especially bacteremia. The best-known relationship is between Streptococcus bovis infection and colon carcinoma, but there is another link, only recently recognized between Cl. septicum and large bowel malignancies. This is associated with hematological malignancies, immunosuppression, neutropenia, and diabetes mellitus. We report an interesting case of a diabetic patient presenting with epigastric pain and fever.

**Case report:** A 69 years old Caucasian woman, with a history of hypertension and diabetes mellitus, presented in the emergency room with fever up to 39°C since 2 hours, tachypnea and epigastric pain. She was febrile, septic with severe abdominal pain located in the right iliac fossa. She had tachypnea (RR25) and metabolic lactic acidosis (pH=7.33, pO<sub>2</sub>=65 mmHg, pCO<sub>2</sub>=18.1 mmHg, HCO<sub>3</sub>=15.2 mmol/L, lactic acid 8.5 mmol/l). The ECG revealed sinus rhythm with no signs of ischemia. The patient was treated with high flow oxygen mask, fluid replacement, calcium gluconate and NaHCO<sub>3</sub> iv, ampicillin/sulbactam 3g x 4 iv and bolus amikacin 1g iv. She responded clinically, temporarily though since an hour after her admission, she developed surgical abdomen with rebound tenderness and positive Mc Burney sign. Acute appendicitis was then diagnosed and a laparoscopic appendectomy was performed. Blood cultures revealed Cl. septicum bacteremia. The patient was treated with penicillin 5 x 10<sup>6</sup> x 6 iv for 7 days. She was discharged and received ciprofloxacin 500 mg x 2 per os for another 7 days. Histology revealed gangrenous appendicitis with presence of colon adenocarcinoma.

**Discussion:** Cl. septicum is a gram positive, anaerobic microorganism. The postulated mechanism of infection in colon cancer involves disruption of the normal mucosal barrier due to tumor-induced ulceration, followed by bloodstream invasion. We wish to alert clinicians to the diverse spectrum and diagnostic difficulties of this rare, potentially catastrophic association and believe that all patients with positive blood cultures for Cl. septicum, even without clinical suspicion of large bowel malignancy, should undergo colonoscopy and evaluated for colon carcinoma.

## Listeriosis mimicking relapse of temporal arteritis

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**Introduction:** Listeria monocytogenes is a bacterial pathogen affecting mostly neonates, immunosuppressed patients, older

adults and pregnant women. It causes invasive disease including meningitis, meningoencephalitis or bacteremia in the above mentioned patients or self-limited febrile gastroenteritis in normal hosts who ingest high numbers of microorganisms. We report a case of a female patient with a prior history of temporal arteritis, which was diagnosed with listerial bacteremia and meningitis.

**Case report:** A 66 years old Caucasian woman, with a history of recently diagnosed temporal arteritis under treatment with methylprednisolone 48 mg/day for the last 2 months and already blind from her right eye, was admitted to our clinic due to fever up to 38.5°C with concomitant left eye blurred vision, diffuse myalgias, fatigue and dysregulation of her blood glucose values. Physical examination was unremarkable, while blood chemistry revealed elevated markers of inflammation (ESR=110 mm/h, CRP=202 mg/l). No signs of ischemic optic neuropathy were identified in fundoscopy. Visual acuity of her left eye was 8/10. Based on the above clinical picture, the patient received a 3 day course of 1g methylprednisolone iv/day. Then, Listeria monocytogenes was isolated from 2 blood cultures. A lumbar puncture was then performed and revealed meningitis with positive PCR of cerebrospinal fluid for Listeria monocytogenes. The patient was then treated with ampicillin 2 g x 6 iv and gentamycin 240 mg x 1 iv with immediate apyrexia. The patient showed impressive clinical response and was discharged in 32 days.

**Discussion:** Listeriosis – though a rare entity- should always be considered in the differential diagnosis of fever in immunosuppressed patients, who may present with symptoms mimicking a relapse of their rheumatologic disease.

## Splenic infarction associated with acute Brucella mellitensis infection

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**Introduction:** Brucellosis is a zoonotic infection caused by the bacterial genus Brucella transmitted from infected animals with high prevalence in the Mediterranean countries. Vascular complication have rarely been associated with brucellosis, we report a case of splenic infarction associated with acute brucellosis.

**Case report:** A 40 years old man presented with pain in left flank and left upper quadrant starting 3 days before admission without fever; his medical history was unremarkable. Physical examination showed only increased tenderness in the upper left abdominal area with no signs of peritoneal irritation. Laboratory tests demonstrate normal CBC, high C-reactive protein, elevated LDH, coagulation tests within normal range. Abdominal ultrasound revealed various hypodense lesions in the spleen. Abdominal CT with contrast shows persistence of these lesions without uptake of contrast, suggesting splenic infarctions. During hospitalization patient recall consuming unpasteurized milk products few weeks before admission, Rose Bengal testing for Brucella was positive, and Brucella agglutination test was positive at titer of 1:640, blood culture was positive for Brucella. Patient was treated with IV gentamycin, oral doxycycline, and analgesia as needed. His

clinical course was favorable. 6 months later Brucella agglutination titer decreased to 1:160.

**Discussion:** Splenic infarction maybe segmental or global caused by hematological disorders and embolic event associated with the presence of anti-phospholipids antibody and infective endocarditis. In brucellosis splenic infarction is extremely rare; only 3 cases were reported in English literature. Endothelial lesions due to local germs infiltration and vasculitis due to direct endothelial damage by this pathogen might be the most plausible explanation. The most common presentation symptoms of splenic infarction is left upper quadrant abdominal pain in up to 70% of cases, CT scan with intravenous contrast is the current diagnostic modality of the disease, the principal mainstay of therapy is conservative analgesia and antibiotic. Brucellosis should be considered in patient with splenic infarction particularly in those living in endemic area.

### **Methicillin-resistant Staphylococcus aureus at a department of infectious diseases in Lisbon 2001-3 and 2011-3**

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**Objectives:** Staphylococcus aureus resistant to methicillin (MRSA) is a leading cause of nosocomial infections, resulting in a worse clinical outcome and putting an increased economic burden on the health system. Further, the situation has become more problematic by an increasing prevalence of intermediate resistant clones towards vancomycin. The prevalence of MRSA in Europe is 17,8%, with important geographical variations. Portugal comes around with a prevalence of 54%, correlated to the predominant clone EMRSA-15 and, conferring cross-resistance towards gentamicin, sulfamethoxazole/trimethoprim and tetracycline in 10 to 20% and towards rifampicin in 10% of the cases. The aim of the study to investigate the clinical impact as well as the actual resistance profile of MRSA at our department of infectious diseases.

**Methods:** The authors proceeded with a retrospective, observational study reviewing the files of all admitted patients in two time frames: 2001-3 and 2011-3. Of these, we selected all cases with confirmed infections by MRSA for further analysis. Parameter like age, gender, HIV status, risk factors, clinical aspects, type of biological specimen – which were culture positive, and their sensibility profile were registered.

**Results:** A total of 127 Staphylococcal infections were registered in 96 patients. Of these, 38 were caused by MRSA, with a significant increase in the incidence for the last three years (23/1000 admissions in 2011-13 versus 7/1000 admissions in the years from 2001-3). In 2001-3 they were responsible for 132 bed-days/1000 bed-days totally, but in 2011-13 they corresponded to 359/1000 bed-days. No MRSA infection was acquired in the community. While the first period was dominated by bloodstream and soft skin tissue infections the last period between 2011-3 had an overwhelming fraction of pulmonary infections, followed by bloodstream infection and to lesser extent osteomyelitis. Sensibility testing revealed resistance towards clindamycin in 74%, against

gentamicin, tetracycline and sulfamethoxazole/trimethoprim in 16% of the cases each. All isolates resistant to gentamicin were also resistant to tetracycline and sulfamethoxazole/trimethoprim. No resistance towards linezolid or daptomycin was apparent. The determination of MIC for vancomycin revealed to be 1 in 23% and 1,5 in 10%. Lacking data on sensibility testing in the first period precluded any comparative study. Nonetheless, gentamicin sensibility had been tested in the first observed period, confirming an overwhelming overall resistance towards this antibiotic.

**Conclusions:** Although the study is small in size, it confirms a growing impact with prolonged admissions of patients with MRSA infections at our hospital. Increasing intermediate sensibility with MIC of 1,5 and clinical more complicated infections might have contributed to this fact. Analysis of the sensibility profile confirms increasing extended resistance towards clindamycin, tetracycline and sulfamethoxazole/trimethoprim compatible with the prevalent clone of EMRSA-15 in Portugal.

### **Tuberculosis – the obvious and the less obvious**

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**Introduction:** Tuberculosis is a multisystemic disease with vast forms of presentations and manifestations. Although typically it consists of pulmonary involvement, virtually any organ might be affected whether in primary or secondary infection.

**Case reports:** Review of 4 cases of tuberculosis in an internal medicine ward. A typical presentation form with pulmonary involvement and 3 cases with pleural, abdominal and cutaneous involvement. A 52 years old man with no relevant medical history, admitted with a history of fever and productive cough in the previous 2 months. Radiologically he had fibrocavitary lesions compatible with pulmonary tuberculosis. Sputum smear positive for acid fast bacilli, confirmed on culture tests. A 93 years old woman without relevant medical history admitted with history of intermittent fever and left cervical anterior adenopathy in the previous month. Sonographic evaluation revealed adenopathy with necrotic center. On CT-scan there was presence of multiple adenopathy on juxta-diaphragmatic, and peri-aortic locations. Ganglionar biopsy – excluded signs of neoplastic process and positivity for acid fast bacilli. A 34 years old woman readmitted to hospital because of fever and dyspnea after completion of broad spectrum antibiotics for community-acquired pneumonia with left pleural effusion, previously interpreted as parapneumonic. Cultural exams for blood, urine, pleural effusion samples – negative. After various drainage sessions, she was submitted to thoracoscopy with identification on Mycobacterium tuberculosis on PCR assay. A 69 years old woman with history of obesity, heart failure, hypertension, atrial fibrillation, various admissions because of heart failure, with ascites, febrile illness of unknown origin and weight loss of 15 kg in the previous 2 months with negative blood culture tests. After drainage of pleural and abdominal fluids – identification of Mycobacterium tuberculosis on PCR assay.



**Conclusion:** The authors intend to alert to other forms of tuberculosis beyond the usual fibrocavitary pulmonary lesions, as the lack of specificity of its symptoms make it a frequently overlooked diagnosis especially with extra-pulmonary involvement.

## Purulent pericardial effusion with cardiac tamponade secondary to methicillin-sensitive *Staphylococcus aureus* infection

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**Introduction:** Pericardial effusion is a common finding in clinical practice, frequently as a manifestation of systemic disease. It has a varied etiology and its approach varies according to its haemodynamic repercussion.

**Case report:** 71 years old male, with a history of alcoholic liver disease, was admitted to the hospital with dyspnea and lower extremity edema. Physical examination: oriented, icteric, afebrile, eupnoeic at rest, hemodynamically stable; auscultation – diminished breath sounds; exuberant lower extremity edema. Blood tests revealed altered hepatic function. He was admitted to internal medicine ward with decompensated chronic liver disease. During hospitalization the patient develops ascites and abdominal pain. After drainage of ascitic fluid compatible with infection he starts a course of cefotaxime. Despite therapy he presents clinical deterioration, with hypotension and necessity of vasopressor support, signs of increased jugular venous pressure and diminished heart sounds on auscultation. A transthoracic echocardiogram showed pericardial effusion with collapse of the right chambers of the heart after which a pericardiocentesis was performed draining 400 cc of hematic liquid with isolation of methicillin-sensitive *Staphylococcus aureus* and subsequent alteration of antibiotic therapy to flucloxacillin and clindamycin with favorable outcome.

**Discussion:** Bacterial etiology can represent up to 30% of pericardial effusions and are related to a high probability of cardiac tamponade. Its diagnosis is frequently made when tamponade is imminent or present, and is confirmed by cultural tests. *Staphylococcus aureus* is among the commonest culprits. The authors report a form of pericardial effusion with dramatic haemodynamic repercussion and intend to alert to the importance of high level of suspicion and interpretation semiologic findings before irreversible haemodynamic deterioration.

## Perceptions and attitudes of patients about adult vaccination and their vaccination status: still long way to go?

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**Objectives:** Immunization is one of the most effective public health measures to prevent disease but vaccination rates in

adult populations still remain below the targets. In this study we aimed to determine the patients' attitudes and perceptions about vaccination and the vaccination status of adult patients who have indications for them.

**Methods:** A cross-sectional study was conducted between October 2014 and May 2015, at general internal medicine outpatient clinics of a university hospital. Adult patients were asked to fill a questionnaire about their perceptions and attitudes about vaccination and their vaccination status.

**Results:** 512 patients were recruited to the study with a mean age of 39±14 years. 15.2% of the patients thought that adults do not need to be vaccinated, whereas 80.1% thought adults should be vaccinated and 4.7% of them had no idea. There was no relationship between patients' attitudes towards vaccination and gender, marital status, educational degree or the place they were living. 45.3% of the patients who thought that adults should not be vaccinated stated that "vaccines are not necessary for adults", 21.9% of them was afraid of the side effects, 14.1% stated that the vaccines are useless. 1 of them told vaccines are not appropriate and 4.7% of them just thought vaccines were money trap. When the patients who thought that adults should be vaccinated were asked about which vaccination should be done to adult patients the top ranking answers were influenza (31.1%), hepatitis B (16.4%), tetanus (15%). Only 36.1% of the patients stated that vaccination was recommended to them in their adult life. The most common vaccine recommendation was influenza and hepatitis B (18%, 10.5%). 48% of them stated that they were vaccinated at least once in their adulthood. The most commonly received vaccination was tetanus in general, while influenza vaccine was the first among patients with chronic lung disease, heart disease and diabetes. But their coverage was still low (34.3%, 62.5%, and 26.5%).

**Conclusions:** This study showed us that there is a lack of knowledge about adult vaccination in patients, inconsistent assessment of vaccination status, low recommendation rate by the physicians and also low vaccination coverage. The physicians should not miss the opportunities like routine visits in outpatient clinics to provide accurate information about vaccination to the patient and for vaccine administration.

## Visceral leishmaniasis in an immunocompetent patient in Southern Europe

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**Introduction:** Visceral leishmaniasis (VL) which is also known as kala-azar, is primarily caused by *Leishmania donovani* and *Leishmania infantum*. Mediterranean VL has a large canine reservoir and the majority of adult cases occur in HIV infected patients. Other forms of immunosuppression also predispose to VL. VL typically presents with fever, splenomegaly, hepatomegaly, lymphadenopathy, asthenia, weight loss, edema, ascites, anemia, leukopenia and thrombocytopenia.

**Case report:** We report the case of an otherwise healthy 74 years old man, who presented with a 5 month history of abdominal

discomfort localized to the right hypochondriac and epigastric regions and postprandial fullness. Physical examination revealed hepatomegaly and splenomegaly. Laboratory tests showed platelet count of  $65 \times 10^9/L$ . Reobserved after 3 weeks, the patient referred a 3 week history of daily low grade vespertine fever and night sweats, as well as progressive asthenia, anorexia and weight loss. Laboratory tests showed pancytopenia. The patient was admitted to the hospital ward for further study. Physical examination showed pale skin, peripheral edema and ascites. Laboratory tests showed polyclonal hypergammaglobulinemia and liver enzymes elevation. The patient was HIV negative. Other serologies (Borrelia, Toxoplasma gondii, Epstein-Barr virus, Cytomegalovirus, Coxiella burnetii, Brucella) were also negative. Hemocultures were negative. Autoimmunity tests were negative. Abdominal ultrasonography showed hepatomegaly and considerable splenomegaly. Bone marrow aspirate showed Leishmania amastigote forms and acute leukaemia was excluded. Serologic studies were also positive for Leishmania spp. When asked retrospectively, the patient referred that his dog had recently passed away with symptoms which were compatible with leishmaniasis. Treatment was successfully performed with liposomal amphotericin B at a dose of 3 mg/kg/day from days 1 to 5, and days 10 and 21. His blood count normalized, and his symptoms improved with regression of hepatomegaly and splenomegaly, regression of ascites, absence of fever, weight gain and progressive recovery of appetite.

**Discussion:** Although the differential diagnosis of conditions that present with constitutional syndrome, hepatomegaly and splenomegaly and thrombocytopenia is vast, the history and clinical presentation, as well as a high level of clinical suspicion, allowed the diagnosis of VL. Prompt appropriate treatment allowed clinical improvement.

### **Necrotizing pneumonia caused by Pantone-Valentine leukocidin-producing methicillin-sensitive Staphylococcus aureus**

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**Introduction:** *S. aureus* producing Pantone-Valentine leukocidin (PVL) is associated with severe skin infections and necrotizing pneumonia in patients with immunological deficits. It is usually associated to methicillin-resistant strains, but methicillin-sensitive strains may also have this feature. We report a case of necrotizing pneumonia by *S. aureus* methicillin-sensitive (MSSA) acquired in community with production of PVL in an immunocompetent patient.

**Case report:** An 81-year-old woman with history of hypertension, who submitted fall with loss of consciousness and disorientation, without infectious clinic previous. She was admitted because of respiratory sepsis. Piperacillin-tazobactam empirical was started. Physical examination showed crackling bilateral scattered right dominance. Chest radiography showed bilateral infiltrates. Laboratory test showed a worsening of renal function and high creatin kinase. MSSA was isolated in blood cultures, so cloxacillin was associated to treatment and transthoracic echocardiogram was requested without vegetations. Differential

diagnosis was made between: respiratory infection of viral etiology, overinfected by *S. aureus* and secondary bacteremia, primary pneumonia by MSSA and secondary bacteremia (most likely), confusion syndrome with aspiration into lungs and pneumonia and secondary bacteremia by *S. aureus*. Influenza virus test was negative; MSSA was isolated in new blood cultures. Transesophageal echocardiogram without evidence of endocarditis was requested to persistent bacteremia. Chest-CT showed bronchiectasis, bilateral infiltrates consistent with disseminated pulmonary microabscesses and consolidation of right upper lobe with cavitation inside. Mantoux was negative. Final diagnosis: bacteremic necrotizing pneumonia by MSSA. Cloxacillin for 4 weeks was remained by complicated bacteremia. PVL determination was requested because of aggressiveness of pneumonia, showing a strain of PVL-producing MSSA.

**Discussion:** PVL has been considered to be a virulence factor associated with severe pneumonia. It's a cytotoxin that appears to be associated with *S. aureus* causing SSTIs and necrotizing pneumonia, pneumonia is frequently severe and rapidly progressive, often leading to septic shock and resulting in high mortality rate (lung necrosis, abscesses and empyema). Make a proper and long-lasting antibiotic treatment and discard concomitant processes that facilitate infection by this type of germ will be important in these cases.

### **Psoas muscle abscess in a hemodialyzed patient: case report**

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**Introduction:** Psoas abscess (PA) – a collection of pus in the iliopsoas muscle is a rare disorder. Primary PA are usually caused by hematogenous/lymphatic spread from a distant site, while the secondary ones result from direct dissemination from an adjacent structure.

**Case report:** 76-year-old man with history of type 2 diabetes mellitus (DM) and end-stage renal failure in hemodialysis (HD) who presented with progressive lumbar back pain that irradiated to the thigh associated with gait limitation, nausea, vomiting and fever for the last 24 hours. He denied trauma, recent travelling and contact with animals. Clinically he presented shivering and polypnea; he was hemodynamically stable, but had hypoxemia. Cardio-pulmonary auscultation revealed crackles and rhonchus. Abdomen, genito-urinary tract and lumbar area examination were normal. No signs of skin/arterio-venous fistulae infection were found. Laboratory showed normocytic normochromic anemia (Hb 9 g/dL), white blood cell  $4,74 \times 10^9/L$ , thrombocytopenia  $50 \times 10^9/L$ , elevated C-reactive protein (93 nmol/L) and myoglobin (298,5 ng/mL). Thorax and lumbar back X-rays and abdomino-reno-pelvic ultrasounds didn't show any sign of infection. 2 sets of blood cultures were collected and ceftriaxone and vancomycin were empirically initiated due the suspicion of osteomyelitis/sacroileitis/PA as the cause of the sepsis. The magnetic resonance showed a right PA and a right piriform abscess. Taking into consideration the small size of the abscess and the isolation of a methicillin-susceptible *Staphylococcus aureus* we changed to an antibiotic therapy

strategy alone with flucloxacillin. The patient remained afebrile, the inflammatory parameters decreased and the lumbar back pain progressively improved. Heart ultrasound excluded endocarditis. He was discharged at day 15 of hospitalization after completing 8 days of flucloxacillin therapy which he continued for more than 4 weeks. At the reevaluation he was completely asymptomatic and had neither clinical nor laboratory signs of infection.

**Discussion:** DM, renal failure, HD and other forms of immunosuppression are risk factors for the development of PA. Although the first line therapy for this condition is its drainage, in those cases where the size of the abscess is less than 35 mm a strategy of antibiotic therapy alone can be tried. Our patient was fully recovered after 5 weeks of antibiotic therapy. Besides being a rare condition, physicians should be aware of this disorder in order to start appropriated treatment as soon as possible.

## Infestation by *Blastocystis hominis*: to treat or not to treat

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**Introduction:** The *Blastocystis hominis* was described almost 80 years ago, but still there are some puzzling aspects about this intestinal parasite, particularly about its taxonomy and pathogenicity. The *Blastocystis hominis* may be isolated in the feces of people with and without gastrointestinal manifestations, immunocompetent or immunocompromised, revealing contaminated water and/or food intake. It has a wide genetic diversity, which could explain the fact that there are asymptomatic carriers and patients with severe symptoms. It can cause fatigue, abdominal pain, change in bowel habits, bloating, skin alterations and arthralgia.

**Case report:** We present the case of a 23 years old male, born in Guinea-Bissau, from where he came to study nonspecific abdominal pain. Physical examination was normal. Laboratory tests: hemoglobin 14.1 g/dL, leukocytes 4.74x10<sup>9</sup>/l, neutrophils 50%, eosinophils 2%, C-reactive protein 0.1 g/dL, anti-HIV 1 and 2 were negative. The stool ova and parasite test revealed the presence of many cysts of *Blastocystis hominis*. The patient was medicated with metronidazole with notorious clinical improvement.

**Discussion:** We consider that this infectious agent should be always considered as potentially pathogenic and that a therapeutic trial should always be carried out, given the potential clinical improvement as in the present case.

## Endocarditis and spondylodiscitis caused by methicillin-resistant *Staphylococcus aureus*: clinical association

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**Introduction:** In the last years, the number of methicillin-resistant *Staphylococcus aureus* (MRSA) infections has been

increasing. Determining whether patients with documented MRSA bacteremia have infective endocarditis or other metastatic focus of infection (as in bone, joints, kidney and/or lung) remains a challenge.

**Case report:** We present a clinical case of infective endocarditis associated with spondylodiscitis, both caused by MRSA, in a 67 years old female patient, with morbid obesity, hypertension, diabetes mellitus type 2, chronic kidney disease stage 3, permanent atrial fibrillation and heart failure. She was recently admitted to another hospital because of sepsis caused by MRSA, having been treated with daptomycin for 21 days. 2 weeks after discharge, she was admitted in our hospital because she presented confusional syndrome, prostration and dehydration, elevated inflammatory parameters (leukocytes 12760x10<sup>9</sup>/L, neutrophils 88%, C-reactive protein 20 mg/dL) and hyperglycemia 10.9 mmol/L. The chest X-ray showed foci of pulmonary condensation and moderate left pleural effusion. MRSA was isolated in blood cultures and the patient was medicated with vancomycin. The transthoracic echocardiogram did not show any vegetation, but transesophageal echocardiogram detected vegetation in native aortic valve. In search of other metastatic focus of infection, we performed thoraco-abdominal-pelvic CT, that revealed spondylodiscitis of D8-D9 with spinal cord compression confirmed by MRI, and the patient was submitted to neurosurgery.

**Discussion:** We conclude that it is very important to perform the systematic search for septic focalizations in patients with MRSA infections, in order to prescribe the appropriate treatment.

## Tuberculous meningitis: a diagnostic and therapeutic challenge

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**Introduction:** Central nervous system (CNS) involvement in tuberculosis (TB) is rare. It often presents with non-specific signs and symptoms, making the diagnosis difficult and frequently post-mortem. A high degree of suspicion is essential to initiate therapy early in the disease course and to minimize long-term sequelae and death.

**Case report:** 72 years old diabetic woman with chronic kidney disease on hemodialysis through an arteriovenous fistula presented to the emergency department with fever, asthenia and anorexia within the last 15 days. She had no respiratory, gastrointestinal or urinary tract symptoms and no history of headache or vomit. In the previous months she had had multiple broad-spectrum antibiotic courses due to relapsing fever associated with urinary tract infections. Blood cultures were repeatedly negative; and endocarditis, spondylodiscitis and intra-abdominal foci were excluded. She had a Glasgow Coma Scale of 14 (E3V5M6), but no focal neurological signs or meningeal signs. Vital signs were normal; there were no skin rashes and no abnormalities on cardiac, pulmonary and abdominal examination. She had no hypoxia or lactic acidosis. Laboratory analysis: microcytic anemia (8,0 g/dL), leucopenia (3,180/microL), elevated C-reactive protein (92,5

mg/L) and erythrocyte sedimentation rate (102 mm/h), normal hepatic parameters and sodium of 133 mEq/L. Chest radiograph was normal. The patient rapidly developed worsening lethargy, confusion and left facial nerve palsy. Cerebral CT had no lesions. Lumbar puncture showed a clear cerebrospinal fluid (CSF) with 216 cells/microL (85% polymorphonuclear), decreased glucose (23 mg/dL) and increased protein count (2,76 g/L); ADA in CSF was 28 U/L. HIV was negative. She was started on a four-drug antituberculous regimen and corticosteroids (60 mg/day prednisolone). Chest CT showed multiple millimetric nodules in the lung parenchyma. She had progressive neurological worsening and died 6 days later. The CSF acid-fast microscopy was negative but the PCR and the culture were positive for *M. tuberculosis* (susceptible to all tested drugs). Gastric aspirate cultures were negative.

**Discussion:** The diagnosis of tuberculous meningitis is difficult since presenting symptoms and findings on examination are often nonspecific. CNS tuberculosis associates with high mortality and should be kept in mind in patients with risk factors, such as diabetes and renal failure, in order to initiate therapy with the least possible delay.

## **A huge clinical dilemma: immunosuppressants or antibiotics? A case report of visceral leishmaniasis**

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**Introduction:** Haemophagocytic lymphohistiocytosis (HL) includes the familiar haemophagocytosis and the secondary haemophagocytic syndrome. Secondary HL may occur at any age, commonly in association with immunosuppressive therapy, secondary to viral infections, protozoal infections and malignancy. These disorders are indistinguishable pathologically and are characterized as 'reactive' disorders of antigen-presenting and antigen-processing histiocytes. The association between HL and visceral Leishmania (VL) has been most frequently described in child, this association is rarely found in adults and when HL and VL are present together the diagnosis of the disease may be difficult. The authors describe a case to call the attention to an infrequently association that can be mortal if the diagnosis does not achieved rapidly.

**Case report:** A 66 years old man who presented complaints of 39°C fever, chills and generalized muscular pain, 1 week before his admission. He had diabetes, hypertension and coronary disease with coronary bypass 1 month before his admission. He referred close contact with dogs and sheep. Without another important antecedents. At physical exam hepatomegaly and splenomegaly were only found. The bloods tests showed, hemoglobin 8,4 g/dL, leucocytes 1900/mm<sup>3</sup> (800 neutrophils 900 lymphocytes), platelets 63.000/mm<sup>3</sup>, fibrinogen 455 mg/dL, ferritin 9400, Leishmania serum serology 1/160. A bone marrow biopsy was performed and it showed compatible findings with HL, the polymerase chain reaction (PCR) of Leishmania in bone marrow was positive. A HL diagnosis was made and began amphotericin B treatment for the Leishmania infection as well as dexamethasone and cyclosporine for the HL treatment. The patient was completely recovered and

discharged after 2 weeks of treatment.

**Discussion:** Visceral leishmaniasis revealed by HL is an extremely rare event that can cause considerable diagnostic difficulty. Furthermore, serologic testing for Leishmania may be negative at the onset of the disease. For our patient, Leishmania infection was confirmed by PCR in the bone marrow. The diagnostic delay plays an important role in the final outcome of these kinds of patients. HL is a potentially fatal entity with a specific treatment that can change the illness natural history.

## **Peritoneal tuberculosis in a Sudanese non-HIV immigrant patient**

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**Introduction:** Tuberculosis (TB) can involve any part of the gastrointestinal tract and is the sixth most frequent site of extrapulmonary involvement. The peritoneum and the ileocecal region are the most likely sites of infection followed by the liver, spleen and lymph nodes.

**Case report:** A 29 years old Sudanese immigrant presented to our department with abdominal pain fever, night sweats and diarrhea for the past 20 days. On physical examination there was evidence of ascites. Chest and abdomen radiography were unremarkable. Abdominal CT scan confirmed the presence of ascites and peritoneal implants. He was empirically started on ceftriaxone. Paracentesis demonstrated ascitic fluid with a serum ascites albumin gradient (SAAG) 0.46 g/dL and 1757 cells  $\mu$ /L with lymphocyte predominance 60%. Blood and fluid cultures for bacteria and TB were negative; Ziehl-Neelsen stain and polymerase chain reaction (PCR) for TB performed on the ascitic fluid were negative. Tuberculin skin and HIV testing were also negative. His condition declined and after surgical consult, peritoneal biopsy was performed. Tissue cultures were positive for *M. tuberculosis*, biopsy revealed caseating granulomas and acid-fast bacilli. Starting a 4-drug anti-TB regimen (rifampicin/isoniazid/ethambutol/pyrazinamide) his status improved. On the 7th day of treatment he abruptly deteriorated, which was attributed to paradoxical reaction to anti-TB treatment followed by respiratory failure and intubation. Hydrocortisone was initiated considering the possibility of adrenal insufficiency. 2 days later, the patient was extubated and eventually discharged.

**Discussion:** Peritoneal TB occurs in three forms: wet type with ascites, dry type with adhesions and fibrotic type with omental thickening and loculated ascites. The peritoneum is usually involved as a result of hematogenous spread from a pulmonary focus or direct spread from adjacent organs. The gold standard for diagnosis is microorganism isolation from ascitic fluid or biopsy specimen. It is of note, that our patient had positive PCR for TB of the omental tissue despite having negative smear, PCR and culture of the ascitic fluid.

**Conclusions:** TB peritonitis should be considered in any patient with abdominal pain, weight loss, fever, and lymphocytic dominant ascites with SAAG <1.1 mg/dL especially when originated from an endemic area regardless of immunocompetence status. Diagnostic yield of smear and culture are low; peritoneal biopsy is helpful and often necessary.

## Cytomegalovirus ileitis in an immunocompetent elderly woman

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**Introduction:** Cytomegalovirus (CMV) is a member of Herpes virus family. Between 40 to 90% of the adult population have IgG seropositivity for CMV, and the disease manifests as atypical viral syndromes or mononucleosis in immunocompetent people. Immunosuppressed individuals, especially HIV infected patients with low CD4 counts or transplanted patients are in a high risk of severe CMV infection, with a high mortality rate. We hereby present a case of an immunocompetent elderly woman with chronic diarrhea due to CMV ileitis.

**Case report:** An 85 years old woman with a history of hypertension and cholecystectomy presented due to weakness, chronic diarrhea, vomiting and weight loss. She was afebrile with normal vital signs. Due to her symptoms persistence for more than 4 weeks, she had undergone endoscopies of the upper and lower gastrointestinal tract as an outpatient. These revealed atrophic gastritis and atypical thickening of the terminal ileum wall. While biopsies were pending, the symptoms persisted, leading to electrolyte disorders, so the patient was admitted to the hospital for intravenous fluid and electrolyte repletion. The third day of her hospitalization, the ileum biopsy revealed ileitis caused by CMV. HIV antibodies were negative and funduscopy was normal. The patient was treated with ganciclovir 2.5 mg/kg twice daily based on creatinine clearance (glomerular filtration rate 55 ml/min) for 21 days, with parallel monitoring of blood cell counts. Her symptoms gradually improved and she was discharged.

**Discussion:** CMV ileitis in immunocompetent people is believed to occur due to age-related B-, T- cells and cytokine dysfunction, along with concomitant impaired mucosal integrity, thus explaining why the disease tends to be more severe in elderly patients. Need for treatment is argued, as it has been shown that the 31.8% of immunocompetent patients aged <55 years old may exhibit spontaneous remission. However, fatal cases have been described, mainly in the elderly, rendering treatment a safe clinical decision.

## Pneumonia: usefulness of a short-term mortality predictor to assess appropriate hospital admissions

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**Objectives:** Pneumonia is an infection of the lower respiratory tract, and it is the most common infectious cause of death in the world. Hospital admission is expensive, particularly when it requires admission in the Intensive Care Unit. The aim is to establish whether the criteria for hospital admission are met

whenever there is a diagnosis of community-acquired pneumonia (CAP) with the use of a short-term mortality predictor.

**Methods:** Descriptive study with retrospective data collection. 100 patients admitted in the Service of Internal Medicine in 2012-2014 with a diagnosis of CAP. Criteria for admission based on CURB-65 scoring, with 1 point for confusion, blood urea nitrogen >20 mg/dL, respiratory rate >30 breaths per minute, blood pressure <90 mmHg or diastolic blood pressure <65 mmHg and age >65 years. A score >3 is considered an indication for admission.

**Results:** In the period observed, 100% of the patients had an age >65 years. 79% of the patients met two admission criteria: age and blood urea nitrogen levels. 16% met 3 criteria for hospital admission, and in 50% of the cases it was age, uremia and tachypnea. The other 50% showed confusion without tachypnea. 5% of the patients presented with more than 3 admission criteria.

**Conclusions:** The appropriate use of CURB-65 may be more objective to determine hospital admission and minimize health costs. Patients with higher scores must be assessed only as candidates to admission in the ICU. Although the patient may be assessed individually in the decision of an admission, a score >3 may complement this decision.

## Mortality and length of stay in hospitalized patients with influenza infection during 2014-2015 season

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**Objective:** The aim of this study is to evaluate the mortality and length of stay associated with all laboratory confirmed cases of influenza virus infection hospitalized during 2014-2015 influenza season.

**Methods:** We recruited all patients with positive laboratory test (either rapid test or PCR) for influenza type A or B during influenza season of 2014-2015 (1st October to 31st March) in our hospital. We analyzed the normal distribution of the sample, the relation between qualitative and quantitative variables using the Wilcoxon-Mann-Whitney test, and the relation between qualitative variables using the Chi-Square test. We assumed significant differences for values of  $p < 0.05$ . The statistical analysis was performed using SPSS v21.0 software.

**Results:** 384 patients were included in the study. The average length of stay was  $14.1 \pm 13.2$  days for influenza type A and  $16.4 \pm 20.2$  for type B, with no significant differences ( $p = 0.727$ ). Total mortality of the sample was 8.3%. Mortality rate was 7.4% for patients with influenza type A and 10% for patients with influenza type B, with no statistically significant differences ( $p = 0.443$ ). Dividing the sample into age groups, we found a mortality rate of 5.9% in the age range 18-65 years, and a mortality rate of 9.3% in patients over 65 years; there was no statistical relation between age and mortality ( $p = 0.285$ ).

**Conclusions:** In patients hospitalized with laboratory confirmed

influenza infection during 2014-2015 season, we found no differences in terms of mortality and length of stay between type A and type B influenza virus. There were no differences in mortality caused by influenza infection between age groups.

### **Acute transverse myelitis: a presentation of primary Human immunodeficiency virus infection**

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**Introduction:** Neurological syndromes are associated with Human Immunodeficiency virus (HIV) infection; however, acute transverse myelitis as a presentation is rare. The differential diagnosis includes a large number of pathologies and the diagnosis can be challenging.

**Case report:** A 47 years old man with medical past history of aortic stenosis and a lacunar stroke in 2009 was referred to the emergency department for one month history of fever, myalgias, headache, constitutional syndrome and a recently dorsal pain associated with a motor deficit on the right inferior limb. On physical examination he was afebrile, haemodynamically stable, revealed a facial erythema, cervical lymph nodes (inferior to 1 cm) and skin lesions compatible with axillar and inguinal dermatophytosis. Neurological examination revealed a left hemiparesis (grade 4/5) and a right crural paresis (grade 4/5) with increased reflexes and clonus and positive Babinski. Laboratory findings revealed a relative lymphocytosis with activated lymphocytes, hepatic cytolysis and he had negative result of western blot analysis for HIV two weeks before. He was admitted for investigation. A magnetic resonance imaging (MRI) of the brain showed ischemic microangiopathy and the medulla. MRI revealed a T2 hyperintensity in D2-D3, with 28mm with nonspecific characteristics. After a broad diagnostic work-up a primary HIV-1 infection was made. The patient initiated methylprednisolone and antiretroviral therapy with clinical improvement.

**Discussion:** The authors highlight the different and varied manifestations of HIV presentation, the importance of suspicion and the dramatic consequences if not diagnosed and treated. In this case, we emphasize also the challenge in diagnosis in a patient with motor deficits complaints and with a prior cerebral vascular event, in which another event could be the easiest diagnosis to think.

### **Infections by atypical Mycobacteria in patients with systemic lupus erythematosus**

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**Introduction:** Patients with systemic lupus erythematosus (SLE) are more prone to develop opportunistic infections due

to immunological defects and immunosuppressive therapy. We report a case of disseminated Mycobacterium avium complex (MAC) infection in a SLE patient together with a review of the literature. We report a clinical case from a tertiary university hospital.

**Case report:** A 37 years old woman presented with 4 months of low-grade fevers, night sweats and paroxysmal episodes of severe abdominal pain. Medical history included SLE with multiple organ involvement requiring steroid therapy and several immunosuppressant drugs, including rituximab. At the time of admission, she was on low dose steroids and mycophenolate. Laboratory findings were remarkable for the presence of pancytopenia, with CD4 cell count of 10/mm<sup>3</sup>. A PET-TC showed hypermetabolism and enlargement of abdominal lymph nodes, intestinal segments and spleen. A laparoscopic biopsy of abdominal lymph nodes led to the diagnosis of infection by MAC. Afterwards, the same microbe was also cultured in blood, feces and sputum samples. Despite the initial therapy with clarithromycin, amikacin and rifabutin, she continued with fever spikes and positive blood cultures. A splenectomy was performed because of the presence of splenic infarction together with persistence of bacteremia and worsening cytopenias. The clinical course was torpid, but eventually she recovered.

**Discussion:** After a review of the literature, we found 14 cases of systemic or disseminated NTM infections in SLE patients. Globally, 87% were female and mean age was 45.5 (SD 16.2). In most cases it was an infection by MAC (60%); other Mycobacteria involved were: *M. xenopi* – 2, *M. chelonae* – 2, *M. kansasii* and *M. marseillense*. 40% of the patients had disease duration of over 10 years and 73% were treated with high dose steroids and/or immunosuppressant drugs. Overall mortality was 20%. Risk of infection seems to increase with SLE duration and aggressiveness of therapy. Delay in diagnosis may lead to severe and disseminated infections. Given the widespread use of immunosuppressant drugs, a growing incidence of these infections among SLE patients will be expected, and clinicians should be more aware of these pathogens.

### **Leishmaniasis in a University hospital. Epidemiological analysis of cases diagnosed in the Hospital Principe de Asturias in Madrid in the period 1987–2012**

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**Objective:** To describe the epidemiological characteristics of diagnosed cases of cutaneous leishmaniasis (CL) and visceral (LV) and to analyze the incidence curve of leishmaniasis.

**Methods:** A retrospective descriptive study of all cases of cutaneous and visceral leishmaniasis diagnosed in the Hospital Principe de Asturias (HUPA) from 1987 to 2012. A data collection sheet was drawn up was conducted in which information is the medical records of region Leishmaniasis patients, these data were analyzed using the SPSS software.

**Results:** In the period studied 60 cases of leishmaniasis, 38 (63%) – were visceral and 22 (37%) – were skin. The overall mean age was 41, the average age was 36 years LV, and LC was 47 years, 97% are Spanish. In the group of LV 31 (82%) were male and 7 (18%) were female, in the group of LC 7 (32%) were male and 15 (68%) are female. In the first 5 years 1987-1991 were diagnosed in June (10%) including 4 leishmaniasis (7%) were LV and 2 (3%) were LC. In the second half 1992-1996 were diagnosed 16 (27%) cases of which 13 (22%) were LV and 3 (5%) LC. In the third 5 year period 1997-2001 they were found 14 (23%) of which 13 (22%) were LV and 1 (1%) was LC. In the fourth year period 2002-2006 11 cases, these 6 (10%) they were LV and 5 (8%) LC were found. In the fifth 5 year period 2007-2012 13 (22%) cases were found, 4 (7%) were LV and 9 (15%) were LC.

**Conclusions:** In our most serious cases were LV; however in the last 15 years have decreased LV cases while cases of LC have increased. Almost all cases were autochthonous. The LV was more common in men between 20 and 40 years while LC was more common in women between 40 and 70 years.

## Anaerobic bacteremia: a clinical problem in internal medicine

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**Objective:** To find out about the incidence and clinical characteristics of anaerobic bacteremia (AB).

**Methods:** Retrospective observational descriptive study about cases of AB from 2008 to 2012, in a 1500-bed tertiary hospital in the northwest of Spain. We made a descriptive statistical analysis of clinical characteristics, risk factors, origin, focal points, microorganisms, medical and surgical treatments and prognostic.

**Results:** We found 235 AB episodes. The mean incidence was  $48 \pm 8.4$  cases/year. The mean age was  $64.5 \pm 16.4$  years (32%,  $\geq 75$  year-old) and the mean Charlson comorbidity index was  $6.3 \pm 3.5$  with an ultimately or rapidly fatal disease of McCabe-Jackson Score in 60% of the cases. 50% patients had a neoplasm (30% hematological, 45% metastatic disease from colorectal cancer as first location in almost half of patients). In 80%, the neoplasm was the AB focal point. Abdominal focal was identified in the 40% but was unknown in almost 20%. 30% patients were admitted in Internal Medicine Department. At the AB time, a third part of them had severe sepsis or septic shock, requiring admission in the ICU. In 30%, the infection was produced by multiple microorganisms, an aerobic microorganism was isolated in the third part of them. The anaerobic microorganisms more frequently isolated were *Bacteroides* spp. (49%), *Clostridium* spp. (25%), *Fusobacterium* spp. (11%). 65% cases needed a surgical treatment, but it was performed only in a bit more than half of them. The 30-day mortality was almost 30% of cases, being the attributable mortality 17%. We could not find differences in the mortality according to comorbidities, except in patients who take corticosteroids. There is an inclination to greater mortality between patients in whom the surgery was indicated but not made.

**Conclusions:** 1) AB is a common entity and it represents a clinical problem in medical departments. 2) Patients are elderly

and have a complex comorbidity. 3) Abdominal focus is the most frequent but in a significant percentage of them we could not identify the focus, restricting the clinical probability of AB suspicion. 4) They are severe infections with elevated septic shock and attributable mortality rates. 5) The mortality was only statistically related with chronically corticosteroid consumption.

## Prevalence of metabolic syndrome in HIV patients under highly active antiretroviral therapy at an outpatient clinic in Lisbon, Portugal

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**Objectives:** Highly active anti-retroviral treatment (HAART) reduced the morbidity and mortality associated with HIV. As the average life expectancy increases, also has increased the prevalence of obesity, high blood pressure, dyslipidemia and diabetes mellitus, known cardiovascular risk factors that bind in the definition of metabolic syndrome (MS). The aim of this study was to evaluate the prevalence of MS in HIV-infected patients under HAART.

**Methods:** Cross-sectional descriptive study, between July and December 2014, including 240 HIV patients on ART  $\geq 6$  months. MS was determined using the definitions: National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III 2001); American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI 2005) and International Diabetes Federation (IDF 2006).

**Results:** The mean age of patients was 47.4 years with a male predominance ( $n=166$ ; 69.2%) and almost all the patients ( $n=233$ ; 97.1%) were infected with HIV-1 (6 with HIV-2 and 1 HIV 1+2). According to the IDF definition, the prevalence of central obesity was 45.8%, high blood pressure 24.6%, hypertriglyceridemia 37.5%, low-HDL 39.2% and glucose intolerance 14.2%. The prevalence of MS according to NCEP/ATP-III 2001, AHA/NHLBI 2005 and IDF 2006 was 24.6%, 26.2% and 28.8% respectively. There seems to be increasing incidence with age, female gender, low level of instruction and long-term HAART, particularly with protease inhibitors.

**Conclusion:** Aging of the HIV population and long-term use of HAART is leading to a higher prevalence of MS in this specific population that should be taken into account particularly regarding the choice of antiretroviral drugs.

## HIV encephalopathy as clinical onset of late diagnosis of HIV infection: report of a case

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**Introduction:** HIV infection is associated with multiple neurological disorders; most of them are related to the involvement of the peripheral nervous system, in relation with the infection itself as well as to the toxicity of antiretroviral

therapy. Furthermore, neurocognitive deficits are more prevalent in HIV-infected regardless of antiretroviral therapy (ART) status or disease state. Despite this, HIV encephalopathy is a rare form of neurologic complication in HIV-infected patients.

**Case report:** We report a case of 55 years old woman, previously healthy, who developed psychotic symptoms of subacute evolution that progressed to acute confusional state. Brain imaging was normal and biochemical analysis and cerebrospinal fluid (CSF) cell counts showed no abnormalities. HIV serologic analysis was positive, being determined CSF viral load with a score of 11,260 c/ml. After making the diagnosis of late-stage AIDS stadium C3, the patient started ART with tenofovir, emtricitabin and cobicistat/elvitegravir. Within 2 months, the patient was examined showing no neurocognitive symptoms.

**Discussion:** HIV must be considered in the differential diagnosis of encephalopathy; owing to the direct effect of the virus in the CNS in along with the predisposition to develop other CNS disorders due to immunodeficiency. Moreover, in Spain, 30% of people infected with HIV are undiagnosed. In the last five years, the number of late diagnoses has not been reduced. This condition favors, individually, a poorer response to treatment and an increased risk of progression and, collectively, represents a public health problem. These circumstances encourage HIV testing in the main risk groups who have contact with the healthcare system.

## Metastatic human alveolar echinococcosis in Switzerland: a case report

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**Introduction:** We report an atypically advanced presentation of human alveolar echinococcosis, an endemic zoonosis in Switzerland.

**Case report:** A 62 years old woman with no relevant past medical history is evaluated for right upper quadrant abdominal pain, weight loss (15% of total body weight in 6 months), progressive dyspnea, itching and jaundice. There is no fever, nausea or diarrhea. Physical examination shows a cachectic patient with generalized jaundice; blood pressure is 100/50 mmHg, pulse rate is 90/min, and respiratory rate is 20/min. Oxygen saturation is 92% breathing ambient air. Abdominal examination discloses massive hepatomegaly. The patient lives in a rural area in Switzerland and usually eats inadequately washed forest fruits. She owns two cats that usually hunt rodents. Laboratory tests show: leukocyte count, platelet count, hemoglobin were normal, alanine aminotransferase 40 U/L, aspartate aminotransferase 49 U/L, alkaline phosphatase 802 U/L, total bilirubin 135 µmol/L, direct bilirubin 64 µmol/L, prothrombine time 45%, factor V 100%. Thoraco-abdominal CT scan shows multiple pulmonary masses up to 8 cm long axis diameter; a big hepatic cyst of 20 cm diameter, intra and extra hepatic bile duct dilatation, moderate ascites. Serological tests are positive for Echinococcus multilocularis. The clinical picture is consistent with human alveolar Echinococcosis, PNM stage IV (P4, N1, M1). Positron emission tomography scan shows high uptake in multiple pulmonary masses as well as in liver lesions. Endoscopic retrograde cholangiopancreatography is performed revealing

extrinsic compression of the common bile duct. After dilatation and drainage of purulent bile a biliary stent is placed. A long-term albendazole treatment is started. The patient subsequently presents bilateral lower limb deep venous thrombosis, biliary fistula, gram-negative sepsis, hemorrhagic shock, neutropenia due to albendazole, and liver failure. The high burden of liver involvement makes the patient non-eligible for surgical treatment. After multidisciplinary consensus palliative care is decided.

**Discussion:** Alveolar echinococcosis is a highly aggressive endemic zoonosis that resembles liver cancer. The disease is caused by the fox tapeworm Echinococcus multilocularis and is highly prevalent in Switzerland and in different regions of Europe. We report an atypically advanced clinical presentation of human alveolar echinococcosis.

## Descriptive study of HCV patients treated in the infectious diseases and digestive units in a secondary hospital in the last 5 years

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**Objectives:** Currently, chronic HCV infection treatment is undergoing significant change because of the fast evolution of treatment. An update of HCV prevalence and genotypes are critical in the development of strategies to act against HCV infection. The aim of this study is to describe HCV genotypes in patients infected with HCV and treated in the hepatology and infectious diseases units in the Health Area of Northern Cadiz.

**Methods:** Retrospective study of patients with active HCV infection, attended by gastroenterology and infectious diseases units during the period 2011-2015. HCV genotype was determined. Clinical, epidemiological and microbiological variables (sex, age, year of diagnosis, mechanism of infection, genotype, HIV/HBV co-infection, treatment and response prior to this) were analyzed. Data were collected from medical history. The genotype was obtained by the technique HCV Genotype 2.0 Assay-LiPA (Versant®HCV). For statistical analysis SPSS v19 was used.

**Results:** We included a total of 364 patients (295 men) in our study, mean age 49.9 years old (range 15-80 y.o.). 284 were mono-infected patients (78%), mean age 49.8 years old (15-80 y.o.) and 224 men. The remaining 80 patients (22%) were co-infected individuals (HCV/HIV), mean age 49.9 years old (range 30-65 y.o.) most frequently men (73/80). The genotypes distribution it was similar in mono-infected and co-infected with a higher prevalence of genotype 1 in both cases, 177 cases (62.3%) (Genotype 1a n=98, (55.4%), 1b n=75, (42.4%), 1 n=4) and 46 (57.5%) (Genotype 1a n=33, (71.7%), 1b n=13, 28.3%) respectively, followed by genotype 3 (n=67 (23.6%) and n=15 (18.8%)), 4 (n=32 (11.3%) and n=16 (20%)) and 2 (n=8 (2.8%) and n=2 (2.5%)). As for the way of transmission are differences between the two groups, patients mono-infected, the most common way of transmission is unknown (52.8%), followed closely by the parenteral way (45.1%); the sexual and vertical transmission were minimal (both 1.1%). The parenteral way was the most frequent for co-infected patients (70%) followed by the



unknown way (17.5%); sexual transmission accounted for 12.5%. **Conclusions:** The most frequent genotype was 1 in both HCV monoinfected subjects and co-infected with HIV (GT1a the most common) followed by 3, 4, 2. The most common way of transmission in our sample was parenteral in co-infected and unknown and parenteral in monoinfected.

## Treatment of *Clostridium difficile* infection in the Alcalá de Henares Hospital (Jan/2014 –March/2015)

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**Objectives:** The aim of this study is to describe how were treated the symptomatic colitis for *C. difficile* infection in the Hospital Príncipe de Asturias in Alcalá de Henares/Madrid.

**Methods:** Retrospective cases review of 79 patients with colitis and positive A/B toxin in faeces by ELISA or toxigenic culture. Concepts, adequate response: absence of symptoms sustained for 3 months. Persistent disease: not response 14 days after antibiotic therapy. Relapsing disease: the relapse of symptoms after 3 weeks of disappearance of the colitis. Severe disease: kidney failure, systemic impairment or sepsis.

**Results:** 70 cases, middle age 76,8 years old. In 78 we identified previous antibiotic exposition. The beta-lactams were the most associated (51 cases, 29 in monotherapy). After them the quinolones were present in 27 cases (14 in monotherapy). Others were identified in combination with the previous one. 52 patients had not severe disease, all of them were treated with metronidazole, 57% had an adequate response, 11% persistent disease and 31% relapsing disease. Severe disease was identified in 27 (34%) cases. 62% was treated with oral vancomycin, we obtained complete response in 17 cases and 30% of them had relapsing disease. The other 10 cases were treated with a combination: metronidazole/vancomycin, 4 (40%) presented relapsing disease. The relapsing disease was treated with oral vancomycin with adequate response. Only one patient received fidaxomicin and had an adequate response.

**Conclusions:** In our hospital the treatment with metronidazole was associated with an important rate of relapses and don't improve the response in association with vancomycin in the severe disease. The vancomycin is a good option to treat the severe disease and have a lowest rate of relapse than metronidazole. Fidaxomicin have better response in relapsing disease but in the clinical practice in our hospital hardly ever was used.

## Pancytopenia as a manifestation of infective endocarditis

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**Introduction:** Infective endocarditis is a systemic disease with an annual incidence of 3-10/100000 inhabitants. About 80% of the cases are caused by *Streptococcus* or *Staphylococcus*. The involvement of the mechanical valves occurs mainly in the first 3 months after surgery.

**Case report:** An 85 years old woman, with mechanical mitral prosthesis for 19 years and a biological aortic prosthesis for 3 months was admitted with a 5-day history of fever, malaise and nausea. Physical examination was unremarkable. There were no murmurs on cardiac auscultation. Blood test revealed a pancytopenia (anemia with hemoglobin (Hb) of 9.5 g/dL, leucopenia (white cell count (WCC) of 2.75/mcL) and thrombocytopenia with platelets (Plt) of 77/mcL) and a C-reactive protein (CRP) of 20 mg/dL. Urea and creatinine were within normal limits. Negative serologies and urine culture. Chest x-rays showed bilateral diffuse reticulonodular interstitial infiltrates which prompted initial empiric antibiotic therapy with amoxicillin/clavulanic acid. Two transthoracic echocardiograms showed no evidence of infective endocarditis. A subsequent transesophageal echocardiogram revealed 3 vegetations on the posterior region of the prosthesis ring, indicating mitral valve endocarditis. Two sets of blood cultures drawn on admission were positive for *Enterococcus faecalis* sensitive to ampicillin and gentamycin. With directed antimicrobial therapy the patient became afebrile and on the 4th day reached normalization of the WCC and Plt Count and a CRP of 3.4 mg/dL. The patient received a 6-week course of directed antimicrobial therapy with resolution of the situation.

**Discussion:** This case highlights the late occurrence of infective endocarditis in mechanical prosthesis valve by an agent that represents only 6% of endocarditis occurring more than 12 months after valve implantation. Although anemia and thrombocytopenia are common, pancytopenia in the context of infective endocarditis is rare, described only in individual cases or small series. We additionally stress the importance of the use of transesophageal echocardiography in the diagnosis of a suspected endocarditis.

## Analysis of ulcers in patients admitted to an internal medicine

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**Objective:** Our study analyses and describes the characteristics of positive cutaneous exudates in patients admitted to an internal medicine department in a six-month period.

**Material and methods:** Retrospective descriptive study of patients admitted to an internal medicine department during a 6 month period (July-December 2014) with positive skin exudates. We analyzed colonization or infection, type of ulcer, demographic data, comorbidities, microorganisms identified, and antibiotic treatment. We used the SPSS19 program to analyze the data.

**Results:** A total of 46 patients were studied during this period, with a total of 62 isolates being analyzed. The mean age was 86 years, a total of 26 women (56.5%), and 36 cases (58.1%)

were community acquired and the rest proceeded from nursing homes. The average length of admission stay was 13.4±10.4 days (1-55). The average index of PROFUND was 9.4, with a significant statistical difference between this and an increasing number of admissions. According to type of ulcer there were 30 (48.4%) pressure ulcers, 15 (24.2%) vascular ulcers, 8 (12.9%) were mixed, 7(11.3%) with cellulitis, and one case with late prosthetic knee infection. There were 48 cases (77.4%) of infection, and 14 cases (22.6%) of colonization, with increasing cases of infection in patients with more hospital admissions. The microorganisms isolated included 34 cases (54.8%) of fermenting gram-negative bacilli, and 27 cases (43.5%) SAMR. Antibiotic resistance was seen in 35 cases (56.5%), mostly being MRSA with increasing statistical significance as the number of admissions increased. The most commonly used empirical antibiotic was amoxicillin-clavulanic acid, needing adjustment in 40% of cases in their first admission. With respect to mortality there were 12 cases (19.4%), of which 9 were admitted from a nursing home.

**Conclusions:** We found that ulcers were more frequent in the elderly, with no difference between sexes, and that cognitive and functional decline were related to more hospital admissions. Pressure ulcers, in particular sacral, were more frequent, and there were more cases of infection compared to colonization. The most frequent microorganisms isolated were gram-positive cocci, in particular MRSA, with progressive increase in antibiotic resistance with each admission. The use of previous antibiogram reports when choosing an empirical treatment for successive admissions was found to have more successful outcomes.

### **Double focal compression bandaging. Local pressure over the wound bed, this avoids application of antibiotics**

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**Background:** The use of antibiotics because of an unfavorable clinical course of ulcers is an important mistake in clinical practice. A common mistake made by physicians is to attribute to the infection, an unfavorable clinical course of the venous ulcer, then, they ask for cell culture of wound bed for which antibiotics are prescribed, according to the test results.

**Objectives:** As a medical expert who is a member of the International Compression Club (ICC), I will demonstrate my experience treating venous leg ulcers, in primary care, and how it is possible to heal the ulcer, using only compression therapy. By using local pressure over the wound bed, the pathogenicity of bacteria can be obviously avoided. I only ask for cell culture of a wound bed if there are signs and symptoms of systemic infection.

**Material and methods:** By using the simple technique of compression therapy named "Double focal compression bandaging". To apply this technique safely in primary care, it is necessary to follow three simple steps: A/ To establish a differential diagnosis. B/ To establish a clinical diagnosis. C/ Measurement of the Ankle Brachial Index. Material: 1º Strong compression inelastic/ elastic bandage. 2º Normal compression bandage. 3º Gauzes, scissors and adhesive tape. 4º Physiological

saline solution. Diagnostic tools: Hand held Doppler ultrasound device / Camera / Tuning fork (128 Hz) /5.07 Monofilament / Scales / Leaflets for making Edinburgh claudication questionnaire.

**Results:** I asked for cell cultures of the wound bed, but despite finding bacteria, I did not prescribe antibiotics and we have achieved to heal the ulcer. In this clinical experience healing ulcers (85 patients), we have not observed infection. As an example, we show the results of cell cultures of five patients with venous ulcers. Result of cell cultures: *Pseudomonas auroginosa*, *Staphylococcus aureus*, *Proteus mirabilis*, *Streptococcus pyogenes*. Photographic sequences of the clinical course of the ulcer till its healing is shown. We achieved to eradicate bacteria in two cases, but not in another three cases. We observed bacteria in the wound bed and this fact means contamination, no infection.

**Conclusions:** No antibiotics should be administered, just because we detect bacteria in the wound bed. Focal compression over wound bed improves tissue perfusion and prevents the pathogenicity of the bacteria. We only use antibiotics, when we observe signs and symptoms of infection, such as cellulitis and/or fever.

### **Streptococcus pneumoniae – the great simulator**

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**Case report:** We present the case of a 62 years old man with past history of aneurysm dissection of the ascending and descending aorta with major aortic insufficiency, motivating the replacement of a mechanical aortic valve and aortic endovascular prosthesis. A month later, the patient was admitted at the hospital because of global aphasia, mutism, conjugate eye and head deviation to the left, right central facial palsy and right hemiparesis. On admission, he presented a status of SIRS, with neck stiffness, no heart murmurs and with decreased breath sounds in the lower 2/3 of the right hemithorax. During the etiologic study, a CT-angiography CE was conducted, revealing an asymmetry in the caliber of the middle cerebral artery (MCA) with less expression in the distal portion on the left. Facing the possibility of CNS infection, he underwent lumbar puncture with the following characteristics: elevated opening pressure, the presence of 12 cells (some PMN), hypoglycorrhachia and hyperproteinorrhachia. In this context, empirical antibiotic therapy was introduced, using ceftriaxone, ampicillin and vancomycin all in meningeal doses, associated with dexamethasone. The patient also underwent chest radiography and CT-scan that confirmed pneumonia of the right upper lobe and, to exclude endocarditis, a transthoracic echocardiography was performed and no suggestive images of vegetations or abscesses were found. Later, the visualization of Gram + diplococci (CSF and blood cultures) suggestive of *S. pneumoniae* (MIC 0012), allowed us to start directed antibiotherapy with penicillin. The study was completed by MRI imaging which demonstrated recent posterior capsulo-lenticular stroke on the left hemisphere (LH) and stenosis of the M1 segment of the left MCA. Finally, there was a good clinical

outcome with complete recovery of the neurological deficits. This allowed the diagnosis of pneumonia to *S. pneumoniae* with haematogenous spread and subsequent meningeal infiltrating, complicated by cerebral vasculitis lesions conditioning a pseudo-stroke of the LH.

## Diagnostic value of clinical predictors for tuberculosis before assessing a screening test

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**Objectives:** Tuberculosis is considered as a serious public health problem in the world, so it is important to use effective criteria for early diagnosis of disease. The aim of this study was to evaluate the effectiveness of single screening measure for TB disease and improve the early diagnostic measures in suspected TB patients.

**Methods:** 80 smear positive and 70 negative patients were enrolled in the study. They were studied according to specific signs and symptoms which are common in TB disease, such as prolonged fever, weight loss, dyspnea, anorexia, night sweats, chest pain, low back pain, sputum production, abnormal radiologic and auscultation findings. The prevalence of each item was compared between two study groups.

**Results:** All of the patients have experienced prolonged cough. The prevalence of fever, weight loss, dyspnea, anorexia and night sweat close contact to TB infected patients and family history of TB disease in patients with positive smear results were significantly higher than the negative smear patients ( $p < 0.001$ ). 85% of the patient had the history of these symptoms during the last weeks. The prevalence of chest pain and sputum production didn't significantly differ in two study groups.

**Conclusions:** Using other predictors such as fever, weight loss, dyspnea, and night sweat in combination with persistent cough (as the main symptom) would increase the quality of diagnostic yields in early TB patients. In addition, a history of close contact to TB infected patients or family members should be considered during the visit of TB suspected patients.

## Herpes simplex virus encephalitis – two case reports

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**Introduction:** Herpes simplex virus type 1 (HSV-1) encephalitis is the most common cause of sporadic fatal encephalitis worldwide. It is often characterized by the rapid onset of fever, headache, seizures, focal neurologic signs, and impaired consciousness. Untreated, the fatality can approach 70%. Even with appropriate diagnosis and treatment, mortality may still be as high as 20 to 30%. The infection arises in all age groups, with one-third of all cases occurring in children and adolescents.

**Case reports:** Here we present two cases: One of a woman of 62 years old, with chronic medication for hypertension and anxiety, which appeared in the emergency department with nausea, vomits, confused speech and then developed right hemiparesis and aphasia. It was performed head computed tomography (CT) scan that revealed left temporal cortical and subcortical hypodensity, so initially it was diagnosed ischemic stroke, but then she developed fever, maintain impaired consciousness and the neurologic deficit, so it was performed lumbar puncture (LP), after another CT. Examination of the cerebrospinal fluid (CSF) showed a lymphocytic pleocytosis and elevated protein, it was also performed a magnetic resonance imaging (MRI), which abnormalities were typical of HSV encephalitis. While awaiting results of PCR testing, treatment was initiated. The other patient was a healthy 68 years old woman that presented headache, nausea, fever, agitation, confusion and then develop focal seizures. It was performed head CT scan, MRI and LP that were suggestive of encephalitis. While awaiting results of PCR testing, treatment for HSV encephalitis was initiated. In both cases CSF HSV-1 PCR was positive. Despite the second case was early diagnosed, both patients developed diminished comprehension, paraphasic spontaneous speech, impaired memory, and loss of emotional control.

**Discussion:** HSV-1 encephalitis is a devastating disease with significant morbidity and mortality, despite available antiviral therapy. It is extremely important that the diagnosis be entertained early in any patient who presents with suggestive signs, symptoms, laboratory, and imaging studies since it is among the more treatable of the infectious etiologies of encephalitis. But even with early administration of therapy most survivors will have significant neurologic deficits like the second case reported.

## Neurosyphilis in the modern era

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**Objectives:** Syphilis is a chronic infectious disease caused by *Treponema pallidum*. The central nervous system is affected early during the infection, and about 30% of untreated individuals develop chronic CNS disease. The incidence of neurosyphilis declined dramatically after the advent of penicillin, but in recent years, the number of reported cases has increased, both in immunocompetent and immunocompromised individuals. **Methods:** The authors present a retrospective analysis of neurosyphilis cases diagnosed between 2004 and 2014 in a regional hospital. Diagnosis was based on symptoms, serum Venereal Disease Research Laboratory (VDRL) and *Treponema pallidum* hemagglutination assay (TPHA) titers, Cerebral Spine Fluid (CSF) cell count and CSF VDRL and TPHA titers.

**Results:** Diagnostic criteria for neurosyphilis were present in 19 cases: of these, 17 were male (89.5%) and 11 were Caucasian (57.9%). The average age at the time of presentation was 46 years (23–67). 9 cases presented with a combination of focal neurological defects, 6 had headache as the main complaint, 3 had visual symptoms, 4 presented with delirium/cognitive impairment and other neuropsychiatric conditions and 2 cases

were asymptomatic. In 6 cases the clinical presentation was acute (<24 hours) whilst the rest presented with symptoms lasting from 3 weeks to 13 years. Uveitis was documented in 4 cases and deafness in 1 case. Most had a serum VDRL titer >1:32 (73.7%) and all of them had a positive TPHA. Lumbar puncture was performed in all cases with a mean CSF white cells count of 114 cells/mL. In 3 cases the CSF VDRL was negative, but CSF TPHA was positive. In 1 case Cryptococcal co-infection was documented and CNS tuberculosis in another. Human Immunodeficiency Virus (HIV) infection was identified in 10 cases with a median CD4 cell count of 183 cells/mL. In 16 patients the treatment instituted was intravenous penicillin, 2 with ceftriaxone and 1 with doxycyclin, and the average treatment duration was 15 days. Of those followed up (8/19 cases), 3 remained with positive CSF VDRL 6 months after treatment. One patient died and 2 were discharged on their own request before treatment was completed.

**Conclusions:** The diagnosis of neurosyphilis can be difficult, as many patients are either asymptomatic or present with non-specific symptoms. A negative CSF VDRL is not 100% sensitive, so a combination of clinical presentation, serum VDRL, CSF pleocytosis, and CSF VDRL are required for a diagnosis and appropriate treatment decisions.

## Atypical clinical presentation of pulmonary tuberculosis

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**Introduction:** Atypical clinical presentation of pulmonary tuberculosis in two immunocompetent patients.

**Case reports:** Patient 1: a 30 years old male patient had a history of inflammatory arthritis of the ankles, knees, wrists and elbows for the past 15 days. He referred night sweats and denied any other signs or symptoms. He had smoking habits but was under no regular medication or had any other underlying disease. After one month of follow-up in consultation he went to the emergency department due to hemoptysis without fever. On physical examination he had only signs of arthritis of the above joints. The lab tests only showed elevated inflammation markers (leukocytosis 12000/uL, C-reactive protein 40 mg/L and sedimentation rate 38 mm/h). The HIV antibodies were negative. The chest X-ray showed a cavitory lesion at the apical pole of the lower lobe of the right lung. The bacteriological examination of sputum isolated an acid-alcohol resistant bacillus. The diagnosis of post-primary pulmonary tuberculosis was assumed. The patient started up on anti-tuberculosis therapy for 9 months and showed good clinical response with complete resolution of the arthritis and night sweats. Patient 2: a 39 years old male patient had a history of night sweats and inflammatory arthritis of the ankles, knees and elbows lasting 10 days. He denied any other complaints, including fever, weight loss, cough and hemoptysis. He was under no chronic medication and had no significant medical history. The physical examination findings only showed signs of arthritis of the above described joints. The lab tests revealed elevated inflammatory markers (leukocytosis

14000/uL, C-reactive protein 100 mg/L and sedimentation rate 75 mm/h) and the HIV antibodies were also negative. The chest X-ray showed enlargement of the pulmonary hila. The thoracic CT revealed bilateral hila lymph node enlargement, lobular areas of consolidation and linear opacities. The patient underwent mediastinoscopy for lymph node biopsy. The histological examination confirmed pulmonary tuberculosis. Antituberculosis therapy was started for 9 months. The patient showed good clinical response with complete resolution of the arthritis.

**Discussion:** Tuberculosis is a major cause of death worldwide. This infectious disease commonly affects the lungs in 70% of patients. Fever, weight loss, night sweats, cough and hemoptysis are the major symptoms and signs. However these two clinical reports demonstrate unusual clinical presentation of the disease.

## Herpes meningoencephalitis in a patient with common variable immunodeficiency – case report

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**Introduction:** Common variable immunodeficiency (CVID) is a primary immunodeficiency characterized by immunological disorders and a cause of recurrent or opportunist infections, autoimmune diseases and neoplasms. The aim of this work is to highlight the importance of early identification of this pathology to prevent these complications.

**Case report:** 27 years old man, Caucasian with multiple upper respiratory tract and ear infections in the last 5 years and 2 recent hospitalizations for acute bacterial pneumonia. No history of epilepsy, chronic medication or drug allergies. No relevant family history. He was admitted in the emergency department with headache and fever. He was uncooperative, with confused speech, and developed a generalized tonic-clonic seizure. The blood test showed leukocytosis 27000 (43% neutrophils) and a creatinekinase 281 U/L. The cranial CT scan had no abnormalities. The cerebrospinal fluid (CSF) presented 18 leukocytes (65% mononuclear), glucose 65% and protein 3.76 g/dL and the microbiological study was inconclusive. We assumed meningoencephalitis diagnosis and he was medicated with acyclovir and ceftriaxone. Later, we found very low values of all immunoglobulins and absence of gamma band on protein electrophoresis. Serology for hepatotropic viruses and HIV was negative with normal lymphocytic subpopulation and no response to vaccination in childhood. The MRI was suggestive of herpes encephalitis. The immunoglobulin replacement therapy was started after CVID diagnosis. On 11th day of hospitalization he had a clinical deterioration with headache and vomiting. It was performed a cranial CT that revealed temporal hemorrhage with edema and mass effect. A lumbar puncture was repeated with PCR for Herpes simplex 1 positive in the CSF, therefore therapy with acyclovir was prolonged for 21 days, with imaging and clinical improvement.

**Discussion:** The CVID must be placed as diagnostic hypothesis when there is a history of recurrent and/or opportunistic infections or with serious clinical impact, as in the case described.

The diagnosis is usually done in childhood, however, and as it was verified in this case, it can only be identified in adulthood. To emphasize the exquisiteness of virus infection in this disease, as the most frequent infections in these patients are by encapsulated bacteria.

## Comparison of clinical and laboratory characteristics and prognosis in patients with right and left sided infective endocarditis

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**Objectives:** Right-sided infective endocarditis (RSIE) accounts for 5–10% of cases of infective endocarditis (IE) and usually occurs among intravenous drug users and patients with foreign bodies (e.g. pacemakers). The purpose of our study was to compare the in hospital mortality of patients with RSIE versus those with left-sided infective endocarditis (LSIE).

**Methods:** We performed a retrospective cohort study of patients with infective endocarditis admitted to Soroka University Medical Center between 1/January 2003 and 1/January 2013. Two groups of patients with infective endocarditis were compared: patients with RSIE and patients with LSIE. The primary outcome was in-hospital mortality. The diagnosis of infective endocarditis was established according to the modified Duke criteria.

**Results:** 215 patients were identified with a diagnosis of infective endocarditis. The majority of these patients has LSIE (176) compared to RSIE (39). Patients with RSIE were younger compared to LSIE (48.1±18.9 vs 61.8±17.0,  $p<0.001$ ). In the group of RSIE, the percentage of IV drug users was higher as compared to LSIE (43.6% vs 4.0%,  $p=0.006$ ) and had a higher percentage of patients with previous endocarditis (15.4% vs 2.8%,  $p=0.006$ ). The level of CRP was higher in RSIE as compared to LSIE (17 [6:32] vs 7.3 [4.7:11.8],  $p=0.008$ ). In-hospital mortality rate was higher in LSIE compared to RSIE (17% vs 2.6%,  $p<0.037$ ). The most common pathogen in patients with RSIE was *S. aureus* (51.3% cases) and the most common pathogens in LSIE were *S. viridans* (14.8%) and *S. coagulase negative* (13.6%).

**Conclusions:** Patients with RSIE were younger and had higher levels of CRP; however mortality was lower as compared to patients with LSIE. These findings might point to a difference in pathogenesis between the two entities and further research is needed.

## Mediastinitis and septic shock as complications of a periodontal abscess in a young patient

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**Introduction:** The objective of this case report is to highlight the potential fatal complications of periodontal abscesses and pharyngeal infections. We describe a case of a healthy young

male who developed mediastinitis and septic shock as a result of a periodontal abscess that extended to the mediastinum. This diagnosis was confirmed after thorough medical workup in our clinic. Furthermore, all the other possible causes of mediastinitis were excluded.

**Case report:** A 28 year old Caucasian male presented to the emergency department of our clinic with a history of a 10-day periodontal abscess and fever. This abscess was previously drained by an ENT surgeon and treated also with amoxicillin and metronidazole. On admission his vital signs were: BP 70/40 mmHg, fever up to 40 °C with chills, heart rate 110 beats per minute. The patient had also tachypnea and his initial laboratory evaluation revealed: WBC 18700, urea 81 mg/dL, creatinine 1 mg/dL, albumin 2.5 g/dL, total protein 5.1 g/dL, LDH 1182 U/L and ESR 60 mm/h. His medical and family history was unremarkable. Chest x-ray showed a widening in the mediastinum and the computed scan of neck and chest that followed, revealed an abscess that extended to the neck, producing right retropharyngeal abscesses and mediastinitis. The patient was treated with urgent thoracotomy and drainage of the mediastinum and parenteral antibiotic therapy. Our patient had an uneventful recovery.

**Discussion:** Oral and pharyngeal infections are very common in the general population and occasionally can cause local and systematic manifestations. This case demonstrated a rare serious complication that these infections may lead to. Available experimental evidence regarding the underlying mechanisms is limited. Even though the widespread use of antibiotics in our era, the mortality rate of mediastinitis still exceeds 20%.

## Atypical mycobacterial and respiratory infections: we think about them? Presentation of 3 unicentric cases

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**Introduction:** New atypical mycobacterial (AM) species with varying degrees of pathogenicity are continuously described although there are diagnostic difficulties and uncertainty about the therapeutic indications and the adequacy form of treatment. Given the controversy in this clinical scenario we present 3 cases of respiratory infection AM. Medical records of patients (P) hospitalized in the Internal Medicine Department of our center with respiratory infection between September 2013 and February 2015 was retrospectively reviewed. We identified 3 cases of immunocompetent P with respiratory AM infection for *Mycobacterium avium*.

**Case reports:** Case 1. Female 85 years old, passive smoking, with chronic obstructive pulmonary disease (COPD) and bronchiectasis (B). She presented an episode of respiratory infection with *M. avium* isolation in sputum culture (SC) and bronchoalveolar lavage (BAL). She was treated with clarithromycin (C) 500 mg twice day, ethambutol (E) 300 mg/8h and rifampin (R) 600 mg/24h daily for 3 months with good response (GR). Case 2. Male 69 years old, ex-smoker, with COPD and history of respiratory infections with multiple microbiological isolates. He presented hemoptysis with Ziehl negative in sputum. Bacterial CS remain positive for *M. avium* being treated with C 500 mg twice day, E 300 mg/8h and R 600 mg/24h three times a week for 3 months with GR. Case

3. Female 60 years old with hypertension, diabetes mellitus and hypercholesterolemia. She presented cough and haemoptoic sputum. Chest CT detected B being isolated *M. avium* in BAL. She was treated 4 months with C 500 mg twice day, E 300 mg/8h and R 600 mg/24h three times a week with GR. 3 P (2 female; 1 male) were presented with a mean age of 71.3 years. Of all P, 2 had COPD and 1 of them had multiple cardiovascular risk factors. Also, 1 of the 2 P with COPD was also presented B being the prevalence of these among P with COPD in our sample of 50%. All they presented a respiratory infection for *M. avium*.

**Discussion:** The presence of B could impact negatively on the natural history of COPD itself, although this fact has not been fully elucidated. B are also a risk factor for infection that can cause functional impairment. We believe that it is justified the screening of AM in patients with COPD and/or B because these germs could be implicated in exacerbations of COPD more often than thought especially when the response to the usual antibiotic treatment is not appropriate.

## Antibiotic sometimes is not the right choice

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**Introduction:** Infectious mononucleosis (IMN) due to Epstein-Barr virus (EBV) infection can be associated with acute hepatitis, which is usually self-limited with mildly elevated transaminases and is sometimes associated with a maculopapular rash. In young adults, EBV infection results in a clinical syndrome of infectious mononucleosis which typical signs and symptoms are fever, pharyngitis, lymphadenopathy, hepatosplenomegaly and a maculopapular rash that can spread throughout the body including palms and plants. A maculopapular rash is present in EBV infection in 5% of the cases, and is usually associated with administration of beta-lactam antibiotics. When initially present, the rash can be exacerbated by the administration of antibiotic. We present a case of IMN having as presentation an exuberant maculopapular rash worsened by the prescription of a beta-lactam antibiotic.

**Case report:** 22 years old male with no relevant antecedents went to the emergency department with a pruritic maculopapular rash and fever with five days of evolution. He was discharged medicated with augmentin and antihistamine. In the next day, he returns to the emergency department with worsening of the rash, high fever and severe prostration. Physical examination showed submandibular lymphadenopathy, hepatomegaly and maculopapular rash dispersed throughout the body. The laboratory investigation showed mild leukocytosis with reactive lymphocytes, hyperbilirubinemia, hepatic cytolysis (30 times the normal upper limit) and EBV IgM positive. It was also documented hepatosplenomegaly on abdominal ultrasound. The patient was admitted to begin supportive therapy and complete the clinical study. There was a marked initial worsening of skin lesions and hepatic cytolysis. We excluded infection by CMV, HIV, Parvovirus, Herpes, Rickettsia, Salmonella and Brucella. He was discharged on the 7th day of hospitalization with significant clinical and analytical improvement. He was subsequently reevaluated in an internal medicine appointment with marked improvement

of cutaneous lesions, analytic markers of hepatic cytolysis and progressive decrease of IgM EBV titer, maintaining a slight fatigue for a few months.

**Discussion:** This IMN case shows that EBV infection can present with acute symptoms and hepatic failure. It's essential to value correctly the symptoms and the physical examination of the patient and avoid the abusive use of antibiotics which can aggravate symptoms.

## Cryptococcal meningoencephalitis as the first clinical manifestation in a patient with AIDS

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**Introduction:** Infections by *Cryptococcus* produce a variety of clinical conditions affecting many systems, with a global distribution. Cryptococcal meningoencephalitis (CM) is the most common fungal infection of the central nervous system and the fourth most frequent opportunistic infection in AIDS patients.

**Case report:** A 37 year old African male presented to our emergency department, complaining of malaise, headache and fever for the past 2 weeks. Physical examination was remarkable for fever and meningeal signs. Awaiting laboratory results, he suffered an episode of generalized tonic-clonic seizures. Lumbar puncture (LP) revealed pleiocytosis, elevated protein and a positive India ink stain. *Cryptococcus neoformans* was isolated from CSF cultures; cryptococcal antigen titre in CSF was elevated (1:6400). HIV testing was offered and he tested positive. His CD4 count was 67/ $\mu$ l and his HIV viral load 210000 copies/ml. He was started on liposomal amphotericin B 4 mg/kg/day plus 5-fluorocytosine 125 mg/kg/day as induction therapy, with subsequent apyrexia and symptom relief within one week. A new LP after 2 weeks revealed no improvement and the patient continued the same therapy for an additional 2 weeks. He was discharged during the 4th week of treatment with a prescription for oral fluconazole 800 mg/day as consolidation therapy. At 10 weeks, highly active antiretroviral therapy (HAART) was initiated (abacavir/lamivudine/darunavir/ritonavir); fluconazole dosage remained at 800 mg/day due to persistent CSF findings. At 6 months the patient remains free of symptoms with an undetectable viral load, a CD4 count at 482/ $\mu$ l and fluconazole has been tapered to 200 mg/day.

**Discussion:** Cryptococcosis is rare amongst immunocompetent patients and should raise strong suspicion for the presence of an underlying immune deficiency. CM presents a challenge regarding the optimal timing of initiation and choice of HAART, due to the possibility of a potentially fatal immune reconstitution inflammatory syndrome (IRIS), characterized by an acute and exacerbated inflammatory process, as the patient's recovering immune system attempts to fight the infection. It remains a controversial issue, but 2-10 weeks of anti-fungal treatment are suggested as optimal before HAART. Initial antifungal treatment should include a combination of amphotericin B plus 5-fluorocytosine. Duration of treatment should be no less than a year in total, with the possible continuation until CD4 count increases.

## Streptococcal toxic shock syndrome associated with necrotizing fasciitis

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**Introduction:** Necrotizing fasciitis refers to a spectrum of infections affecting deep layers of the soft tissues. It is caused by multiple (type 1) or single (type 2) bacteria, the most common causative agent of the latter being group A beta hemolytic *Streptococcus* (*S. pyogenes*), also infrequently implicated in the occurrence of toxic shock syndrome (TSS).

**Case report:** An 85 years old male with a medical history of chronic atrial fibrillation under coumadin therapy presented to our emergency department due to painful swelling of his right forearm and palm. The skin of the area appeared completely intact. Ulnar and radial arterial flow appeared biphasic in Doppler study. The lesion was initially considered a spontaneous hematoma associated with Coumadin therapy. Within hours, the patient became febrile, disoriented and hemodynamically unstable, while the swelling affected the whole length of his arm and blisters appeared on the affected area. His laboratory studies showed pancytopenia suggestively due to DIC, renal impairment, elevated liver enzymes and C-reactive protein. Restoration of his hemodynamic stability was achieved through aggressive IV hydration with colloids and crystalloids and conservative vasopressor infusion rates, in an attempt to minimize tissue hypoperfusion. He was started on piperacillin/tazobactam plus clindamycin promptly after blood cultures were obtained, from which *S. pyogenes* was isolated. Clindamycin dose was raised to 900 mg TID to treat a probable TSS. Necrotizing fasciitis was suspected due to the patient's LRINEC score of 10 (>6) and was confirmed through a CT scan. The patient underwent shoulder level right arm amputation. He expired in the ICU during the post operative period due to heart-related complications.

**Discussion:** Streptococcal necrotizing fasciitis constitutes a surgical emergency, the successful clinical course of which depends on a high level of alertness from the part of the evaluating physician. Emergency tissue debridement is necessary while broader scale surgery is often required. Coexistent streptococcal TSS makes hemodynamic stabilization a challenging task and it may require, apart from antibiotic therapy per se, agents that halt toxin production (clindamycin) or ameliorate its effects (intravenous gamma globulin).

## Melioidosis in Bangladesh

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**Background:** Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, a Gram negative non-aeruginosa pseudomonas bacillus found in water and soil. Transmission to human is by contact and it causes disease mostly in the immunocompromised state. Melioidosis closely mimics

tuberculosis. In Bangladesh as tuberculosis is common, melioidosis is often misdiagnosed and empirically treated as tuberculosis. Although climate in Bangladesh is favorable for this organism, there are limited numbers of published cases among Bangladeshies. Detection of melioidosis cases and recent isolation of *B. pseudomallei* in the soil of Gazipur district has not only confirmed Bangladesh as a "definite country for melioidosis" but also has deepened its importance in our clinical practice.

**Objective:** This study was aimed to investigate melioidosis occurring in Bangladeshi residents and in travelers returning from Bangladesh.

**Methods:** Retrospective analysis of melioidosis confirmed cases in and from Bangladesh from 1988 to 2015 was done. Medline search for cases published in overseas journals was done using key words melioidosis, Bangladesh and *Burkholderia pseudomallei*. A systematic online search through "Banglajol" for locally published articles was also done. Total 24 cases were identified from which 2 were excluded due to repetition. Among the 22 cases 19 were published and 3 local cases are yet to be published.

**Results:** Among the cases 21 were diabetic and 18 were male. 16 cases were classified as endemic while 6 cases were reported as returning travelers from Bangladesh. Common presentations were fever (21, 95.4%), arthritis (9, 40.9%), weight loss (9, 40.9%) and cough (7, 31.8%). Common radiological findings showed lung involvement (8, 36.3%) and organ abscess (6, 27.2%). 14 cases responded to ceftazidime/imipenem/meropenem as initial therapy followed by a combination of doxycycline and trimethoprim-sulfamethoxazole or amoxicillin-clavulanic acid. In 3 cases treatment was not mentioned and 5 patients died despite treatment.

**Conclusions:** Observation revealed that this disease if remained untreated can cause life threatening complications, even death. Therefore, suspicion of melioidosis should be considered in appropriate clinical scenario. It is now a grave question whether melioidosis should be considered as an emerging disease in Bangladesh.

## Renal tolerability and efficacy of telaprevir-based triple therapy in HIV/HCV co-infected patients

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**Objective:** This study was aimed to evaluate the renal tolerability and efficacy of triple therapy including telaprevir (TVR) in a small group of HIV/HCV co-infected patients in real-life conditions.

**Material and methods:** We designed a retrospectively study to investigate the kidney function and clinical outcome of chronic hepatitis C, genotype 1 co-infected patients with HIV, who received TVR plus pegylated interferon (PegIFN) and ribavirin (RBV) treatment. Clinical and biological data at TVR initiation and every following visit during 48 weeks were retrospectively recorded from the medical files. We used the Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI) to evaluated renal function and Wilcoxon's signed-rank test

for repeated measures was used for comparisons between follow-up and baseline results, using the SPSS statistical analysis software.

Results: 17 patients have been included; 13/17 (76.4%) male and 4/17 23.5% females, median age 49.3 years old, 12/17 (70.5%) were IL-28B genotype CC, 3/17 (17.6%) CT and 1/17 (5.8 TT), in 1 case we found no data. Cirrhosis was present in 12/17 (70.6%) and F3 grade fibrosis in 5/17 (29.4%). Infection whit genotype 1a was observed in 76.5% of patients. The most commonly used antiretroviral (ARV) drugs were tenofovir/emtricitabine [6/17 (35.3%) patients], abacavir/lamivudine [5/17 (29.4%) patients], efavirenz/tenofovir/emtricitabine [5/17 (29.4%) patients]. 94.1% of the patients showed anemia at some point of treatment. Only 1 patient discontinued HCV therapy during week 4, due to poor adherence to treatment, not related to toxicity. We observed a non-statistically significant median (interquartile range) reduction in eGFR (ml/min/1.73m<sup>2</sup>) relative to the baseline value [102 (96.3–108.0)], at weeks 4 [96.2 (89.4–105.0), p=0.084] and 8 [96.1 (91.4–103.7), p=0.053] but a significant median (interquartile range) reduction at 12 weeks [95.6 (92.6–105.5), p=0.03]. These changes reversed after TVR discontinuation, as was seen at week 24. The sustained viral response (SVR) on week 48 was 76.5% (13/17). One patient discontinued HCV therapy during week 4, 1 patient had relapse on week 36.

**Conclusions:** Even though only a small number of patients were evaluated, TVR based triple therapy in HIV/HCV co-infected patients was significantly associated with a reversible decrease in eGFR only on week 12. Response rates to triple therapy with TVR plus PegIFN and RBV in HIV/HCV co-infected patients under real-life conditions, are similar to the clinical trials, and so we believe it could be an adequate therapeutic option in special situations and in countries where there is no access to the new direct antiviral agents (DAAs).

### Infective endocarditis: experience from a 3 year old hospital

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**Objectives:** The incidence of infective endocarditis (IE) ranges from 2,6 to 7 cases per 100 000 population in developed countries. The predisposing conditions have shifted from rheumatic disease to IV drug use, valvular degeneration and intracardiac devices. IE has a high prevalence of complications, leading to high mortality especially in the elderly. We aimed to assess and characterize all cases of IE in a 3 year period of a district hospital.

**Methods:** Review of all cases of IE in patients hospitalized in the Medical Department of a Hospital between February 2012 and December 2014. Descriptive statistic of demographics and characterization of IE (type of IE, echocardiographic findings, blood cultures results, complications, antibiotic regimen).

**Results:** We included 53 patients with the diagnosis of IE, with an incidence of 6,3 cases/10000/year, 70% were men. Mean age was 65,3 years. The most prevalent risk factor was immunosuppression (diabetes, cancer, HIV). The most

frequent cardiac disease was valvular disease. Blood cultures were positive in 79% of cases, with 53% Streptococcus, 42% Staphylococcus (53% MRSA) and 5% Enterococcus. The most frequent Streptococcus was *S. gallolyticus* (90% had a colonoscopy performed, 60% with abnormalities). 92% of patients had a transthoracic echocardiogram (60% sensitivity) and 83% had a transesophageal one (93% sensitivity). The most affected valve was the mitral (n=16) and aortic (n=13). 76% of patients had a definitive diagnosis according to Duke Criteria. 77% had a native valve IE, 15% a prosthetic valve (6% <1 year valve). Most patients didn't have the right antibiotic regimen according to the ESC guidelines, due to excessive use of vancomycin. 30% were submitted to cardiac surgery, most due to acute cardiac failure. 75% of patients had complication, mainly acute cardiac failure due to valvular insufficiency. Ischemic stroke occurred in 8 patients. There was one case of cerebral mycotic aneurism, splenic infarction, septic arthritis and renal infarction.

**Conclusions:** IE is a common disease and is associated with serious complications. The transesophageal echocardiogram is the most accurate diagnostic method for identifying vegetations. Transthoracic echocardiogram has a sensibility of only 60%. Blood cultures are crucial for the adequate antibiotic regimen in IE. Most common microorganisms are Staphylococcus and Streptococcus. The Duke criteria, not being ideal, are a good method for identifying clinical IE.

### Spontaneous community-acquired Escherichia coli meningitis

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**Introduction:** Despite widely described in the pediatric population, Escherichia coli (*E. coli*) meningitis is considered rare among adults. The majority of reported cases are associated with cranial-encephalic trauma, neurosurgery, immunosuppression or other invasive procedures. Literature reports an estimated mortality of over 90%. We present a case of spontaneous community-acquired *E. coli* meningitis.

**Case report:** A previously healthy 60 years old man presenting with left hemiface paresthesia, diplopia and vertigo with 48 hours (h) of evolution was admitted. Neurological examination revealed hypoesthesia of the right hemiface and gait instability. Laboratorial findings included leukocytosis with neutrophilia and negative CRP; cerebrospinal fluid (CSF) analysis showed cloudy liquid, 1050 cells with a predominance of polymorphonuclears, proteinorrachia 129 mg/dL and glucorrhachia 67 mg/dL. Cranial computed tomography scan (CT-scan) was normal. Empirical therapy was initiated with ceftriaxone (2 g 12/12h) and ampicillin (1 g 4/4h). On the third day of treatment, the patient maintained diplopia and headache, and fever occurred. CSF cultures came positive for *E. coli*, resistant to ampicillin and ceftriaxone. The antibiotic regimen was changed to meropenem (2g 8/8h) and ceftazidime (2 g 6/6h), with clinical and laboratory improvement after 14 days of therapy. To study possible underlying causes, the following complementary exams were requested: urine culture,



blood cultures and echocardiography, all of which showed no alterations; sinus and ears CT-scan, which showed periodontitis of the upper left second molar; cranial-encephalic magnetic resonance imaging (MRI), which documented a "lesional area in posterolateral right bulb-protuberancial transition extending to middle cerebellar peduncle and, particularly on the fourth ventricle, no recent vascular nature? vs. small capillary telangiectasia?".

**Discussion:** The limited information available on this etiology in adult patients represents a challenge. Taking into account the previously reported mortality, the response were surprisingly positive. The clinical relevance of the lesion presented in the MRI is still unknown. For full clarification of this finding, an MRI angiography would have been required. With the available data, we can only suppose it may correspond either to a complication of meningitis or to a primitive central nervous system injury.

## Human immunodeficiency virus epidemiology in Portalegre district

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**Objectives:** There is a lack of trials of prevalence of human immunodeficiency virus (HIV) in Portugal, however, the calculated prevalence in all the country is close to 0,2%. The aim of the study is to characterize population with HIV in Portalegre district.

**Methods:** Transverse trial based in medication given records for HIV treatment in Elvas and Portalegre pharmacies. Patients were excluded if they did not live in Portalegre or had passed away. They were analyzed age, gender, nationality, address, co-infections and co-morbidities, viral load, HIV type and to have or not a family doctor. A manual questionnaire was designed and a digital base was filled out. Applications Info 7 and Excel 2011 were used to qualify the variables. Measures of central tendency and dispersion were utilized, frequencies, prevalence risks for ages, genders, using population projections of Portuguese National Statistics institute (INE). Chi-square and T-student were used to establish differences among comparison groups, with 0,05 of alfa.

**Results:** There were 109 registered patients, who picked up medication. 102 of them filled criteria for the trial. There was a prevalence of 8,88 out of 10000 people, being higher in men (RP: 2,88; IC 95%: 1,87-4,45;  $p=0,000$ ), the age's mean of  $45,6\pm 9,8$  years, without gender significant difference ( $p=0,2$ ), The highest prevalence in Fronteira and Alter de Chão councils. Portuguese nationality (96,1%) was predominant, besides HCV co-infection (87,3%), psychiatric comorbidities and type 1 HIV. In addition, 88,8% had negative viral load and 26,5% did not have a family doctor.

**Conclusions:** Social HIV stigmata hinders local trials of its prevalence. Although these studies help to identify own population features and some shared with other towns, helping to develop trials and programs to improve the follow-up of these patients.

## Pneumococcal pneumonia associated with laboratory-confirmed influenza hospitalizations during 2014-2015 season

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**Objectives:** Bacterial pneumonia is a common complication of influenza virus infection and contributes substantially to morbidity and mortality, particularly among older individuals than 65 years of age. The aim of this study was to evaluate whether pneumococcal pneumonia had clinically significant relevance on the length of hospital stay and mortality in patients hospitalized with laboratory-confirmed influenza infection.

**Methods:** We reviewed all patients older than 16 with laboratory-confirmed influenza infection hospitalized from November 1, 2014 to March 31, 2015. Patients were included in our study if they had confirmed pneumococcal pneumonia: a positive test for *S. pneumoniae* (either antigen detection in urine or a positive culture in sputum, BAL or blood) and a new infiltrate in chest X-ray. Statistical analysis was performed with SPSS version 21.0.

**Results:** During influenza season 2014-2015, we found 384 patients hospitalized with laboratory confirmed influenza infection. 38 (9,8%) had confirmed pneumococcal pneumonia. Diagnosis of *S. pneumoniae* was performed by antigen detection in urine (92,1%), blood culture (2,4%), sputum culture (2,6%) or both (2,6%). In the group of patients with influenza infection without pneumococcal pneumonia, the average length of stay it was 16.95 days, while in the group of co-infected patients the average stay was 15.05 days, with no statistically significant differences ( $p=0.97$ ). In the group of patients with influenza infection without pneumococcal pneumonia, mortality was 9%, while in the group of co-infected patients was 2,6% ( $p=0.34$ ).

**Conclusions:** We found a high incidence of influenza virus and pneumococcal pneumonia co-infection. Although in previous studies there is a relation between increased mortality in patients with flu and bacterial pneumonia, in our study we found no significant differences in mortality or length of stay among patients with co-infection during influenza season in our center. In patients hospitalized with influenza virus infection during 2014-2015 season, there was a high incidence of pneumococcal pneumonia co-infection. Nonetheless, there were no statistical differences in terms of mortality and length of stay between both groups.

## "Isn't one enough?"

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**Introduction:** Lyme's disease is a systemic, potentially chronic infectious disease caused by the spirochete *Borrelia burgdorferi* which is transmitted to humans by a tick from the genus *Ixodes*. The prognosis is usually benign if early treated. In Portugal, it

is still a relatively common disease, especially during spring and early summer.

**Case report:** 53 years old, homeless, Caucasian, male, diagnosed with hypertension and alcoholism was hospitalized in the psychiatry ward for a rehabilitation program. The patient referred substantial weight loss and asthenia, and presented light fever, ataxic walking pattern, lack of balance and diminished strength in the lower limbs. The blood analysis revealed neutrophilic leukocytosis, macrocytic anemia, sedimentation rate of 114 mm/h, C-reactive protein of 68 mg/dL, iron deficiency, hypercalcemia and hyperphosphatemia and adenosine deaminase of 16 IU/L. The endoscopic study didn't reveal any lesions. The chest X-ray and CT-scan showed multiple nodular images especially in the right lung, some of them with cavitations. The patient was submitted to a bronchoscopy and bronchoalveolar lavage. The direct microscopic exam for acid-alcohol-fast bacilli was negative, but the interferon gamma release assay was positive as was the blood serology for *Borrelia burgdorferi*, revealing acute infection. Despite not having the full results from the cerebrospinal fluid analysis, as the patient presented with neurologic symptoms, the authors opted for treating for neurologic Lyme's disease with ceftriaxone 2 g once daily during 21 days (the polymerase chain reaction for *Borrelia burgdorferi* in the cerebrospinal fluid arrived later and was negative), as well as initiating the treatment for the pulmonary tuberculosis with isoniazid 300 mg once daily, pyrazinamide 1,5 g once daily, ethambutol 800 mg once daily, rifampin 600 mg once daily and pyridoxine hydrochloride. Later were obtained the results from the multiple bronchoalveolar lavage cultures for *Mycobacterium tuberculosis* which were all positive, with no drug resistances.

**Discussion:** The authors believe this case is particularly interesting because, even though the patient's symptoms were broad and could be justified by the pulmonary tuberculosis only, the high susceptibility of the patient derived from his living conditions, originated the necessity to pursue other diagnosis and proceed to a more exhaustive investigation.

## Malaria – a global disease

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**Introduction:** Malaria is a disease caused by the *Plasmodium*, a parasite transmitted to humans by the bite of the female *Anopheles* mosquito. It is a disease increasingly present in European hospitals, especially in countries where migratory movements are frequent as is Portugal.

**Case reports:** The authors describe a case series of 5 patients hospitalized for malaria, in charge of a work team in the infectious diseases department of a central hospital during a 3 months period. One female and four male patients were treated, with an average age of 40.2 years, all Caucasians and living periodically in Angola for work reasons. They've all had previous episodes of malaria (were partially immune) and all claimed having done prophylaxis. The initial symptoms were fever in 100% of cases, nausea and vomiting in 40%, diarrhea in 40%, asthenia and myalgia in 40%, headache in 40% and confusion in 20%. In the first determination, parasitemias

were: 0.03%, <0.1%, 2%, 13% and 18%. However, some of the patients had started therapy right after the thick blood smear exam, and the first parasitemia determination was performed after the initiation of treatment. All cases were caused by *Plasmodium falciparum*, one of the cases treated was a mixed infection with *Plasmodium vivax* as well. Analytically, both thrombocytopenia and normochromic normocytic anemia were present in 100% of cases, the increase in lactate dehydrogenase was present in 60%, liver dysfunction was present in 40% of the cases as well as kidney dysfunction. According to the World Health Organization criteria 2 of the cases corresponded to severe malaria. One case presented with shock with need of organ support. In 80% of cases, initial treatment was with quinine and doxycycline which were subsequently replaced with artemether and lumefantrine. In 20% of cases the initial treatment was with artemether and lumefantrine. In 40% of cases there was need for transfusion of red blood cells due to hemolytic anemia.

**Discussion:** The authors consider relevant to describe the previous cases because being a potentially fatal disease, malaria has a favorable prognosis if diagnosed early and properly treated. As a matter of fact, malaria remains one of the main diagnoses to be considered in newcomers from countries where malaria is endemic presenting with fever.

## Infective endocarditis – 8 years in review

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**Objectives:** Infective endocarditis is still a diagnostic challenge and a condition with a moderate mortality rate. Its incidence in Europe is about 3-10 episodes/10000 person-years, and its epidemiological profile has been changing afflicting an increasingly older population. This analysis intends to characterize this population and identify factors associated with worse prognosis in infective endocarditis.

**Methods:** It was done a retrospective review of 8 years of clinical practice in our hospital and we included all patients admitted in ward with definitive or probable diagnosis of bacterial endocarditis (according to the revised Duke criteria).

**Results:** 74 patients were included in the study, most were males (53%) with a mean age of 73 years old. 38 patients developed any type of complication, including 3 patients with perivalvular abscess, 28 patients with severe heart failure and 21 patients required valvular replacement surgery. 11 patients died during in stay, all but 2 were diagnosed with complications of the infectious endocarditis. Patients that developed complications were more likely to have definitive diagnosis of bacterial endocarditis, compared to those who had probable diagnosis ( $p=0.01$ ), to have higher serum levels of C-reactive protein ( $p<0.001$ ) and a lower count of white blood cells ( $p<0.05$ ). There was no association between complications of the infection and the presence of fever, a worse performance status, renal insufficiency, electrolyte disturbance (sodium and potassium). We also could not find a statistically significant correlation between a higher neutrophil/leukocyte ratio and a higher mortality or development of complications.

**Conclusion:** With this study we summed an 8 year experience in infective endocarditis in order to characterize the patient's

demographics, valvular involvement, microbiological types, comorbidities and which features were associated with most complications and greater mortality.

## High prevalence of vitamin D deficiency in patients with HIV infection in the north of Spain

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**Objective:** Estimate the prevalence and establish the factors associated with deficiency of vitamin D in adults with infection by HIV seen in an outpatient clinic.

**Methods:** A cross-sectional study in patients with HIV infection treated in an outpatient clinic determining levels of cholecalciferol (25-OH vitamin D) and parathyroid hormone (PTH). Vitamin D deficiency was defined as levels <10 ng/ml, insufficient levels between 10 and 30 ng/ml, and the diagnosis of secondary hyperparathyroidism was established when PTH >65 pg/ml.

**Results:** The study included 100 consecutive patients. Mean age 47.1±11.1 years. 74% were male, 99% of Caucasian origin, 69% (32% MSM) due to sexual transmission of HIV, 30% due to intravenous drug use (IVDU). Median duration of HIV infection 14 years. Median CD4 + lymphocytes levels 607/microL, and in 85% of cases >200/microL. 40% were coinfecting with HCV. 95% of patients were taking antiretroviral treatment, of these 93% had an undetectable viral load. Current therapy included tenofovir (62%), efavirenz (27%), and both (68%), and medium duration of antiretroviral treatment 9 years. Vitamin D levels were in normal range (18%), deficient (15%), insufficient (67%), and 22% had secondary hyperparathyroidism. The level of vitamin D in patients with CD4 > 500, between 200 and 500, and <200/microL were 21.7, 14.8 and 12.1, respectively (p=0, 0016). No association was established between levels of vitamin D and factors including age, sex, type of transmission, HCV co-infection, viral load, duration or type of treatment.

**Conclusion:** There is a high prevalence of vitamin D deficiency/insufficiency in patients with well-controlled HIV, and there is an association between vitamin D levels and the degree of immune deficiency.

## Potential impact of the introduction of direct-acting antiviral agents against HCV in a cohort of patients infected with controlled HIV in a hospital in the north of Spain

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**Objective:** To estimate the percentage of patients with HIV infection that should be treated within a short period of time

with direct-acting antiviral agents (DAAs) against HCV in a general hospital.

**Methods:** A cross-sectional study in consecutive patients with HIV infection attending an outpatient internal medicine clinic, determining the current situation of co-infection before the introduction of direct-acting antiviral agents.

**Results:** The study included 100 consecutive patients. Mean age 47.1±11.1 years. 74% males, 99% Caucasian. Transmission of HIV was sexual in 69% (32% MSM) and intravenous drug use (IVDU) – in 30%. Median duration of HIV infection was 14 years. Median CD4+ lymphocytes 607/microL, 85% had CD4+ lymphocytes >200/microL. 95% undergoing antiretroviral treatment, of which 93% had undetectable viral load, median duration of antiretroviral treatment was 9 years. Positive serology for HCV in 40% cases. Of which 17 patients (42.5%) had a negative HCV viral load (41.2% had spontaneous clearance and 58.8% had sustained virological response after treatment based on interferon). Positive viral load for HCV in 23 patients (60%). Relative contraindication to immediate treatment in 8 patients (34.8%) which included an active neoplasia (1), active drug addiction (2), active alcoholism (1), non-adherence (1), unstable psychiatric disease (3). Refusal of treatment in 3 patients (13%). Patients susceptible to immediate treatment with DAAs 12 cases, 52.2% (12% of all cases). Genotype 1 – 7 cases, G3 – 2 cases, G4 – 3 cases. Patients with F2 or greater fibrosis (elastography or biopsy) – 7 cases.

**Conclusions:** In this cohort of patients with HIV infection, 12% of patients require treatment with DAAs against HCV, are willing to be treated and have no contra-indications. If we restrict to F2 or higher fibrosis the percentage of patients decreases to 7%.

## Larynx paracoccidioidomycosis in immunosuppressed patient: case report

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**Introduction:** Paracoccidioidomycosis (PCM) is a severe systemic disease caused by the fungus *Paracoccidioides brasiliensis*. It is an endemic infection in Latin America and is the main cause of death through systemic mycosis in immunosuppressed patients in Brazil. It has widespread clinical manifestations. Larynx involvement is common and may be the initial sign.

**Case report:** Female patient, 39 years old, Brazilian. Initiated two months ago with dry cough, asthenia, nocturnal sweating and weight loss. Evolved to dysphonia and dysphagia. Assessed by the otorhinolaryngologist who identified the granulomatous lesion in the larynx through indirect laryngoscopy. HIV diagnosed during hospital admission, CD4 97 cells/mm<sup>3</sup>. Submitted to a biopsy of the lesion which demonstrated fungus compatible to PCM. Upper gastrointestinal endoscopy revealed unusual duodenal ulcers and the biopsy was compatible to PCM. Treatment was initiated with amphotericin B. Patient demonstrated clinical improvement. After hospital discharge, treatment was maintained with trimethoprim-sulfamethoxazole.

**Discussion:** PCM is a systemic mycosis endemic of Latin America of which Brazil is responsible for 80% of the cases. Due to HIV pandemic, an even larger number of paracoccidioidomycosis/HIV

cases are depicted, once HIV currently presents itself in rural regions where *Paracoccidioides brasiliensis* is found. PCM in HIV patients is directly related to reduction of immunosuppression rates. On average 83.7% of the patients showed a CD4 less than 200 cells/mcL. In these patients the clinical decline is faster and multiple extra pulmonary manifestations may occur. The first reference to larynx involvement by the fungus was found in the study of Lutz who described a patient with larynx involvement at necropsy. The oral mucosa and the larynx are affected in 70% of the cases. When the larynx is affected, dysphonia is a common symptom. The most affected structures of the larynx are the vocal folds and the epiglottis. Complications due to lesions of the larynx cause limitation to daily activities, therefore this illness should be considered a public health issue.

### **mRNA gene expression of surviving, PDGFA, PDGFB, PDGFRA and PDGFRB in lung cancer cell lines**

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**Objectives:** Lung cancer is one of the leading causes of death worldwide, with an increasing incidence and poor prognosis. Angiogenesis, the process of forming new blood vessels, as well as apoptosis evasion and imbalanced cell cycle regulation resulting in cell proliferation, are hallmarks in the pathology of cancer. Proto-oncogene SURVIVIN is a member of the IAP (inhibitor-of-apoptosis) family of proteins. SURVIVIN has dual function on inhibition of apoptosis and regulation on cell cycle (phase G2/M). SURVIVIN is overexpressed in various cancers, and has been suggested to be involved in cancer development, progression and resistance to treatment. PDGF/PDGFR signaling has been recognized to have a major role in angiogenesis. Activation of platelet-derived growth factor receptors (PDGF) by ligand-induced dimerization, leading to autophosphorylation on specific tyrosine residues promotes cell growth, survival, and migration. Pathway's overactivity or mutations of PDGF receptors is seen in tumor cells and malignancies. Controversial studies show the expression of SURVIVIN, PDGFA, PDGFB, PDGFRA and PDGFRB in cancer lung cell lines. In this study SURVIVIN, PDGFA, PDGFB, PDGFRA and PDGFRB expression was quantified in cell lines with small and non small lung cancer (SCLC and NSCLC) compared to normal lung fibroblasts.

**Methods:** Total RNA was isolated from the A549, NCI-H1299, NCI-H460 (NSCLC) and NCI-H69, DMS-114 (SCLC), as well as the MRC-5 normal lung fibroblasts cell line. Then cDNA synthesis and Real-time PCR was used to quantify mRNA gene expression of PDGF-A, PDGF-B, PDGFR-A, PDGFR-B and Survivin by mean of SYBR green detection (CFX96, Biorad) and hybridization probes (LightCycler, Roche). Results were compared to lung fibroblasts and analyzed by using t-test. There are expressed as: mean value $\pm$ SEM (p<0,05).

Results: Increased mRNA levels of SURVIVIN, PDGFA and PDGFB have been expressed in all cell lines compared to normal lung fibroblasts, while of PDGFRA and PDGFRB were minimally

expressed. However, the SURVIVIN, PDGFA and PDGFB increased expression is in accordance with experimental data of two-pathway synergy and paracrine interaction with tumor cell microenvironment.

**Conclusions:** The increased mRNA levels SURVIVIN, PDGF and PDGF B have a very important role in tumorigenesis and angiogenesis. They could be useful biomarkers for monitoring patients with cancer. Further investigation is needed to improve understanding disease appearance and progression.

### **Spontaneous bacterial peritonitis. Is it necessary to change empirical treatment?**

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**Objectives:** Recent publications have described an increase in the incidence of spontaneous bacterial peritonitis (SBP) caused by microorganisms resistant to cephalosporins and increased mortality in patients with SBP associated with health care or nosocomial. The objective of this study is to describe the clinical and microbiological characteristics of patients diagnosed of PBE in our hospital.

**Material and methods:** Retrospective study by reviewing the medical records of all patients with SBP in POVISA Hospital between 2005 and 2014. We collected clinical, microbiological and therapeutical data and we analyzed mortality related factors.

**Results:** We included 36 patients, 81% males, mean age 65 years. 86% of patients had at least one concomitant disease, the most common liver cancer (36%), renal failure (22%), HIV (11%), DM (11%) and refractory ascites (11%). In 53% cirrhosis was related with alcohol, and in 36% with HCV. SBP was community acquired in 28%, related to health care in 36% and nosocomial in 36%. The most frequent symptoms were abdominal distension (78%), abdominal pain (30%) and fever (22%). The mean duration of symptoms was 5 days. The most common stage in Child-Pugh classification was B (53%), and stage C in 47%. The mean value on MELD-Na scale was 21. 6 patients had received antibiotics in the previous 3 months, mostly cephalosporins. The peritoneal fluid culture was positive in 41% of cases, and blood cultures in 33% of which were made. The most frequently isolated microorganism was *E. coli* (53%); others were *K. pneumoniae*, *K. oxytoca*, *Proteus mirabilis*, *S. mitis*, *E. faecalis* and *E. faecium*. All were sensitive to amoxicillin, cefotaxime and ciprofloxacin, except *S. hominis* and enterococci. The three patients with resistant organisms had taken previously antibiotics as the only significant statistically difference compared to patients with susceptible organisms. The most commonly used antibiotics were third-generation cephalosporins. 48% developed renal failure. 35% had a new SBP. 31% died, 45% of deaths attributable to SBP. The only independent predictor of hospital mortality factor was kidney failure. Mean time to death was 7 months.

**Conclusions:** In our country there is an increase frequency of less common microorganisms in patients who have received previously antimicrobial therapy. It should be reasonable a modification of the empirical antibiotic treatment in this patients. In our study renal failure was the only factor associated with increased mortality.

## Preview of diabetic nephropathy at cellular level: analysis of diabetes related renal changes in streptozotocin induced diabetic rats

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**Objectives:** Diabetic nephropathy has been extensively studied but early stage of renal changes in diabetes and their prevention have not been studied widely. In this experimental study, we aimed to perform a histological analysis of renal changes in diabetic rats and search for the possibility of prevention of these changes at an early stage.

**Methods:** 30 Sprague Dawley male rats weighing 200–220 grams were included in the study. Diabetes was induced in 24 rats by a single intraperitoneal injection of 65 mg/kg streptozotocin (STZ), 6 animals constituting the control group. At the end of 2nd day, the induction of diabetes was confirmed by measurement of blood glucose levels and  $\geq 200$  mg/dl were considered diabetic. Induction of diabetes failed in 3 animals which were excluded from the study. 10 rats from diabetic group were started treatment with NPH insulin 5 units/day and the remaining were followed untreated. After 21 days, all rats which completed the study were sacrificed. Their kidneys were removed with dissection, sections were obtained for microscopic study and histological evaluation was performed.

**Results:** Light microscopic study revealed dense collection and closure in capillaries forming glomerulus in non-treated diabetic group when compared to control group. There was eosinophilic collections and cellular enhancement in extracellular mesangium. There wasn't a significant change in proximal tubules compared to control group. In distal tubules and collecting ducts there was extreme widening of lumen and injury in some cells. There was dense PAS (+) collection and degeneration in cell cytoplasm. There was no enhancement of basal lamina. In treated diabetic group; the capillaries forming glomerulus were similar to control group with their intact texture. There was no collection in mesangium or cellular increase. The cells, nucleus and cytoplasm of proximal tubules, distal tubules, and collective tubules were intact. There was no PAS (+) collection in the cytoplasm. Basal laminae of glomerulus and tubules were distinctive and widening of the lumen was present in this group also.

**Conclusions:** In our study, in a short time like 21 days, renal pathological changes were observed in diabetes. But the striking point is that it could be reversed to an important degree with treatment. Thus, it is vital to provide and maintain blood glucose regulation urgently in diabetic patients to prevent possible complications related to the disease.

## Nephrotic syndrome: a case report of primary focal segmental glomerulosclerosis

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**Introduction:** Many primary and secondary renal diseases manifest as nephrotic syndrome (NS). Primary focal segmental

glomerulosclerosis (FSGS) is the most important cause of idiopathic NS in the adult patient and the most common cause of glomerulonephritis-associated end stage renal disease. Recently, it was noted that patients have a better response to treatment with corticoid therapy (CCT) and, consequently, a better prognosis, than previously thought.

**Case report:** The patient was 48 years old, female. She sought medical attention because of worsening ankle edema, for nearly one year. She had history of hypertension and dyslipidemia that had been of difficult management by her general physician since the edema developed. She also complained of hoarseness and was a smoker. There were no other symptoms, relevant personal/family history or medication. On physical examination, she had anasarca and was hypertensive. Relevant data from initial tests include: hypoalbuminemia (17.8 g/L);  $>4$  g of proteins in spot urine; normal kidney function. Nephrotic range proteinuria was confirmed in a 24h urine specimen (8.17 g/24h). Dyslipidemia was documented: total cholesterol 411 mg/dL, HDL-cholesterol 63 mg/dL, triglycerides 263 mg/dL. The NS was managed with high dose diuretic therapy, an angiotensin converting enzyme inhibitor (ACEi) and a statin. To exclude secondary causes, the patient was examined by an ENT doctor – there were no suspicious lesions; a palpable nodule on the right lobe of the thyroid gland was studied – colloid nodule, thyroid function was normal; the immunologic study was negative except for rheumatoid factor; screening for HIV and hepatitis virus B and C was negative; the most common types of cancer for age group and sex were ruled out. Renal biopsy revealed FSGS and electronic microscopy showed effacement of podocyte foot processes and no immune deposits. The presenting features and the findings in the renal biopsy were suggestive of primary FSGS. CCT was instituted and the patient is currently on the 9th week of therapy, with improving NS but experiencing side effects from CCT. The patient developed a post-biopsy renal hematoma, so the decision to initiate anti-coagulation was postponed.

**Discussion:** Treatment of the NS requires high dose diuretic therapy, blood pressure control and ACEi. The decision to initiate anti-coagulation is guided by the serum albumin concentration. Up to 66% of patients with primary FSGS, respond to CCT.

## Low-protein diets supplemented with soy protein or essential amino acids/ketoanalogues in renal failure

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**Objective:** We attempted to evaluate the effects of the low-protein diets (LPD), supplemented with soy proteins or essential amino acids/ketoanalogues on blood pressure (BP) level, myocardial hypertrophy and biochemical indices of the severity

of uremia in Wistar rats with reduction of nephron number.

**Methods:** The study was performed on adult male Wistar rats (body mass 200-300 g). Model of the renal failure (RF) created by 5/6 nephrectomy (NE). Four groups experimental animals were studied: (1) sham operated rats (control – C) received 20% animal protein (standard diet; n=10); (2) NE rats kept out on standard ration (n=12); (3) NE rats received LPD1 (10% essential amino acids/ketoanalogues; n=9) and (4) NE rats received LPD2 (10% soy protein; n=7). Animals were taken out of the experiment, two months after NE or sham operation. Blood pressure (BP, mmHg) was measured in awaked rats by tail cuff method. In blood serum concentrations of urea (Ur, mmol/l), creatinine (Cr, mmol/l), total cholesterol (TC, mmol/l), inorganic phosphorus (Pi, mmol/l), total calcium (Ca, mmol/l) and albumin (Alb, g/l) were determined. The degree of myocardial hypertrophy was assessed by the left ventricular mass index (LVMI): left ventricular mass/body mass (mg/g). Data are presented as mean±SE. Unpaired Student t-test was used.

**Results:** Two months after NE in rats received a standard diet the levels of Ur (1.60±0.16), Cr (0.06±0.004, Pi (2.59±0.09), TC (1.60±0.12), BP (153.0±3.0) and LVMI (2.94±0.12) were significantly higher than in C (5.64±0.07, p<0.001; 0.034±0.004, p<0.001; 1.72±0.1; p<0.001; 1.34±0.08, p<0.01; 122.0±5.0, p<0.001; 2.06±0.13, p<0.01, respectively). By contrast, the level of Ca (1.92±0.09) in group (2) was lower than in C (2.35±0.15, p<0.05). In the NE rats kept out on LPD1 or LPD2 Ur (7.5±0.75 and 11.49±0.69, respectively) and Pi (2.09±0.07; 2.10±0.006, respectively) were significantly lower than in C (p<0.001 in all cases). In the same groups Ca did not differ from C (2.39±0.15, p=NS and 2.43±0.07, p=NS, respectively). In group (3) Ur value was less than in group (4); p<0.01. In NE animals received LPD1 or LPD2 levels of TC (1.44±0.17 and 1.49±0.07, respectively) were comparable with C (p=NS in both cases). The same was observed in respect Alb (LPD1 vs C: 29.0±1.59 and 26.44±1.18, p=NS; LPD2 vs C: 27.4±0.87 and 26.44±1.18, p=NS). BP in groups (3) and (4) were significantly lower in comparison the NE rats kept out on standard diet (125.0±5.0 and 135.0±3.0; p<0.01 in both cases). LVMI in groups (3) and (4) were less than in C.

**Conclusions:** Therefore, LPD, supplemented with soy proteins or essential amino acids/ketoanalogues in experimental RF exhibit cardioprotective and antihypertensive effects, prevent secondary hyperparathyroidism, lipid metabolism disturbances and not induce the protein-energy wasting. LPD, supplemented with essential amino acids/ketoanalogues more effective for prevention serum urea level rise than LPD, supplemented with soy proteins.

## Frequency and structure of etiopathogenetic causes of secondary amyloidosis with renal impairment

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**Objective:** To study the incidence and structure of the diseases, etiologically and pathogenically associated with the development

of renal amyloidosis in patients of the Nephrological department.

**Methods:** Case histories of 2577 patients with chronic kidney disease (CKD) of Nizhny Novgorod Regional Clinical Hospital named after N.A. Semashko during the period of 5 years (from 2009 to 2013) were analyzed. 56 admissions (from which 25 repeated) about amyloidosis with renal impairment were recorded. Thus, 31 patients (21 women and 10 men) were recorded. The average age of patients was 54±12,3 years. The diagnosis of amyloidosis in all investigated patients was morphologically verified (biopsy of gums, the abdomen wall and kidneys). To analyze the data statistical processing of the program «Statistica 6,0» was used. In addition, the structure of the pathology was evaluated in percentage.

**Results:** As a result it was found that the incidence of amyloidosis in patients with renal disease was 2,2% among patients with CKD. Among them the following diseases were predominated: rheumatoid arthritis (RA) – 23,3%, chronic tubulointerstitial nephritis (CTIN) – 25,6% and chronic obstructive pulmonary disease (COPD) – 18,6%. In rare cases there were: bronchiectasis – 7,0%, type 2 diabetes – 5,0%, bronchial asthma – 4,6%, chronic glomerulonephritis – 4,0%, ankylosing spondylitis – 2,3%. In 4,6% of the cases amyloidosis was concurrent with Friedreich's ataxia syndrome and obliterating atherosclerosis of the lower extremities with chronic arterial insufficiency. In the rest 5,0% of the cases the causes of renal amyloidosis were not found. Among them there were likely to be the cases of primary amyloidosis. In turn, the structure of CTIN in these patients was presented: primary chronic disease – 54,5%, in combination with urolithiasis – 18,2%, due to congenital abnormalities of the urinary tract (doubling of both kidneys) – 9,1%, in combination of stone disease and urinary tract malformations (horseshoe kidney) – 9,1%, in combination with polycystic kidney disease – 9,1%. The average duration of the main diseases led to renal amyloidosis was: in CTIN – 19,5±10,5, in RA – 11,6±7,4, in COPD – 9,4±7,7 years.

**Conclusion:** In the structure of the diseases etiopathogenically led to amyloidosis with renal impairment RA, CTIN and COPD prevailed.

## Nephrotic syndrome associated with lymph node tuberculosis

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**Introduction:** Tuberculosis (TB) is a systemic infectious disease known as “the great pretender”, with several possible atypical presentations that can lead to death if clinical suspicion is low. The authors present a case which thoroughly portrays such diagnostic complexity.

**Case report:** 70 years old Caucasian male, active smoker (40 pack/years), was admitted to an internal medicine ward for study of progressive fatigue, anorexia, nausea, non-quantified weight loss and foamy urine. Physical observation with no relevant findings. Laboratory findings: nephrotic proteinuria (glomerular and tubular – 3993 mg/24h) with granular and hyaline rods; sedimentation rate 28 mm/h; creatinine 1,56 mg/dL, serum

albumine 2,8 g/dL, negative serologies for cytomegalovirus, Epstein-Barr virus and human immunodeficiency virus; acid-fast bacilli and urine cytology negative. The initial study of secondary glomerulonephritis revealed monoclonal gammopathy (MG) of undetermined significance IgG-K; MG of renal significance was ruled out as was amyloidosis. Search for occult primary tumors was negative; IGRA test and tuberculin skin test negative; full autoimmunity testing negative. Imaging studies: infracentimetric mediastinal adenopathies; mild-to-moderate pericardial effusion with signs of chronic pericardial thickening. Renal biopsy was inconclusive (insufficient sample). The patient developed severe nephrotic syndrome (protein/creatinine ratio 8-10 g/day) and progressive malnutrition. Still with no conclusive diagnosis at that time, a mediastinoscopy was performed with excision of mediastinal lymph node; biopsy revealed necrotizing granulomatous lymphadenitis, compatible specifically with lymph node TB. Treatment was started with isoniazid, rifampicin, pyrazinamide and ethambutol. However, the patient developed a respiratory tract infection which progressed into severe sepsis, passing away before evidence of therapeutic response was observed. Despite the outcome, both the wasting and nephrotic syndromes (as a result of secondary glomerulonephritis) were attributed to lymph node and pericardial TB.

**Discussion:** Lymph node TB is the most common extrapulmonary form of the disease. Membranous glomerulonephritis is the most prevalent cause of nephrotic syndrome in this patient's age group, and is usually secondary to diabetes mellitus or underlying malignant, inflammatory or infectious disease, as occurred in this case, despite the scarce amount of literature relating nephrotic syndrome and lymph node TB.

## Hematuria and acute kidney injury associated with warfarin anticoagulation

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**Introduction:** Over anticoagulation (international normalized ratio (INR) >3.0) is often associated with an unexplained acute increase in serum creatinine and an accelerated progression of chronic kidney disease (CKD) but robust prospective data is lacking. Hematuria in warfarin-treated patients may result from glomerular leak or urothelial hemorrhage. We present a case of hematuria and acute kidney injury (AKI) associated with warfarin anticoagulation along with a review of the literature.

**Case report:** A 60 years old woman under warfarin therapy after aortic valvuloplasty with placement of mechanical prosthesis 30 years ago was admitted because of acute loss of kidney function together with persistent microscopic hematuria and proteinuria and also sputum haemoptysis. She was hemodynamically stable and oxygen saturation was 98%. Her blood tests revealed Hb 8,5 g/dL, INR 12, creatinine 12,5 mg/dL (normal last month). Radiographic study showed bilateral heterogeneous opacities of the lower lungs. Other causes of AKI such as obstruction, dehydration or infection were ruled out. Supratherapeutic INR was corrected with vitamin K. Serology for hepatitis B virus, hepatitis C virus and human immunodeficiency virus was negative. Anti-neutrophil cytoplasmic antibody and anti-

glomerular basement membrane antibody were negative. Light microscopy of a needle biopsy containing 25 glomeruli showed diffuse mesangial proliferation. Red blood cells (RBC) were found within the tubular lumina with formation of occlusive RBC casts in 10% of tubules. She became oliguric and emergent hemodialysis was initiated. The patient did not recover renal function and remained on chronic dialysis.

**Conclusions:** This case highlights the importance of monitoring kidney function and coagulation parameters in patients under warfarin therapy. Prospective studies are needed to clarify the actual impact of overanticoagulation on AKI and hematuria.

## Vascular determinants of dementia in diabetics

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**Objectives:** Recent evidence suggests that carotid ultrasound combined findings denoting atherosclerosis are associated with dementia. The aim of the present study was to determine the association of carotid and femoral ultrasound findings with dementia.

**Methods:** Analysis involved imaging by triplex of carotid femoral arteries of 80 diabetics with and without albuminuria in longitudinal fashion, to detect the presence of atheromatic plaque and to assess the intima-media thickness (IMT). Each artery was assigned a score/presence of plaque = 1 IMT <0,8 mm = 0.1 MT ≥0,8 mm = 1) and the total score of the four vessels was calculated per patient (atherosclerotic ultrasonic score – ATHUS) according to Thomas Tegos method. Subsequently the Mini-mental state examination (MMSE) of every patient was evaluated.

**Results:** Group A (ATHUS=0-2, 30 patients without albuminuria) was associated with median MMSE of 30 and interquartile range of 3. The corresponding values for Group B (ATHUS=3-5, 30 patients with microalbuminuria) and Group C (ATHUS=6-8, 20 patients with albuminuria) were: 27 (3) and 25 (4) respectively (p<0,05).

**Conclusion:** Our study suggests that the degree of atherosclerosis and albuminuria were inversely related to MMSE.

## Clinical characteristics, quality of life and prognosis of patients with chronic cardiorenal syndrome

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**Objectives:** Decrease of kidney function is associated with more severe chronic heart failure (CHF), an increase of re-hospitalizations, reduced social activity. The aim of this study

was to investigate comorbidity clinical and psychological characteristics and quality of life in patients with CHF and patients with CHF associated with chronic kidney disease (CKD).

**Methods:** 203 patients with CHF (130 males and 73 females, mean age  $61,8 \pm 9,6$  years) were examined. CHF was defined according to the Russian guidelines for the diagnosis and treatment of chronic heart failure (2012). Glomerular filtration rate (GFR) was calculated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula and chronic kidney disease (CKD) was defined according to the National guidelines for the diagnosis, prevention and treatment of CKD (2012). Group of chronic cardiorenal syndrome (CRS) was included patients with CHF GFR  $<60$  mL/min/ $1,73\text{m}^2$ . Charlson comorbidity index was calculated. Standard 2-dimension echocardiography was performed. Left atrial diameter (LAD) was measured and indexed on  $\text{m}^2$  of height (LADI). Left ventricular systolic function was defined as preserved if left ventricular ejection fraction was  $>50\%$ . Number of hospitalizations during 1 year follow-up period, psychological state, quality of life of patients with chronic cardiorenal syndrome were assessed.

**Results:** Charlson comorbidity index for age was  $5 \pm 2,1$  points. 89 (43,8%) patients had CKD with GFR  $<60$  mL/min/ $1,73\text{m}^2$ . CKD was the most frequent component in the structure of comorbidity of patients with CHF. Patients with CRS had a higher comorbidity. Systolic dysfunction was diagnosed in 58 (27,6%) patients. Patients with CRS were hospitalized due to exacerbation CHF for year more often than patients without CRS. Patients with CRS had higher mean LADI than patients without CKD:  $22,7 \pm 3,1$  and  $21,8 \pm 2,9$  mm/ $\text{m}^2$  resp. ( $p=0.03$ ). There was positive correlation between Charlson comorbidity index and LADI ( $r=0.40$ ,  $p=0.003$ ). CKD was the main factor determined influence comorbidity on LADI. Multivariate regression analysis showed that female gender and decrease of kidney function (GFR  $<60$  mL/min/ $1.73\text{m}^2$ ) were independently associated with enlargement of LADI. Patients with CRS had expressed emotional discomfort, the presence of depressive, dysadaptative trends, decreased of quality of life, both in the physical and the psychological aspects.

**Conclusions:** CKD has a negative impact both in the clinical course and quality of life, psychological status and prognosis of patients with CHF. At the same time, patients with CRS have a high comorbidity, they are characterized by the presence of hypochondria and depression and low quality of life, which should be taken into account in the development of guidelines for the diagnosis and treatment of this group and assessment of prognosis.

### Comparing the efficacy of carvedilol therapy with angiotensin converting enzyme inhibitors in type 2 diabetic patients with microalbuminuria and stage 1 hypertension taking angiotensin receptor blockers

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**Objectives:** Angiotensin receptor blockers (ARB) and angiotensin converting enzyme inhibitors (ACEI) are currently used in the

treatment of diabetic nephropathy. Recent studies suggest that additional benefits may be achieved with the administration of third generation beta-blockers in diabetic patients. Although carvedilol is known to have antiproteinuric activity in patients with essential hypertension, this activity was not investigated in patients with diabetic nephropathy. The present study was planned to compare the efficacy of carvedilol therapy with ACEI in type 2 diabetic patients with microalbuminuria and stage 1 hypertension taking ARB.

**Methods:** 56 patients with type 2 diabetes, stage 1 hypertension and microalbuminuria, were enrolled. All patients were included in a follow-up period of 2 weeks prior to treatment and randomization. After this period, all patients were started on losartan 50 mg/day as a single dose. Patients receiving this treatment for approximately 6 weeks were randomized to 3 groups. Patients in the first group had a losartan dose increase to 100 mg/day. Patients in the second group were started on carvedilol 25 mg/day in addition to losartan 50 mg/day. Cilazapril 5 mg/day was started in the third group in addition to losartan 50 mg/day treatment. Patients were followed-up for 6 weeks post-randomization.

**Results:** Age, gender, diabetes and hypertension durations, oral antidiabetic and insulin usage among the groups were similar. In all three groups, during the losartan 50 mg treatment period and post-randomization treatment period, the decreases in systolic and diastolic BPs were statistically significant. In the post-treatment period greatest decreases in systolic and diastolic BPs were seen in group 3 (systolic BP  $16.5 \pm 7.4$  mmHg, diastolic BP  $10.5 \pm 2.8$  mmHg), and smallest decreases were seen in group 1 (systolic BP  $9 \pm 6.1$  mmHg, diastolic BP  $3 \pm 4.8$  mmHg). In all three groups significant decreases were found in microalbuminuria in the post-randomization period, as opposed to the period when losartan 50 mg was administered. Serum urea, creatinine, sodium, potassium, total protein and albumin levels of the groups did not change significantly.

**Conclusions:** Our findings show that in hypertensive type 2 diabetics with microalbuminuria, carvedilol can be combined with ARB treatment with established efficacy. This combination was not found to be different than other combination treatments, in terms of efficacy and side effects.

### Acute renal failure secondary NSAIDs in patient with inflammatory bowel disease

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**Introduction:** Description of a case of acute interstitial nephritis (AIN) in patients with chronic inflammatory bowel disease, and tests performed to reach the diagnosis and treatment.

**Case report:** We present a 24 year old woman diagnosed with ulcerative colitis 4 years of evolution with good control with mesalazine without intake of other NSAIDs in the past 8 month. She was admitted because progressive deterioration of renal function (serum creatinine maximum 1.87 mg/dL)



with normal kidneys size and morphology, and asymptomatic. After detecting elevated plasma levels of IgA, proteinuria and improve renal function partially after decreasing the dose of mesalazine, secondary to mesalazine AIN is suspected and virological study of autoimmunity and resulting negative are made, a renal biopsy confirmed the diagnosis. Treatment was initiated with prednisone 60 mg a day, reaching the normal patient plasma creatinine figures. Laboratory Results: urea 31 mg/dL, creatinine 1.87 mg/dL, Ca 9,3 mg/dL, P 3,6 mg/dL, Na 138 mEq/L, K 5 mEq/L, hemoglobin 13.8 g/l, hematocrit 40%, prothrombin activity 100%, VSG 5 mm/h, PCR 4 mg/l, ASO 44 IU/ml, Latex <10 IU/ml; ANAS, ANCAS, Serology HCV, HBV and HIV negative. Increase in IgA polyclonal serum protein, complement C3 90 mg/dL, C4 16 mg/dL, IgG 1480 mg/dL, IgA 444 mg/dL, IgM 55 mg/dL, negative anti-GBM. Urine: proteinuria 159 mg/g, microalbuminuria 40 mg/g. Sediment: evidence of proteinuria. Ultrasonography: both kidneys of normal size, location and normal morphology, distinct both cortical and normal thickness. No dilatation of the excretory system. Renal biopsy: cylinder kidney glomeruli 26, 1 sclerotic, optimally regular rest. Mild nonspecific interstitial infiltrate and focal tubular atrophy with focal amyloid deposition and interstitial level vessel wall.

**Discussion:** The NIA can have a longer latency to 18 months with the NSAID. It usually presents with fever, skin rash and eosinophilia but can occur only with elevated serum creatinine. The treatment of choice is to stop taking the drug causes; corticosteroids are used if not decrease serum creatinine after treatment discontinuation. In patients with inflammatory bowel disease it is advisable to assess renal function periodically for NIA secondary to mesalazine.

## Disseminated sarcoidosis: a diagnosis not to be missed

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**Introduction:** Chronic Kidney Disease (CKD) in young patients without predisposing factors (hypertension, diabetes mellitus, renal artery stenosis, urinary tract obstruction, autoimmune disease/ vasculitis, post-infectious glomerulonephritis and consumption of nephrotoxic drugs) remains a diagnostic challenge.

**Case report:** A 32 years old man with a 2-year history of calcium oxalate kidney stone disease and CKD (glomerular filtration rate 43 ml/min), presented due to incidentally discovered severe hypercalcemia (serum calcium 13 mg/dL) with low parathormone and 25(OH) vitamin D levels. Laboratory tests revealed a mild normocytic anemia, leukopenia with normal neutrophils and lymphopenia, elevated urine calcium, normal serum phosphorus, mild elevation of the IgG and a normal urine microscopy. Imaging studies demonstrated nonspecific fibroatelectatic lesions in the lungs, lymph nodes smaller than 1 cm in the abdomen and mild splenomegaly. Serum SACE and 1,25 vitamin D were significantly elevated, consistent with either sarcoidosis or a lymphoproliferative disease, which produce 1 $\alpha$  hydroxylase, leading to autonomous increase of dihydroxyvitamin D, despite

hypercalcemia. A bone marrow examination was also performed, revealing a non caseating granuloma with a negative Ziehl-Nielsen stain, while a marrow immunophenotyping showed a relative decrease of the CD4 count, a finding commonly met in sarcoidosis. Following these, a bronchoscopy revealed a CD4:CD8 ratio 3.2:1, likewise consistent with sarcoidosis. After steroid administration, serum calcium is normal and the patient's renal function has returned to normal.

**Discussion:** Sarcoidosis is a multisystem disease, mainly involving the respiratory system. It may also affect the kidneys, causing lithiasis in 4%, acute or chronic renal failure with an incidence varying from 3 to 48% in the literature, hypercalcemia in 10-13% and more often, hypercalciuria. Renal biopsy may be not diagnostic in the 29% of patients. Diagnosis may be then based on clinical, laboratory and histological findings from other organs which may be affected, even though the patient may be asymptomatic. Renal sarcoidosis usually responds adequately to steroids, but rarely evolves to end-stage renal disease.

## Glomerular affectation and nephrocalcinosis: a rare case of Dent's disease

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**Introduction:** Dent's disease is an X-linked recessive disorder of the proximal kidney tubules characterized by hypercalciuria, nephrocalcinosis, kidney stones, renal failure, and rickets. 250 families in the world are affected by Dent's disease, but diagnosis sometimes goes unnoticed over years. We describe a case of Dent's disease of difficult diagnosis.

**Case report:** A 19 years old man was admitted to nephrology ward. He had consulted for an episode of macroscopic hematuria. Physical examination was normal, including BP 120/60 mmHg. The urinalysis and blood test showed proteinuria 2.2 g/24 h, preserved glomerular filtration rate, 1-5 red blood cells per high power field (RBC/HPF), negative immunological study and negative urine culture. In addition, hypercalciuria (400 mg/24 h), calcium oxalate crystals, and serum calcium 10 mg/dL, serum phosphate 2,5 mg/dL with high vitamin D (90 ng/mL) and low PTH (12 pg/mL) were documented. The renal ultrasonography and the intravenous urography revealed incipient signs of nephrocalcinosis. He was discharged on enalapril 5 mg daily and hydrochlorothiazide 12,5 mg daily. Subsequent controls in the outpatient clinic showed maintained hypercalciuria and proteinuria not rich in albumin, nephrocalcinosis progression and slow worsening of renal function to 46 mL/min. Several episodes of urethral colic were also documented. 15 years later, a second-degree male relative is diagnosed with Dent's disease, thus genetic testing is also carried out in our patient, resulting positive for p.G466D mutation in CLCN5 gen, establishing the diagnosis of type 1 Dent's disease. This mutation leads to stop reabsorbing low molecular weight proteins, which explains proteinuria without albumin. One such protein is human PTH, which reaches portions of the following renal tubule and promotes all the calcium-phosphate alterations including nephrocalcinosis.

In the familial research, two grandmother's brothers of our patient, already deceased, had unknown renal disease. His grandmother and mother were asymptomatic carriers and none of his siblings had the disease.

**Discussion:** Hereditary tubulopathies are rare diseases. Clinical suspicion is difficult in the absence of a family context. Nonetheless, the joint presentation of proteinuria (characteristically not rich in albumin) and nephrocalcinosis in a young patient may be indicative of Dent's disease. No other treatments than common nephro-protectors are available, but early diagnosis allows changes in lifestyle and the use of drugs designed to slow the progression of the disease.

## Renal artery thrombosis

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**Introduction:** Renal artery thrombosis is a rare condition, serious and often underdiagnosed due to its non-specific clinical presentation.

**Case report:** We present a case report of a 73 years old patient, male, with pathological history of hypertension, dyslipidemia, myocardial infarction, stroke and transient ischemic attack. Treated with enalapril, acetylsalicylic acid, clopidogrel, pantoprazole, simvastatin, nebivolol, transdermal nitroglycerin and zolpidem. Admitted by intense abdominal pain in left quadrants, radiating to lumbar and left inguinal regions and sudden decrease of the urinary debit, progressing to anuria, with 48 hours of evolution. At the entrance was afebrile, hemodynamically stable, distended abdomen, painful on palpation in the left iliac fossa and left upper quadrant. Analytically: microcytic and hypochromic anemia with 11.0 g/dL hemoglobin; without leukocytosis or neutrophilia, potassium 5.9 mEq/L; urea 120 mg/dL, creatinine 7.4 mg/dL; C-reactive protein 15.7 mg/dL. Negative urine culture. Abdominal CT scan: features suggestive of complete thrombosis of the left renal artery, extending a small thrombus to the lumen of the aorta in the renal ostium, calcium atheromatous of the aorta artery with extension to the iliac. He was transferred to the reference hospital, to vascular surgery, where intra-arterial thrombolysis was performed. Control angiography: permeability of the left renal artery. After 24h he makes a new angiography: new thrombosis of the right renal artery. Treated with intra-arterial aspiration of the thrombus and introduction of alteplase. He also presented a new thrombosis of the left renal artery, which was treated with instillation of alteplase. As complications, he suffered a hemorrhagic stroke that reabsorbed spontaneously. There was a need for treatment with renal replacement therapy. He was again transferred to the hospital of his residence area, with the diagnosis of acute kidney injury due to left cortical necrosis perfusion deficit and right acute tubular necrosis. Currently without dialysis support, with still high creatinine values but decreasing and without neurological deficits. The prothrombotic study was negative.

**Discussion:** Thrombosis of renal arteries is a major cause of deterioration of kidney function, usually being difficult to establish the diagnosis.

## Estimation of electrophoretic activity of erythrocytes with arterial hypertension patients undergoing routine hemodialysis

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**Objective:** To estimate electrophoretic activity of erythrocytes (EAE) in patients suffering from the 5th stage of the chronic kidney disease (CKD) with arterial hypertension (AH) undergoing routine hemodialysis (HD).

**Methods:** 60 patients with the 5th stage of CKD (55% of women and 45% of men) were examined. The average age of the patients is 48,8±11,4. 42 conditionally healthy respondents among blood donors of Udmurt Republic were included in the control group. The hemodialysis procedures were implemented on device 4008S (Fresenius, Germany) in the department of hemodialysis in the City Hospital of Izhevsk №6. Estimation of EAE was held using the set "CytoExpert" (OJSC Axion Holding, Izhevsk, 2010). The average range of erythrocytes fluctuation (AREF), asymmetry and excess were assessed.

**Results:** Comparing the results of the research in the main and control groups a significant increase of AREF with the patients undergoing the hemodialysis was marked: 49,7±6,3 microns versus 28,4±3,2 microns with the donors ( $p<0,01$ ). The increase of AREF with the patients undergoing the routine hemodialysis might be caused by frequent injections of anticoagulants and mechanic damage of erythrocytes when injecting dialyzer. There were no major differences in asymmetry and excess indicators in the main and the sampling groups discovered: -0,98±1,3, -1,37±0,2 ( $p>0,1$ ) 5,1±6,9, 9,62±1,7 ( $p>0,1$ ) respectively. The percentage of active erythrocytes in the main and the sampling groups was almost equal: - 98,3±2,9%, 99,2±0,2% ( $p>0,1$ ) respectively. There was no gender factor affecting AREF discovered either: 50,6±6,9 microns with men, 49±7,6 microns with women ( $p>0,5$ ). The AREF and asymmetry of erythrocytes indicators were lower with AH patients in comparison with people with normal arterial tension: 47,4±6,3 microns and 52,8±3,9 microns ( $p<0,01$ ); -1,3±1,2 and -0,35±0,8 ( $p<0,01$ ) respectively. The percentage of active erythrocytes was of no difference. The AREF indicator was different depending on the stage of AH: the 1st stage - 47,5±6,1microns, the 2nd stage - 47,6±10,2 microns, the 3rd stage - 52,7±5,7 microns ( $p<0,01$ ). The AREF indicator was higher with patients taking calcium channels blockers (CCB) (51,5±5,4 microns) compare with patients taking angiotensin converting enzyme inhibitors (ACEI) (44,6±5,8 microns  $p1<0,05$ ) and beta-blockers (BB) (46,6±1,1 microns  $p3<0,05$ ). The asymmetry of erythrocytes fluctuation indicator was clearly lower with patients taking ACEI (-2,4±0,3,  $p2<0,05$ ,  $p3<0,05$ ), versus those with patients taking CCB (-0,6±1,4) and BB (0,2±0,3).

**Conclusions:** Peculiar features of EAE with patients undergoing the routine hemodialysis were determined. A remarkable alteration of indicators was discovered with AH patients. CCB affect EAE in the most positive way. The data on EAE could be of great use when differentiated selection in performed as well as for studying the effectiveness of antihypertensive therapy.

## Cardioprotective effect of low-protein diet supplemented with essential amino acids and ketoanalogues in chronic renal dysfunction

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**Objective:** We evaluated the effects of long term low-protein diet (LPD) supplemented with of essential amino acids and ketoanalogues on serum biochemical parameters, blood pressure (BP) and myocardium morphology in 5/6 nephrectomized (NE) Wistar rats.

**Methods:** Adult male Wistar rats, weighing 200–250 g were studied. Experimental groups: 1 – sham-operated (control, C) receiving standard diet, containing 20% animal proteins (n=9); 2 – NE rats on standard diet (n=10); 3 – NE rats receiving LPD and ketosteril (n=11). The animals were observed in 4 mo after NE. Serum urea (Ur), total calcium (Ca), phosphorus (Pi), albumin (Al), total protein (TP) and urine protein levels were investigated. Mean BP was measured in the awaked rats by the tail cuff method. The degree of left ventricular hypertrophy was estimated as a ratio: left ventricular mass/body mass (LVH; mg/g). Morphological and morphometric investigations of myocardium (light microscopy) were performed.

**Results:** NE in rats on the standard diet was associated with significant rise Ur (mean±SE; 17.8±0.9 in group 2 vs 5.4±0.7 mmol/l in C; p<0.001). LPD with ketosteril prevented a significant increase Ur in rats after NE (9.97±1.0 mmol/l, p<0.01). Pi level increased in rats after NE, receiving standard diet: 2.62±0.01 mmol/l in group 2 vs C – 2.05±0.05 mmol/l (p<0.01). Serum Pi level in group 3 didn't increase significantly (2.20±0.08 mmol/l). Total Ca level in group 2 was lower, than in group 3 (2.07±0.05 and 2.34±0.08 mmol/l respectively; p<0.01), whereas in C – 2.35±0.15 mmol/l (p=NS vs group 3). LPD didn't influence on the TP and Al levels. LPD with ketosteril decreased proteinuria in rats after NE (in group 2 – 9.8±2.2 g/l; in group 3 -1.5±0.9 g/l, p<0.01). BP in group 2 was significantly higher, than in C (165±5 vs 125±10 mmHg, p<0.001). LPD with ketosteril prevented increase in BP (130±5 mmHg) compared with NE rats on standard diet (p<0.001). LVH in group 3 was less than in other groups (1.96±0.15 mg/g vs – 2.72±0.11 mg/g (p<0.01) in group 2, and vs 2.35±0.09 mg/g in C rats). After NE in groups 2 and 3 morphological findings showed disintegration of myocardium cells and signs of apoptosis, fragmentation of myocardium fibers, severe cellular cloudy degeneration, perivascular sclerosis. Hypertrophy of myocardium cells was not revealed. But increasing in conjunctive tissue area was significantly more in NE rats on standard diet (3636 ±8,81µm<sup>2</sup>) vs control (2750.5±6.57; p<0.01) and vs groups on LPD and ketosteril (2837.6±6.2 µm<sup>2</sup>, p<0.01). Vascular walls didn't thicken in rats on LPD and ketosteril.

**Conclusions:** Long term LPD with ketosteril delayed myocardial fibrosis and showed antihypertensive effects in 5/6 NE Wistar rats. Long term LPD with ketosteril delayed myocardial fibrosis and showed antihypertensive effects in 5/6 NE Wistar rats.

## Uromodulin and severity of tubulointerstitial lesions in patients with nephropathies

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**Objectives:** Is traditionally believed that uromodulin (Umo) may participate in urinary stone formation. However, there is evidence that Umo can be operated in other mechanisms, especially damaging tubulointerstitial renal compartment and promotional arterial hypertension. In this regard, we attempt to compare the levels of the Umo in urine and blood serum with the morphological characteristics of kidney lesions and some clinical functional parameters in patients with various nephropathies.

**Methods:** 28 patients (Pts; M:F 11:17), age 28–74 years were studied. The severity of sings of renal damage were assess semi-quantitatively in nephrobiopates (light microscopy) by independent morphologist. Urinary (UUmo) and serum (SUmo) Umo concentrations were measure by Human Uromodulin ELISA kit ("BioVendor", Czech Republic). Levels of creatinine (Scr) and urea (Sur) in blood serum, proteinuria (Ptr) and estimated glomerular filtration rate (eGFR; CKD-EPI) been established. In 20 Pts 24-hour blood pressure monitoring was performed.

**Results:** UUmo significantly inverse correlated (Spearman rank correlation coefficient) with degree of tubular atrophy (TA; rs=-0.39; p=0.038), mononuclear infiltration of interstitium (rs=-0.37; p=0.05) and mean systolic BP at the day time (mSBPday; rs=-0.49; p=0.028). SUmo was directly associated with eGFR (rs=0.53; p=0.007) and inverse – with TA (rs=-0.39; p=0.038), degree of perivascular stromal fibrosis (rs=-0.44; p=0.019), Scr (rs=-0.64; p<0.001) and Sur (rs=-0.60; p<0.002). TA directly correlated with mSBPday (rs=-0.50; p<0.001). There were no any links between SUmo and UUmo, SUmo or UUmo and glomerular lesions or Ptr. In Pts with the presence hyaline casts in the tubular lumen according to morphological date SUmo was significantly lower than in Pts with no casts.

**Conclusions:** Umo concentrations in urine and serum are associated with the severity of tubulointerstitial lesions in patients with different nephropathies. Reduction the urinary and serum Umo levels may reflect a decrease the nephron mass and more local tubulointerstitial damages.

## The chicken or the egg: a patient with rapidly progressive renal and heart failure

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**Introduction:** Acute renal failure requires a systematic diagnostic approach. The following case report illustrates that the heart does not always play a 'prerenal' role in kidney failure.

**Case report:** A 78 years old man presented with rapidly progressive renal failure. His medical history mentioned an urothelial cell carcinoma for which the patient had twice undergone transurethral resection. The past month, he had been treated with antibiotics for a leg ulcer. While under antibiotic treatment, the patient developed peripheral edema and progressive dyspnea. He was admitted to a local hospital where a transthoracic ultrasound showed a diminished left ventricular function of unknown cause with an ejection fraction of 30% and a moderate aortic valve stenosis. The patient's creatinine level had increased in one month time from 62 to 330  $\mu\text{mol/l}$ , first thought to be due to forward failure. However, the patient also appeared to have a nephrotic syndrome with a serum albumin of 27 g/l and proteinuria of 9 g/24h. No erythrocytes or erythrocyte casts were found in his urine and a renal ultrasound was unremarkable. The differential diagnosis at that moment included a glomerulonephritis/vasculitis or a tubulointerstitial nephritis caused by his antibiotic treatment. Unfortunately, treatment with diuretics was unsuccessful; the patient's urine output decreased and he was transferred to our hospital for further work up. A kidney biopsy was done and the patient was started on methylprednisolone. Despite this, his kidney function did not improve and after three days the patient developed a fever. His blood cultures were positive for an *Enterococcus faecalis* and intravenous amoxicillin was promptly started. A transesophageal ultrasound showed aortic valve vegetation and an abscess at the non-coronary cusp. The kidney biopsy showed an immune complex mediated diffuse proliferative glomerulonephritis, consistent with a postinfectious glomerulonephritis. The patient was diagnosed with an *Enterococcus faecalis* endocarditis; possible route of infection was a cystoscopy a week before presentation. The patient underwent long-term intravenous antibiotic treatment and an aortic valve replacement. He had a full recovery of his kidney function and his left ventricular function is currently improving.

**Discussion:** When a patient presents with rapidly progressive renal failure and heart failure of unknown cause, the possibility of an endocarditis should be considered.

## Hepatorenal syndrome – a review on the subject through a clinical case

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**Introduction:** The hepatorenal syndrome (HRS) is one of the many potential causes of AKI in patients with acute or chronic liver disease. Arterial vasodilatation in the splanchnic circulation, which is triggered by portal hypertension, appears to play a central role in the hemodynamic changes and the decline in renal function. The diagnosis is based upon clinical criteria and is essentially one of exclusion, entertained only after other potential causes of acute or subacute kidney injury (AKI) have been ruled out. The ideal therapy is improvement of liver function either from treatment of the underlying disease or liver transplantation. When improvement of liver function is not possible in the short

term, medical therapy should be instituted in an attempt to reverse the AKI associated with HRS. Medical therapy includes norepinephrine or terlipressin in combination with albumin. Treatment options for patients who do not respond to medical therapies include TIPS (transjugular intrahepatic portosystemic shunt) and dialysis.

**Case report:** The authors report a case of HRS, referring to a 36 years old woman who presented with jaundice, ascites, oliguria, AKI, hyperbilirubinemia, coagulopathy and peripheral edemas. She had a previous diagnosis of chronic alcoholic liver disease with cirrhosis. After excluding other causes of liver disease decompensation, such as infection, gastrointestinal bleeding and diuretic therapy, she started treatment with terlipressin/norepinephrine in combination with albumin. However, she failed to respond to the therapy, developed severely impaired renal function with shock, anuria and severe respiratory failure, which implied admission in an intensive care unit. In this unit, she started vasopressor support, invasive mechanical ventilation and continuous renal replacement therapy (RRT), leading to favorable clinical outcome, with reversal of the hepatic failure and recovery of kidney function within roughly a week from admission.

**Discussion:** The authors review and discuss the current evidence in the management of the HRS. Although its prognosis is still dismal, the presented case was successful.

## Parvovirus B19 infection in kidney transplantation. A case report

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**Introduction:** Infections represent a relevant cause of morbidity and mortality after renal transplantation. In this respect, viral infections are the most common cause of infections within the first 6 months after the procedure. Parvovirus B19 has been related to refractory anemia, pancytopenia and thrombotic microangiopathy. PCR is widely used as a diagnostic tool of Parvovirus infection and intravenous immunoglobulins may be quiet effective in its treatment.

**Case report:** 45 years old male patient with a previous medical history of chronic renal failure. He started hemodialysis in 2012 which was pursued until 2014. At that time, he received a cadaver donor renal transplant. The procedure had no relevant complications. At discharge, blood tests showed a serum creatinine of 1.56 mg/dL and hemoglobin was 8.2 g/dL. Erythropoietin was prescribed but despite it, hemoglobin ranges between 8-9 g/dL in a context of fluctuant lymphopenia. 1 month later, hemoglobin dropped to 7.1 g/dL requiring blood transfusion and increase dose of erythropoietin. At day 64, the patient was hospitalized because of fever and general weakness but all the tests came back negative. At day 120, in a context of persistent fever, the patient was re-admitted and same lab test results obtained including PCR for parvovirus B19. The patient continued to be febrile showing the complete

blood pannel marked anemia (6.2 g/dL), thrombopenia and lymphopenia. At day 142, considering the overall picture, another determination of PCR for parvovirus B19 was ordered which came back positive and then confirmed through a bone marrow aspirate. Cellcept was discontinued and intravenous immunoglobulins were daily administered during 10 days. A complete clinical and biological recovery was obtained, thus erythropoietin discontinued.

**Discussion:** Parvovirus B19 infection in a cadaver donor renal transplant should be suspected in the setting of hematological abnormalities requiring adjustment of the immunosuppressive.

## Microalbuminuria and renal hemodynamic status in patients with metabolic syndrome

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**Objectives:** Metabolic syndrome (MS) is a major risk factor for the development of type 2 diabetes and cardiovascular disease. Patients with the MS are at significantly higher risk for microalbuminuria and/or chronic kidney disease (CKD). It is important to study intra-renal hemodynamics by ultrasound, where renal parenchymal damage in obesity may be reflected by intra-renal resistive indices.

**Methods:** We examined 108 patients with MS (90 women and 18 men, mean age 54,6±0,4 years). All patients were divided into 3 groups (III classes of obesity, divided by body mass index). They underwent clinical and laboratory examination, which included lipidogram, insulin, plasma homocysteine levels, microalbuminuria (MAU) in the morning urine. The result was determined directly, without any recalculation. MAU identified in excess of index higher than 20 mg/l. Study of intrarenal blood flow was performed by color Doppler with pulsed dopplerometry on the device Aloka SSD-5500. We studied the main and intrarenal renal artery (segmental and interlobar) in the projection of the three segments of both kidneys. We determined the resistive characteristics of the arterial blood flow (RI and PI), calculated automatically by the standard formulas.

**Results:** The average level of insulin plasma and homocysteine exceeded the normal laboratory data in the III class – 31,6±0,4 mE/l (p<0,001) and 18,4±0,6 mol/l (p<0,001). The level of MAU exceeded in the II class – 20,4±0,5 mg/l (p<0,05) and III class – 53,1±7,9 mg/l (p<0,001). In the study of intrarenal blood flow RI and PI in the segmental and interlobar level of the arteries in these groups of patients were above normal values. In the segmental level: I class – RI=0,64±0,01 (p<0,05) and PI=0,99±0,2 (p<0,001); II class – RI=0,71±0,01 (p<0,05) and PI=1,24±0,03 (p<0,001); III class – RI=0,7±0,01 (p<0,05) and PI=1,33±0,04 (p<0,001). In the interlobar level: I class – RI=0,63±0,01 (p<0,05) and PI=0,99±0,2 (p<0,001); II class – RI=0,7±0,01 (p<0,05) and PI=1,24±0,03 (p<0,001); III class – RI=0,68±0,01 (p<0,05) and PI=1,31±0,04 (p<0,001).

**Conclusion:** These results suggest that patients with MS have a sign of intravascular renal resistance and an increased risk for CKD.

## The protective effects of amifostine, curcumin and melatonin against cisplatin-induced rat renal tissue damage: a light and electron microscopic study

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**Objectives:** Cisplatin clinical oncology in the testis, ovary, bladder, is an effective antineoplastic agents commonly used in the treatment of many types of cancers of the lung. The most important side effect is that restrict the use of cisplatin nephrotoxicity. Nephrotoxicity is known to be caused by increased oxidative stress occurred due to free oxygen radicals. This in renal injury induced by cisplatin in rats study starting from the basic idea, known to have antioxidant properties amifostine protective effects of curcumin and melatonin examined.

**Methods:** Single intraperitoneal (i.p.) dose of cisplatin group way 5 mg/kg will be cisplatin. Starting 24 hours before the cisplatin injection cisplatin + amifostine group, for 7 days after i.p. injection of cisplatin injection of 400 mg/kg/day amifostine (etyhol) apply. Cisplatin + curcumin group, starting 24 hours before the cisplatin injection curcumin set up to cut after the cisplatin injection orally. Cisplatin + melatonin group was started 24 hours before the cisplatin injection, i.p. injection of melatonin (ML) 4 mg/kg/day was administered for 7 days before slaughter. **Results:** We observed that at the same time create damage in the basal membrane thickening and glomerular podocyte foot extension of tubular damage caused by cisplatin nephrotoxicity in a variety of pathways. We made for each pathway observations we made with immunohistochemical staining of we observed the protective effect of amifostine.

**Conclusions:** Our study demonstrated that amifostine significantly decreased the nephrotoxicity of cisplatin. With the antioxidant effect of curcumin and melatonin observed that provides limited protection.

## Thromboembolic complications in membranous glomerulonephritis: a Tunisian experience

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**Objectives:** Thromboembolic events are frequent in nephrotic syndrome. They are even more frequent in membranous glomerulonephritis (MGN) and severe hypoalbuminemia. Our study aims to describe the prevalence and the characteristics of this complication in patients with MGN in an internal medicine department.

**Methods:** We retrospectively reviewed the records of patients with MGN and included those who were hospitalized in our

department for thromboembolic accidents confirmed by a radiological examination between January 2010 and January 2015.

**Results:** 8 patients were hospitalized for MGN between January 2010 and January 2015. 7 thromboembolic events were noted in 4 patients (50%): pulmonary embolism in 3 cases, cephalic vein thrombosis in 2 cases, left renal vein thrombosis in 1 case and deep vein thrombosis of an inferior extremity vein in 1 case. The thromboembolic disease revealed the MGN in 1 case while it occurred in the first 6 months of the disease in 6 cases. 2 patients presented a thromboembolic complication although having an anticoagulant treatment. All the patients with thromboembolic events had a hypoalbuminemia under 20 g/L (under 15 g/L in 2 cases), massive proteinuria superior to 5 g/24h and a pre-terminal renal failure was noted in 2 cases. Patients were treated by anti-vitamin K. A favorable evolution was noted in 2 patients and a relapse occurred in 2 other patients. An overdose of anti-vitamin K was noted in 2 patients: it was asymptomatic in one case and in the other case the patients had an upper gastrointestinal hemorrhage.

**Conclusion:** The presence of thromboembolic events in nephrotic syndrome should suggest MGN, and looking for the thromboembolic complications should be part of the monitoring of patients with MGN, especially in the first 6 months of the disease.

## Prevalence of chronic kidney disease and its related risk factors in Gonabad, Iran

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**Objectives:** Chronic kidney disease (CKD) is one of the most important health problems worldwide and in our country with increasing prevalence rate. Knowledge about the prevalence of this disease in various parts and investigating the relationship between it and clinical and paraclinical data can help in planning to control this condition.

**Material and Methods:** In this cross sectional study 1285 individuals of 20 to 60 year-old age group who live in Gonabad, Iran, were selected via simple random sampling in 2012. Laboratory tests such as blood urea nitrogen, creatinine, uric acid, cholesterol and urine analysis were performed. Demographic data were collected. Glomerular filtration rate was estimated. T-test and Mann-Whitney test were applied in normal and non-normal distributions, respectively. To examine the association between categorical data, we used Chi-square and Fisher's exact tests.

**Results:** 65 persons (5.1%) had CKD. The number of males and females with CKD were 27 persons (5.1%) and 38 persons (5%) respectively. The difference was not meaningful ( $p=0.9$ ). In CKD population, 27 persons (42%) were males, and 38 persons (58%) were females. This difference was meaningful ( $p<0.01$ ). Elevated blood pressure, history of diabetes and hypertension, older age and presence of proteinuria were

significantly related to CKD, whereas history of urinary tract infection, nephrolithiasis, smoking, uric acid, cholesterol, triglycerides and glucose concentrations were not related to the presence of CKD.

**Conclusions:** CKD has a high prevalence rate in this part of Iran. We suggest further studies in other parts of our country for the better estimation of the prevalence of CKD in Iran and for better planning for its control.

## Successful medical treatment of emphysematous pyelonephritis in a transplanted kidney recipient

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**Introduction:** Emphysematous pyelonephritis (EP) is a kind of urinary tract infections (UTI) that affects both native and transplanted kidneys. It usually requires nephrectomy in addition to antibiotic therapy for treatment.

**Case report:** Our patient was a 66 years old man with a transplanted kidney since 7 years ago. He presented with low grade fever, dysuria and malaise. His urinalysis showed pyuria and bacteriuria. His urine culture showed E.coli with colony count about 105/ml. In computed tomography (CT) scanning of this patient there was gas density in his pyelocaliceal system in his transplanted kidney. He treated successfully with meropenem without any surgical intervention. We followed him for about 2 years and his UTI did not recur in that period. He died 2 years after his EP because of a cardiac disease.

**Discussion:** EP is a relatively rare presentation of UTI that usually requires both antibiotic therapy and nephrectomy for complete treatment; however we present an old man with EP in his transplanted kidney who cures only with antibiotic therapy. We suggest physicians to consider antibiotic therapy alone in the management of EP in transplanted kidney recipients.

## The correlation of donor/recipient body-mass index ratio and 6-month post-transplant kidney function in known end-stage renal disease patients

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**Objectives:** Kidney transplantation (KT) is the preferred treatment in end-stage renal disease (ESRD) curbing costs and complications of prolonged hemodialysis. The challenge rests in finding appropriate donors. Donor-recipient size mismatch was shown to correspond to donor-recipient nephron supply mismatch, affecting prognosis in KT patients. Matching nephron supply to recipient needs was proposed to improve outcomes. Patients with a higher body mass index (BMI) relative to their donors were shown to have poorer long-term graft function. Determining whether measures, such as BMI, are valid predictors

of outcomes thus becomes a legitimate area of study. This research sought to determine if there is an association and correlation between the donor-recipient BMI Ratio and the 6-month post-KT creatinine.

**Methods:** A review of donors and recipients who underwent KT in 2005-2014 at the Cardinal Santos Medical Centre, Philippines, was done. Inclusion criteria were Filipinos aged 18 years and above with a graft, coming from a living donor, functioning for at least 6 months post-KT (25 donor-recipient pairs). Association using Chi-Square and correlation using multiple linear regression analysis between the donor-recipient BMI and renal function based on 6 months post-KT creatinine were determined.

**Results:** Data showed no statistically significant association ( $p=0.64$ ) and correlation ( $p=0.77$ ) between donor-recipient BMI ratio and post-KT creatinine. Statistically significant correlations ( $p<0.10$ ), were noted between the post-KT creatinine and the recipient BMI and donor BMI, with an overall strong correlation of 0.78. There was a 22.5  $\mu\text{mol/L}$  increase in post-KT creatinine per 1 point increase in the donor BMI, and a 13.5  $\mu\text{mol/L}$  decrease in post-KT creatinine per 1 point increase in recipient BMI.

**Conclusions:** The data support 2 general schools of thought on BMI correlations and donor-recipient selection in improving outcomes. First, recipients are encouraged to lose weight to improve BMI prior to KT due to the increased risk of graft damage from hyperfiltration and lipotoxicity. Second, patients with larger BMI's are better donors than having a higher nephron reserve. It could be surmised from the study that the donor and recipient BMI's influence the 6-month post-KT creatinine. The appropriate mathematical instrument defining the relationship between these measures of body size predicting KT outcomes more accurately, however, is yet to be universally established.

## The eye-kidney challenge

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**Introduction:** A unique subset of patients with tubulointerstitial nephritis also has ophthalmologic involvement, more specifically uveitis. This rare entity, more frequent in adolescents, with about 250 cases reported worldwide, is known as the TINU syndrome.

**Case report:** 39 years old woman without relevant medical past presents with a 2 month history of bilateral anterior uveitis and an acute kidney injury. The urinalysis tested positive for leucocytes, erythrocytes and proteins. Infectious causes as well as abnormal thyroid function were excluded. Autoimmune and vasculitic screens showed an isolated positivity for the antinuclear antibody. The renal biopsy revealed a lymphocytic and eosinophilic tubulointerstitial infiltration. The patient started therapy with corticosteroids showing a good clinical response.

**Discussion:** The TINU's etiopathophysiology remains unknown. This eye-kidney connection emphasizes the value of a holistic view of the patient. Although the median age of onset is 15 years, it mustn't be forgotten in the differential diagnosis of an adult patient with uveitis.

## Late-onset tenofovir-induced acquired Fanconi's syndrome in a chronic hepatitis B monoinfected individual

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**Introduction:** Tenofovir disoproxil fumarate (TDF) is a nucleotide reverse transcriptase inhibitor used widely for the treatment of HIV and ultimately chronic hepatitis B (CHBV) infection. Acquired Fanconi's syndrome (FS) is a well described adverse effect associated with TDF treatment in HIV infected individuals, though similar cases in CHBV monoinfected patients are scarce in current bibliography.

**Case report:** An 81 years old male was referred to our hospital for further investigation of progressive fatigue, malaise and a weight loss of 21% of total body weight over the past four months, associated with an observed rise in serum creatinine. He denied diuretic or laxative use. Past medical history was notable for CHBV infection diagnosed 25 years ago, under treatment with TDF 245 mg plus telbivudin 600 mg daily for the past 4 years. Physical examination was unremarkable. Laboratory studies revealed renal impairment (eGFR 23 ml/min, sodium fractional excretion 2.9%), hypokalemia (potassium 2.5mmol/l) and hypophosphatemia (phosphate 1.6 mg/dL) suggestively due to renal wasting, normoglycaemic glycosuria, hypouricemia (uric acid 3.0 mg/dL) and proteinuria (1.65 g/24h). Moreover a normal anion gap metabolic acidosis with a negative urine anion gap was present. Administering bicarbonate resulted in alkaline urine at a serum threshold of  $[\text{HCO}_3^-]$  of 18 mEq/l, highly indicative of proximal renal tubular acidosis. Lacking a profound causative agent other than TDF, the diagnosis of FS associated with TDF therapy was made. The patient's antiviral treatment was discontinued and entecavir 0.5 mg/day was started, while potassium, phosphate and bicarbonate oral supplements were prescribed. At 2 months the patient reports significant improvement of his constitutional symptoms, his renal function parameters appear improved (eGFR 56 ml/min) and maintains an excellent electrolytic and acid/base profile while the dose of the electrolyte supplements is gradually being tapered.

**Discussion:** TDF use has been implicated in the occurrence of FS in HIV infected individuals, possibly due to coexisting risk factors for renal disease or pharmacokinetic interactions. Though rarer, the same has been lately observed in HBV monoinfected patients. Despite the fact that several risk factors that facilitate the latter have been recognized, to the best of our knowledge this is the first case of a FS manifesting after such a prolonged time interval of TDF usage.

## Renal amyloidosis Prince of Asturias Hospital in Madrid in the period 2002-2012

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**Objective:** To describe the clinical and epidemiological characteristics of patients with amyloidosis in the Prince of

Asturias Hospital (HUPA) in the period 2002-2012. Set the time from the onset of symptoms until diagnosis.

**Methods:** A descriptive study of all cases of amyloidosis with renal involvement diagnosed beginning in the HUPA. Computer data histories were reviewed. A sheet of Excel data collection that were analyzed with SPSS software was developed.

**Results:** During the study period 10 cases of amyloidosis were diagnosed, all cases were diagnosed with renal biopsy. In 7 cases (70%) were type AL in 2 (20%) was familiar and 1 (10%) was AA. The average age of diagnosis was 53 years with a range between 37 and 67 years. In 6 cases (60%) were female, in 4 (40%) were male. In 4 cases (40%) impairment goal kidney function secondary to amyloidosis of which three were female and one male. Between onset of symptoms and diagnosis the average time was 6 months. Regarding the clinical picture, all patients had edema and proteinuria, 3 (30%) presented digestive symptoms and constitutional clinic, 2 (20%) polyarthralgia clinic, 2 (20%) symptomatic congestive heart failure and one said signs of impairment dermatological. In 7 patients (70%) was found more than an affection at the time of diagnosis apparatus and diagnosis affected organs were kidney (100%), heart (20%) and liver (10%). In our series, most of the patients had nephrotic syndrome and 40% deterioration of renal function at diagnosis, in addition, the average number of months from the onset of symptoms to diagnosis was 6 months with a range from 3 and 10 months, a considerable time that could explain the results of our study as to the deterioration of renal function.

**Conclusions:** The most common type of amyloidosis was AL in older adults and in females, the clinical presentation is nonspecific and difficult to diagnose, being the most frequent renal involvement. In our series, the female sex was associated with deterioration of renal function at the time of diagnosis.

### **Breach respiratory function and prognosis in patients with end-stage renal disease receiving hemodialysis**

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**Objective:** The predictive value of lung ventilation functions in patients with end-stage chronic renal failure in a prospective study.

**Methods:** The study included 100 patients with end-stage renal disease receiving hemodialysis, aged from 21 to 68 years (mean age 49.7±12.8 years). Among them, 54 males (mean age 48.8±13.2 years) and 46 women (average age of 50.7±12.3 years). During the annual prospective study the relationship of all-cause mortality and the combined endpoint of the severity of respiratory dysfunction were evaluated.

**Results:** Analyzing the effect of reducing lung ventilation function we found a significant increase in both all-cause mortality and the combined endpoint in reducing lung capacity ( $p=0.021$  and  $p=0.001$ , respectively). The relative risk of the combined endpoint increased in 6.5 times at the range vital capacity 0 to 2.75 liters (95% OR 6.56 (2.45-17.57,  $p<0.001$ )). The amount of vital capacity from 3.0 to 3.2 liters lower relative risk of the combined endpoint of 30 times (95% OR 0.38 (0.14-0.99),  $p=0.048$ ). The level vital

capacity in the range of 0 to 2.75 liters increased relative risk of mortality within one year is 5 times (95% OR 5, 4 (1.55-19.18),  $p=0.008$ ). Thus, it was found an increase in the relative risk of an endpoint and mortality from worsening of respiratory function and found a direct correlation between the decrease in lung capacity and frequency of endpoints.

**Conclusions:** It's suggest that a significant increase of adverse outcomes with an increase degree respiratory failure. The decline in respiratory function parameters has an adverse prognostic value in patients receiving hemodialysis. The data will make possible to develop measures to prevent the progression of secondary vital capacity decline and reduce the adverse outcomes.

### **Kidney diseases in North Israel according to kidney biopsies – Bnai-Zion medical center 14 years' experience**

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**Objectives:** Little is known about the prevalence of kidney diseases according to renal biopsy in Israel. Since updated literature worldwide emphasizes changing etiologies of chronic kidney disease, it is crucial to research and define the epidemiology and pathology of kidney disease in Israel. Hereby we introduce an original review of the prevalence of kidney diseases in our study population, which we believe reflecting the prevalence of kidney diseases in the population of Israel. The aim of the study is to investigate the prevalence of kidney diseases diagnosed by renal biopsy, according to age, gender, race and clinical symptoms.

**Methods:** 155 kidney biopsies were conducted in the years 2000-2014 in Bnai-Zion Medical Center in Haifa, according to formal accepted indications. Most of the biopsies (65%) were niddle aspiration in retroperitoneal approach, in which 90% were ultrasound guided and the rest computed tomography guided, while other 35% of biopsies involved laparoscopic approach.

**Results:** Most common indications for kidney biopsy were nephrotic syndrome, nephritic syndrome and proteinuria (37.4%, 25.8% and 24.5%, respectively). Average glomeruli number per biopsy was 17.5 vs. 82.2 for niddle aspiration and laparoscopic approach, respectively (statistically significant). Most common diagnosis was focal segmental glumerulosclerosis (FSGS), followed by chronic glomerulonephritis, IgA nephropathy, lupus nephritis, minimal change disease (MCD), membranous nephropathy and tubular interstitial disease (20%, 11.5%, 11.5%, 10.1%, 9.5%, 8.1% and 6.1%, respectively).

**Conclusions:** FSGS was the most common diagnosis in patients presented with nephrotic syndrome or proteinuria, men, and patients with age >60. Patients with age <30 were diagnosed mainly with IgA nephropathy. In recent years, FSGS is becoming more prevalent compared with other chronic kidney disease especially in the older population. IgA nephropathy is still the most common diagnosis in young patient and in patients presented with hematuria. To the best of our knowledge no data exists on the prevalence of kidney diseases in Israel, and our study is an important contribution to the epidemiological and clinical knowledge on the subject.



## Purple urine bag syndrome: a case report

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**Introduction:** Discoloration of urine is not uncommonly encountered in clinical practice and may indicate a potential pathology. Discoloration occurs as the result of trauma to the urological system during procedures or ingestions of substances such as medication or food. Purple color of a urinary catheter bag is rare and can be alarming to both patients and doctors. The purple urine bag syndrome is associated with urinary tract infections occurring in catheterized patients, generally elderly females with comorbidities and constipation.

**Case report:** A 78 years old male admitted to emergency department with a history of three days purple discoloration of urine. His past medical history included end stage renal disease. He received hemodialysis twice a week. He had urinary catheter because of benign hyperplasia of prostate. His medication includes antiaggregant, beta blocker, erythropoietin, calcitriol, and piracetam. Results of the urinary analysis were as follows: density 1012, pH 8.0, leukocyte esterase: ++, erythrocyte: 4/HPF, leukocyte: 11/HPF, nitrite: negative. He was hospitalized with urinary tract infection and IV ceftriaxone 2 g once daily was started on an empirical basis. Urine sample was obtained for urine culture and extended-spectrum beta-lactamase positive *Escherichia coli* was determined. The catheter was changed into new one. Urine color changed back to his normal yellow color on fifth day of treatment and leukocyte esterase was determined negative in urine sample.

**Discussion:** Dietary tryptophan is metabolized by bacteria in the gastrointestinal tract to produce indole. Indole is absorbed into the blood by the intestine and passes to the liver. There, indole is converted to indoxyl sulfate. Indoxyl sulfate is excreted in the urine. In purple urine bag syndrome, bacteria that colonize the urinary catheter convert the indoxyl sulfate to indirubin and indigo. It is more common in female nursing home residents. Other risk factors include alkaline urine, constipation, and polyvinyl chloride catheter use. The most commonly implicated bacteria are *Providencia stuartii*, *Providencia rettgeri*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Escherichia coli*, *Morganella morganii* and *Pseudomonas aeruginosa*. It is treated with proper antibiotics and urinary catheter change.

## Incidence of acute kidney injury in patients with acute coronary syndrome

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**Objectives:** We investigated the incidence of acute kidney injury (AKI) in patients with acute coronary syndrome (ACS) and

assessed the diagnostic performance of urinary biomarkers: kidney injury molecule-1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) for AKI in ACS.

**Methods:** We examined 70 patients with ACS, aged 63 (53; 74) years. Serum creatinine (SCr) and estimated glomerular filtration rate using CKD-EPI formula (eGFR) were estimated in all patients during the hospital stay and after 3 months follow up. The presence of AKI was diagnosed in accordance with KDIGO recommendations (2012). We measured urinary excretion rates of KIM-1 and NGAL by enzyme linked immunosorbent assay.

**Results:** In the studied group of patients admitted to the hospital with ACS (n=70) mean eGFR was 58 (21; 103) mL/min/1.73m<sup>2</sup>, mean serum creatinine level 103 (76; 197) umol/L. Decreased eGFR (<90 mL/min/1.73m<sup>2</sup>) was present in 66 (94%) patients with ACS, while only 21 (30%) patient had hypercreatininemia. According to KDIGO definition AKI was present in 62 patients (89%). 23 patients with decreased eGFR already had chronic kidney disease (CKD) by the time of admission, only 10 of them developed AKI on top of CKD. Thus the exact incidence of AKI in patients with ACS with or without preexisting CKD was 70% (49 out of 70). Only 3 patients with AKI (7.6%) developed CKD de novo. Mean urinary levels of the biomarkers of structural damage were significantly higher in patients with ACS and AKI than in patients with preserved kidney function: 1.18 (0.78; 2.32) ng/mL vs 0.45 (0.24; 0.72) ng/mL respectively for KIM-1 (U=62, p=0.0005), and 47 (34.14; 85.2) ng/mL vs 18.2 (10.7; 24.07) ng/mL respectively for NGAL (U=10, p=0.0009). ROC analyses showed that urinary KIM-1  $\geq 0.88$  ng/mL predicts AKI development, the sensitivity was 78% and the specificity was 72% (AUC 0.79). Urinary NGAL  $\geq 42.5$  ng/mL also showed to be a predictor of AKI, but its sensitivity and specificity were lower (65% and 56% respectively), AUC was 0.54.

**Conclusions:** The majority of patients admitted to hospital with ACS have decreased renal function. But only thorough study of medical history and long-term (3.5 months) follow-up allows estimating the exact incidence of AKI and CKD in this group of patients. Very few patients with ACS and AKI develop CKD de novo. Increased urinary excretion rates of KIM-1 and NGAL are predictors of AKI. However elevated urinary KIM-1 showed to be more sensitive and specific than NGAL.

## Gitelman's syndrome: case report

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**Introduction:** Gitelman's syndrome is an autosomic recessive renal tubular disorder characterized by metabolic alkalosis, hypocalciuria, hypomagnesaemia and hyperreninaemic hyperaldosteronism. The genetic abnormality behind this syndrome is a mutation in the gene that encodes for the sodium/chloride co-transporter and magnesium channels located in the distal convoluted tubules.

**Case report:** 30 years old female of African origin, born in Cape Verde, with a past medical history of rheumatic valve

disease for which she needed mechanic aortic and mitral replacements, performed in 2003. She started anticoagulation therapy with warfarin after the procedure. She also has a past medical history of persistent hypokalemia without previous precipitating factors (including diuretic therapy). 3 months after the valvular replacement she was admitted to the hospital and diagnosed with bacterial endocarditis of the prosthetic valves, which had to be replaced again. During her stay in the hospital and despite an uneventful post-operative period, she complained of fatigue, cramps and involuntary muscle spasms. She also had persistent hypotension despite adequate fluid resuscitation. Blood analysis showed a normal renal

function, hypokalemia (2.48 mmol/L), renin of 35.3 pg/ml, aldosterone of 31.5 ng/dL, urinary density of 1010 and normal urine sediment. 24 hours urine sample was collected, which revealed calcium 48 mg/24h and chlorine 103 mmol/24h. Blood gas analysis revealed metabolic alkalosis (pH 7.50) and a serum bicarbonate of 35.9 mmol/L. She was not under diuretic therapy. A renal ultrasound was performed, which did not reveal relevant pathologic findings. It was requested a genetic test for Gitelman's syndrome. The patient was discharged from the hospital medicated with spironolactone, oral potassium and magnesium supplementation and was referred to the outpatient clinic.

## Wernicke-Korsakoff syndrome in a non-alcoholic patient

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**Introduction:** Wernicke-Korsakoff syndrome is a potentially life-threatening neurological condition caused by thiamine deficiency. It has been described mostly in alcoholic patients, but recently there has been an increasing trend amongst psychiatric patients.

**Case report:** We present a case of a middle-aged homeless woman found on the street and brought in our emergency department by our ambulatory service. She first appeared with aphasia, confusion and hypothermia. The latter was assumed to be the cause of her condition and was treated with warm intravenous fluids. She further deteriorated and went into coma. Excluding other common causes of coma, she was started on thiamine intravenously with a dramatic improvement over the next few days revealing upon awakening that she was in fact a psychiatric patient. She was transferred to a psychiatric hospital and on 6 months follow-up she has no neurologic signs.

**Discussion:** Thiamine is an important nutrient that plays a crucial part in the process of glycolysis and the citric acid cycle. Thiamine deficiency can manifest as Beriberi, characterized by polyneuropathy (dry Beriberi) and heart failure (wet Beriberi) or as Wernicke-Korsakoff syndrome (WKS), which constitutes a continuum of neurological signs and symptoms ranging from reversible confusion, ataxia and ophthalmoplegia to irreversible memory loss. WKS mortality reaches 15%, while 40% of patients will have irreversible damage to the central nervous system requiring long term institutionalization. Diagnosis is clinical and based on a set of criteria. It is suggested that on suspected cases treatment be started without delay since thiamine has no important adverse effects and can prevent serious complications. Alcoholics are more prone to developing thiamine deficiency because alcohol directly inhibits thiamine absorption and its metabolism to the active molecule thiamine pyrophosphate. Psychiatric patients present a population at risk because the neurological symptoms of WKS can be masked by or attributed to the psychiatric condition. These two populations may be undernourished due to inability to care for themselves and thus more likely to develop vitamin deficiencies. On comatose patients one should always keep in mind the possibility of thiamine deficiency and start treatment with thiamine as soon as possible to prevent permanent neurological damage or death.

## Intracranial hemorrhage and oral anticoagulants: are there any predictors of mortality and/or morbidity?

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**Objectives:** Intracranial hemorrhage (ICH) is the cerebral vascular accident with the highest mortality rates. Several scores have been developed to determine prognosis. However, it is not known if these scales apply indiscriminately to patients under oral anticoagulation or if factors determining mortality also influence morbidity. The aim of the study was to determine if there are any predictors of mortality and morbidity in patients with ICH under oral anticoagulation.

**Methods:** Patients taking oral anticoagulants who were admitted in a tertiary hospital due to ICH during the years of 2010 to 2014 were included, while those taking antiplatelet or non-steroidal anti-inflammatory drugs, submitted to neurosurgical procedures after admission, taking oral anticoagulants for less than three months or with known traumatic brain injury, were excluded. Demographical, clinical, analytical and tomographic data concerning the time of hospital admission was obtained.

**Results:** Among the total of 73 patients included, 80,8% (n=59) was taking warfarin. The mean INR value at admission was 3,29. Only 13 patients recovered their baseline neurological status at discharge. The univariate analysis showed statistically significant associations between  $\Delta mR$  (variation of the modified Rankin scale between discharge and admission) and the following factors at hospital admission: presence of chronic kidney disease ( $p < 0.01$ ), previous medication with insulin ( $p < 0.01$ ), diastolic blood pressure ( $p = 0.04$ ), INR ( $p < 0.01$ ), hemoglobin ( $p < 0.01$ ) and C-reactive protein ( $p < 0.01$ ) values, hemorrhage longest diameter ( $p < 0.01$ ) and administration of prothrombinic complex ( $p < 0.01$ ). When excluding deceased patients (mRankin 6), previous medication with calcium channel blockers also appeared to prevent neurological dysfunction ( $p = 0.04$ ).

**Conclusion:** In the studied population, several factors have been found that might be useful as predictors of mortality and/or morbidity.

## Computed tomography scan in the emergency room: are the reasons behind the requests related to the findings?

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**Objective:** To evaluate the main reasons that led physicians to request computed tomography scans (CT-scans) and the main findings on such diagnostic tests during the course of a month in an emergency room.

**Methods:** Retrospective analysis of data from patients who sought medical attention in the month of April 2015 in a major hospital emergency room and who underwent a CT-scan. Eligible patients were all those who were 18 years or older. We extracted data from our local electronic medical record in order to find all CT-scans performed in our hospital in afore mentioned period and selected the ones that met our criteria.

**Results:** A total of 117 patient charts were evaluated and revealed that the most common reason for asking for a CT-scan was head trauma (36), followed by focal neurological deficits (32), altering state of consciousness (17) and headache (15). Focal neurological deficits were the reason that led more frequently to acute abnormal findings on CT-scan: 59.3% of tests requested for that reason were abnormal, being ischemic stroke the most common alteration (11 cases) followed by hemorrhages (6 cases) and tumors (2 cases). Other reasons with a high occurrence of acute alterations were altered state of consciousness (23.5% - 3 ischemic strokes and 1 hemorrhage) and head trauma (11.1% - all 4 were hemorrhages). In our series, none of the 15 tests requested because of headache showed acute alterations. Vertigo was another reason for requesting a CT-scan (10 cases) and no tests showed abnormalities leading us to think vertigo as a single symptom does not correlate frequently to an abnormal CT-scan.

**Conclusions:** Although a small number of cases were evaluated, we were led to believe that the reason for requesting the test alone does not correlate well to the likeliness of an abnormal test. Most possibly, other variants (such as comorbidities and risk factors) must be taken into account when performing such a diagnostic test. Focal neurological deficits were most implicated in altered CT-scans stressing the relevance of these findings. We would like to highlight the importance of careful patient evaluation and criterious decision making when deciding to request a diagnostic test.

## We saw, but did we really see?

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**Case report:** We present a clinical case of a 23 years old female patient who firstly came to our consultation in primary care setting about a year ago because she was pregnant. She denied any pathology of her own or of the family. The pregnancy went well but after 6 months of breastfeeding she came for another consultation referring fatigue, diplopia and heavy eyelids at the end of the day. After a thorough investigation we learned that she was operated to her left eyelid ptosis by an ophthalmologist but with no other diagnosis. After the consultation we referred her to a neurologist with the hypothesis of a myasthenia gravis which was confirmed and treated. We had seen the patient for 1 year but never really given importance to her ptosis until it got worse and she complained about it.

**Discussion:** The present clinical case should raise the clinicians' awareness towards physical examination cues that, though important, are not always mentioned in the patient's complaints. Do we really look at our patients or do we automatically undervalue what we see?

## Neuro-borreliosis triggering a neurosarcoidosis

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**Introduction:** Neurological involvement in sarcoidosis is estimated between 2 and 9%. However, in half the cases, neurological involvement is indicative of the disease. We report a case triggered by neuro-borreliosis.

**Case report:** 62 years old woman with history of angina pectoris hospitalized in 2011 for confusion and hyponatremia (127 mmol/l). She was dysphasic with severe cognitive troubles and weight loss. Biology was normal (immunological including antineuronal antibodies and NMDA, angiotensin conversion enzyme (ACE), viral, rickettsial, bacterial, metabolic profile). Lyme serology was positive (ELISA & Western Blot). Thoracoabdominal CTscan (TACT): aorto-pulmonary adenopathies and bilateral septal thickening. Electroencephalography: bitemporal focalizations. Lumbar puncture (LP): lymphocytic meningitis (13 cells, protein 1.44 g/l), positive IgG and IgM Borrelia. Whipple and all other viruses were negatives. ACE 1,42 U/l. Magnetic resonance imaging (MRI): bitemporal hypersignal Flair with contrast enhancement. Positron emission tomography FDG scan: negative. Accessory salivary gland biopsy (ASGB): negative. Empirical treatment with acyclovir then ceftriaxone for 4 weeks with real improvement. 3rd LP negative except protein 0.8 g/l. MRI late 2012: complete disappearance of contrast enhancement and stability of left temporoparietal Flair hyperintensity. 2013: petechial panuveitis with lupus pernio and erythema nodosum. Biology: ECA 135/l. LP: acellular, protein 0.46 g/L, ACE, serologies, electrophoresis negative. MRI: stable without contrast enhancement. ASGB: sarcoidosis granuloma. TACT: thoracic adenopathies, splenomegaly and hypodense splenic nodules. 3 bolus corticoïdes then oral relay + methotrexate (MTX) optimal dose (25 mg/week) with good improvement and clear ocular fundus. Because of lymphocytosis 14000/mm<sup>3</sup>, lymphocytic immunophenotyping shows a low grade marginal zone lymphoma confirmed by bone marrow biopsy and gastrointestinal exploration with therapeutic abstention.

**Discussion:** Neurosarcoidosis sometimes precede by several years the systemic involvement which makes diagnosis difficult especially if there is other concomitant hemopathies or cerebral infections like in our case. Neurolyme may be the trigger of the sarcoidosis. MRI has all its interest to show the central affection. Corticosteroid therapy remains the reference treatment as well as MTX.

## Irreversible lithium-effectuated neurotoxicity: a case report

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**Introduction:** Lithium is widely used, and most of its side effects are well established and recognized. Chronic lithium toxicity is usually precipitated with introduction of new medication that may impair renal function or cause a hypovolemic state. Symptoms

are primarily neurologic. Severely poisoned patients can develop a syndrome of irreversible lithium-effectuated neurotoxicity (SILENT) such as cognitive impairment, sensorimotor peripheral neuropathy, and cerebellar dysfunction. We present a case of irreversible lithium-effectuated neurotoxicity along with a review of the literature.

**Case report:** A 60 years old woman with history of manic-depressive disorder was brought to the emergency room for altered mental status of 3 days duration. Positive physical exam findings: dry mucous membranes, disorientation to place and time with GCS of 13/15, nystagmus, dysarthria and tremor of both hands. Serum lithium levels were elevated at 3.4 mEq/l. Serum alcohol, tylenol, salicylate levels were undetectable. CT head and MRI of brain did not reveal any acute pathology. Lithium was stopped and patient was started on high infusion of normal saline. Hemodialysis was not initiated as her lithium levels trended down to normal range within a few hours of admission. Her altered mental status improved but her neurological signs persisted, so syndrome of irreversible lithium-effectuated neurotoxicity was considered. Patient was discharged after one week. 5 months after initial presentation, physical exam was still positive for tremors, nystagmus and other cerebellar signs.

**Discussion:** Persistent neurologic handicaps greatly reduce the quality of life and are difficult to manage. Lithium toxicity can be avoided by conservative prescribing, care in combining drug therapies, and, above all, educating the patient and caregivers to recognize early signs of the condition. Risk factors are sometimes present and recognizable, but more often they are not well identified.

## Retrospective analysis of stroke in an internal medicine service

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**Objective:** Cerebrovascular diseases have been a leading cause of morbidity and mortality worldwide and continue to be the main cause of mortality in Portugal.

**Methods:** The authors present a retrospective study focusing on patients admitted in the Internal Medicine Service in the period between January 1st and December 31th, 2013, with the primary diagnosis of cerebral vascular accident (CVA). They were characterized by gender, age, provenience, "Via Verde AVC" activation, ischemic stroke, hemorrhagic stroke, thrombolysis, anticoagulation/antiplatelet prior therapy, electrocardiogram (ECG) at admission. Data were extracted from medical records.

**Results:** 98 patients were admitted with a primary diagnosis of stroke, 67 women (68%) and 31 men (32%). Most were transferred from the emergency room, about 91%. Via Verde stroke was activated in 18 cases (18%), thrombolysis performed in 6 patients. Identified 78 ischemic stroke (79%) and 20 hemorrhagic stroke (20%). Having regard to classification TOAST 20% were classified etiologically as a result of atherosclerosis in large vessels and 52% were cardioembolic. About 14% were previously anticoagulated and 64% of these had infratherapeutic INR value. ECG showed 59 cases of atrial fibrillation, 19 new cases. Approximately 72% of patients maintained neurological deficits.

**Conclusion:** It stands out a high number of cardioembolic stroke origin, alerting to the need to apply the treatment recommendations with regard to thromboembolic prophylaxis in high-risk patients.

## Ultrasound for measuring transorbital axonal damage optic nerve in patients with multiple sclerosis, comparative study with optical coherence tomography

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**Objectives:** Compare the measurement of optic nerve (ON) by transorbital echo (TOE) with optical coherence tomography (OCT) and assess whether the TOE is useful as a marker of axonal damage in patients with multiple sclerosis (MS).

**Methods:** Prospective observational case-control study by ETO of NO and OCT of patients diagnosed with MS (n=45) and healthy controls (n=25).

**Results:** As the diameter of the measured ON by TOE, differences between cases and controls were found in both right ON ( $2.65 \pm 0.26$  mm in the case,  $3.20 \pm 0.17$  mm in controls,  $p=0.0001$ ) and the left NO ( $2.66 \pm 0.27$  mm in the case,  $3.21 \pm 0.17$  mm in controls,  $p=0.0001$ ). There is a negative correlation between scale disease (EDSS) and both size of the optic nerve with right ON measured by TOE ( $r=-631$ ;  $p=0.01$ ) and OCT ( $r=-622$ ,  $p=0.01$ ), as measured by TOE left ON ( $r=-632$ ;  $p=0.01$ ) and OCT ( $r=-595$ ,  $p=0.01$ ) ON to smaller, more EDSS. We found a negative correlation between years of evolution of the disease and the size of the ON. Both the right ON measured by TOE ( $r=-563$ ,  $p=0.001$ ) and OCT ( $r=-651$ ,  $p=0.0001$ ); left ON as measured by TOE ( $r=-575$ ,  $p=0.0007$ ) and OCT ( $r=-631$ ,  $p=0.0006$ ); how many more years of evolution, smaller size ON. Finally a positive correlation between the size measurement by optic nerve and OCT TOE seen in both optic nerves (right ON:  $r=736$ ,  $p=0.009$ ); (left ON:  $r=738$ ,  $p=0.009$ ).

**Conclusion:** The TOE is a tool useful and noninvasive paragraph to assess the axonal damage to the ON of MS patients.

## Neurological impairment syndrome secondary to carbon monoxide poisoning, case report

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**Introduction:** Description of a case of late neurological syndrome (LNS) in a patient, five weeks after suffered from carbon monoxide poisoning, treatment and evolution.

**Case report:** A 43 years old Cameroonian man with a history of chronic hepatitis B and positive Mantoux, who lives in foster care for immigrants and developed a normal life. He was admitted because of carbon monoxide poisoning by poor combustion fireplace, featuring Glasgow 6, miotic pupils with conjugate gaze deviation to the left and extensor response to noxious stimuli in arms. That after a month of stay in intensive care with supportive measures, it is discharged without neurological sequelae. 1 week following table presents suddenly off the medium, sleeplessness, muteness with ocular response to verbal stimulation, obey simple commands, increased muscle tone paratónicas prone positions and occasional urinary incontinence. Suspecting LNS, treatment with citicoline and levodopa starts, presenting progressive improvement, being transferred to hospital care means with verbal response to simple questions with mild motor dysphasia, independent food intake, walking with bilateral support and muscle rehabilitation. Continuing good performance. Arterial blood gas: pH 7.43, pCO<sub>2</sub> 27 mmHg, pO<sub>2</sub> 126 mmHg, HCO<sub>3</sub> 17.9 mmol/L, COHb 36.6%. Cranial CT: hypodense both pale, compatible with necrosis likely etiology hypoxemic balloons. Cerebral magnetic resonance: leucopatía bihemispheric with diffusion restriction. Electroencephalogram: signs of diffuse cerebral suffering cortico-subcortical predominantly in frontotemporal areas of the left hemisphere. Cerebrospinal fluid: normal appearance, erythrocytes 20 /mm<sup>3</sup>, leukocytes 1 /mm<sup>3</sup>, protein 51 mg/dL, glucose 75 mg/dL, adenosine deaminase 3 U/L.

**Discussion:** The LNS is observed in 3-40% of victims of acute carbon monoxide poisoning, with variable prognosis. The LNS is observed: 13% severe neuropsychiatric disorders, 30% personality deterioration, 40% memory impairment. The intensive hyperbaric oxygen therapy can completely prevent neurological sequelae after acute carbon monoxide poisoning. It is important to think about the LNS carbon monoxide poisoning in order to prevent their occurrence in the short-medium term.

## Slightly changes and major morbidity. Clinical case

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**Case report:** A 48 years old women presented herself to emergency department with abdominal pain and hypocalcemia. She was a hypertensive lady that 3 months ago went for a total thyroidectomy due to a coloidal goiter. Her medication was perindopril, L-thyroxin and calcium. She had 4 days with epigastric pain, started after ingestion of medlar. Pain worse with food. She had also paresthesias in both hands and legs. There was no fever, nausea, vomiting, pyrose, diarrhea or blood loss. Objectively she was complaining, apyretical, not hypotensive, with tenderness at epigastric depression. Her laboratory values were slightly disturbed: 15200 leucocytes, with no neutrophilia, normal amylase. CK 331, troponin T - normal, CRP 2.4, and 6.4 calcium for albumin 4. She was put on observation, calcium correction and performed a CT and a gastric endoscopy that were otherwise normal. PTH was 19.8. TSH 43.6 and FT4 1.15. Therapeutical adjustment was made with calcium gluconate 1 g

tid, oral calcium 3 g once a day. Rocalthrol 0.5 mcg once a day and L-thyroxin mcg also daily. Blood pressure was controlled. After 48 hours she started clonic-tonic seizures complicated with coma (GCS 3), and respiratory failure, and initiated mechanical ventilation. Angio-CT showed subaracnoidal hemorrhage with cysternal evolvment.

**Discussion:** There are several causes for abdominal pain in this case. Also hypocalcemia in post-thyroidectomy is usually multifactorial. Patients under medication with inhibitors of conversion enzyme and calcium also can have abdominal pain. Hypocalcemia per se can produce the same symptoms. Intracranial hemorrhage can also be started with atypical abdominal pain localization, even without intracranial hypertensive state. This dramatic case illustrated how slightly changes can be involved with complicated course and potentially fatal evolution.

## Percheron's syndrome - case report

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**Introduction:** The synchronous bilateral paramedian thalamic infarction usually is associated with Percheron's artery occlusion. The authors propose to emphasize the diagnostic difficulties of this uncommon syndrome.

**Case report:** Male patient aged 78, previously autonomous comes to the emergency department due to sudden onset of disorientation and decreased strength of the left body, with 6 hours of evolution. The CT scan of the brain did not reveal significant abnormalities. During hospitalization, the patient showed consciousness fluctuations, hypersomnia, apathy, loss of initiative, mild left dysmetria and paresis of conjugate vertically gaze. 24 hours after the initial CT scan, an imaging control scan was performed and this time revealed synchronous bilateral thalamic strokes.

**Discussion:** Since the initial cerebral CT scan in Percheron's syndrome has low sensitivity, the physician must be aware of the presentation triad of this condition composed by impaired consciousness, disabled eye movements and behavioral/cognitive changes.

## Fever and asthenia

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**Introduction:** Show the clinical case of encephalomyelitis management with review of this rare pathology.

**Case report:** 12 years old patient without previous medical history, who is carried to Emergency owing to an intense asthenia, anuria and high temperature (39°C measured at home). 2 weeks ago, he had suffered from a cold which was treated with amoxicillin 10 days; however the patient consulted many times in emergency for persistence of the fever. To the

physical exploration highlighted a great asthenia that prevented ambulation with an unsteady gait, nystagmus to both a sides and vertical. On abdominal exploration there was defense on hipogastrio suggesting a vesical bolus which should be evacuated through urinary catheterization. The initial study was based on complete analyses, lumbar puncture with CSF analysis and a brain TC as well abdominal contrast TC to rule out obstructive disease. The following differential diagnoses were raised: viral encephalitis (Herpes virus encephalitis), sclerosis multiple, sarcoidosis, vasculitis, progressive multifocal leukoencephalopathy, Behçet's syndrome, acute disseminated encephalomyelitis. CSF analysis did not reveal any herpes virus infection, being PCR negatives. Other imaging studies were requested, cerebral and spinal RM. Brain RM was informed as "multiple hyperintense cortico-subcortical lesions in flair a T2, frontal and in protuberance in a bilateral way with restricted diffusion, suggestive of encephalitis". Spinal RM could not be done due to the patient had bad tolerance to the test. Due to the symptoms and the results of those proofs and the fact that the patient suffered for a cold 2 weeks before symptoms started, and it was suspected to be a viral infection as the patient did not improve with the antibiotic treatment so the main diagnosis was acute disseminated encephalomyelitis.

**Discussion:** Acute disseminated encephalomyelitis is also known as postinfectious encephalomyelitis. It is an uncommon illness that consists on an autoimmune demyelination of the central nervous system. Commonly triggered by viral infections and immunizations, although the pathogenesis is incompletely understood. The diagnosis is considered in patients with acute multifocal neurologic signs and symptoms. Tough there are no specific biomarkers or confirmatory tests to establish the diagnosis; this is supported by the presence of one or more supratentorial or infratentorial demyelinating lesions on brain MRI. Immune suppression is the mainstay of treatment: glucocorticoids, intravenous immune globulin, and plasma exchange. The prognosis is uncertain; nevertheless most of patient improves with treatment.

## Inability to walk

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**Introduction:** Exposing through a clinical case the differential diagnosis of weakness in lower members taking into account all the factors that could influence on a mid-age patient.

**Case report:** Obese, 50 years old patient, who is carried to emergencies owing to the fact that in the last 3 months he was suffering for a progressive weakness in lower members with awkwardness and frequent falls, as well as inability to maintain standing. In the last month, he started with weakness in upper members too, with difficulty to feed himself. About his medical history highlighted a hypertension, an alcoholic habit up to 3 months, schizophrenia. 4 months before this episode, he was diagnosed of diabetes mellitus type 2 with glycosylated hemoglobin of 12.5%. Physical exploration showed less strength on carpal in a bilateral way being 3/5, with strength of 4+/5 in lower member;

global arreflexia and dysmetria in upper members' proportional to paresthesia level. Severe astasia-abasia. Taking all those points into account the differential diagnosis was focus on Guillain-Barré syndrome; demyelination associated to systemic disease, demyelination associated to toxic; autoimmune disease and neoplasia. Like complementary proofs a complete analyze was demanded with autoimmunity and serologies, cerebrospinal fluid (CSF) analysis, imaging test like brain TC, and electromyography. Electromyography showed a severe sensitive and motor polyneuropathy with demyelination predominance, such in lower members like in upper members, in an acute stage. So, the patient was diagnosed of Inflammatory demyelinating polyneuropathy.

**Discussion:** The patient is chronically ill, with toxic and metabolic problems that can cause the symptomatology; however the tests revealed that this patient was suffering for inflammatory demyelinating polyneuropathy which is an acquired disorder of peripheral nerves and nerve roots. There is a temporal continuum between acute inflammatory demyelinating polyneuropathy, the demyelinating form of Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy; nonetheless the last one usually is present for greater than eight weeks, like in this patient. The initial diagnosis of inflammatory demyelinating polyneuropathy is clinical, however it is confirmed by evidence from electrodiagnostic studies, and in some cases by CSF analysis, nerve biopsy findings, and other laboratory investigations.

## Tirofiban and acute ischemic stroke: one center experience

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**Objectives:** Thrombolytic therapy with intravenous alteplase reduces the risk of death and disability. However is associated with a definite risk of symptomatic cerebral hemorrhage and is deliverable to only a minority of people in a short time window after symptom onset. Tirofiban is a selective nonpeptide glycoprotein IIb/IIIa platelet receptor antagonist which reversibly and effectively prevents platelet aggregation. Effective for the treatment of acute coronary syndromes it may favor endogenous thrombolysis by reducing thrombus growth and preventing thrombus reformation and, therefore, may aid reperfusion and clinical improvement if administered early after an ischemic stroke. Safety and efficacy in acute ischemic stroke (AIS) remain uncertain. This was addressed in this study.

**Methods:** We conducted a retrospective observational study. Were included all consecutive patients with acute ischemic stroke who where submitted to tirofiban at our Stroke Unit between 2010 and 2014. Demographic, clinical, laboratorial and imagiological data were collected. Intracerebral bleeding events were assessed by CT and other bleedings were registered in order to evaluate the safety. Efficacy was assessed with National Institute of Health Stroke Scale (NIHSS) at presentation and discharge and modified Rankin Scale (mRS) before the admission and 3 months after discharge.

**Results:** Were included 38 patients, 19 women, with 59±12 years. All received an initial infusion of 0.4 µg/kg body

weight/minute over 30 minutes followed by a continuous infusion of 0.1 µg/kg body weight/minute for 48 hours: 17 after arterial angioplasty and stenting, 6 after balloon angioplasty, 5 after mechanical thrombectomy, 4 after intravenous thrombolysis and 6 patients only received tirofiban. 20 patients (52,6%) with posterior circulation AIS and 18 patients (47,4%) with anterior circulation AIS. NIHSS at admission was in average 10±6. Tirofiban was initiated 7±3 hours after symptom onset. At 3 months majority of patients (92,1%) had favorable outcome (mRS 0-2). Two patients (5,3%) developed intracerebral hemorrhage and just one had a minor hemorrhage. One patient died due to a respiratory infection. Multivariate statistical analysis showed that unfavorable outcome was just related with NIHSS at admission (p=0.018).

**Conclusion:** We conclude that acute ischemic stroke treatment with tirofiban is safe and effective even when administered within a large time window after symptom onset.

## Monoclonal gammopathy of undetermined significance related axonal neuropathy as a possible differential diagnoses

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**Introduction:** The neuropathy associated with monoclonal gammopathy of undetermined significance (MGUS) is typically a predominantly demyelinating process that may have additional features of axonal degeneration. Pure axonal neuropathies in patients with MGUS are considered rare, comprising only a few cases in large series. But can association between patients with axonal neuropathy and MGUS be only chance? Data showed that MGUS patients had greater involvement of the arms, worse disability on the Rankin score, and a higher frequency of denervation. There are reports of improvement of axonal neuropathy in patients treated with immunomodulating therapy.

**Case report:** An 82 year old man was sent to the internal medicine outpatient clinic of our hospital with information of sensitive axonal neuropathy in probable relation to chronic alcohol consumption and type 2 diabetes. He complained of paresthesia and sensation of coldness of the right feet for the past 2 years. History of type 2 diabetes mellitus, chronic alcoholism abstinent for over a year, myocardopathy, macrocytic anemia, right foot ulcer, non-invasive papillary urothelial carcinoma. Usually medicated with bisoprolol 2.5 mg, oxazepam 15 mg id, metformin+sitagliptin 850/50 mg id, folic acid 5 mg, acetylsalicylic acid 100 mg, quetiapine 100 mg. On physical examination he presented cefalic tremor, pale complexion, cardiac auscultation: systolic murmur grade III/VI, pulmonary auscultation: audible pulmonary murmur with rales in the right apex. No peripheral edema. Ulcer in the internal face of the calcaneum without inflammatory signs. Maintains normal sensibility and proprioception. Blood tests showed Hb A1c 5,2%, serum immunofixation: biclonal gammopathy IgA kappa and IgG kappa. Urine immunofixation: kappa light chains <0.01 g/L,

lambda light chains <0.01 g/dL. Bone marrow (phenotype): 0,7% plasma cells, 92,5% of which presented an abnormal phenotype. This suggests the presence of MGUS.

**Conclusion:** This is a patient with three possible causes for the existence of axonal neuropathy. Despite being more likely to be an alcoholic neuropathy, there is a chance of being an IgA and IgG MGUS, since it's difficult to distinguish between the various causes. We could test immunosuppressant therapy but few are the patients with MGUS related axonal neuropathy that have a significant response.

## Investigation and diagnosis in cases of high protein level in cerebrospinal fluid found on lumbar puncture in a United Kingdom medical assessment unit

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**Objectives:** Raised cerebrospinal fluid (CSF) protein levels are observed following many lumbar punctures (LP) performed in MAU. The purpose of this study is to correlate the diagnosis, investigations and follow up of such patients and to establish best practice when analyzing samples to ensure accuracy.

**Methods:** Anonymous data were collected retrospectively of patients who had raised CSF protein (>0.45 g/l) using lab reports and electronic discharge summaries/letters. Two cycles of data were collected, first during April-October 2013 with the second in June-October 2014. Following the 1st cycle an analysis of mean protein levels by bottle number were carried out.

**Results:** A total of 157 patients were included, with 3 excluded due to missing lab reports. High CSF protein were found in 55 (35%) of samples, of which 34 (61.8%) had no correlating diagnosis. Protein range when elevated was from 0.5-2.2, the mean around 0.8. The commonest diagnosis were migraine/headache (n=18, mean CSF protein 0.5) and viral meningoencephalitis (n=11, mean CSF protein 0.7), but they were cases as Shigella diarrhea and depression when protein was elevated to 0.8 (normal white cell count and red cell count in CSF). 8 patients had unknown diagnosis of which 6 were missing discharge summaries and 2 had ongoing investigations. 10 patients had CSF protein >1g/l, only one had no correlating diagnosis or follow up/imaging. 89% cases have CT scan on admission. Neurology follow up rates were 31% and 26% respectively, however neuroimaging in the form of MRI was requested more often, 30% compared to 9%. Lab analysis showed a difference in mean protein levels between bottles. Bottle 2 was used most commonly (n=114) with a mean of 0.68±0.68, compared to bottle 4 (n=33) in which the mean was 0.38±0.22.

**Conclusions:** Many patients with raised CSF protein have no correlating diagnosis. Protein levels in earlier bottles are likely raised due to red cells. Accurate assessment of CSF protein is more likely to be gained when analyzing later bottles (3 or 4). Practice now implemented in our lab. Neurological advice is that all cases with CSF protein >1 g/l need further neurological investigation (MRI brain/spine) and discussion with neurologist. Completion of discharge summaries and organization of follow up MRI has improved in the second cycle.



## Central nervous system infiltration as first manifestations of a disseminated Burkitt lymphoma

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**Introduction:** Burkitt lymphoma (BL) is an extremely infrequent high proliferative neoplasm considered as one of the most aggressive non-Hodgkin lymphomas (nHL). In our center, we had registered only 4 cases (3.4% of B-cell nHL), throughout the last 24 years (1991-2015). Of them, 2 cases (50%) had neurologic symptoms as first clinic presentation, with normal magnetic resonance imaging (MRI). The diagnostic key was the cerebrospinal fluid (CSF).

**Case reports:** Case 1: male, 39 years old, HIV+, with 380 CD4+ T-lymphocyte and viral load 10.000 copies/ml, with a low back pain for two month diagnoses as sciatic lesion. After hospital intake, fever appeared. Lumbar spine MRI was considered normal. Atypical white cell were observed in CSF. Located a lesion in ilion, a biopsy found BL cells. Case 2: female, 19 years old, healthy, with binocular diplopia after several days with pain in shoulder and paraesthesias in pharynx. A posterior internuclear ophthalmoplegia (pINO) was seen: abduction paresis of right eye with adduction nystagmus of the left eye; as well as depressed abdominal cutaneous reflexes and absence of left achilles reflex. Cranial MRI was normal. A CSF study had 50 atypical white cell per mm<sup>3</sup>, and high protein (4 g/L). Flow cytometric analysis confirmed BL cells. After that, body CT-scan found involvement in kidneys, ovaries, and pancreas.

**Discussion:** In BL, the central nervous system involvement is suggested by signs, neuroimaging studies, and cytology studies. However neurological presentation is not specific and it can mimic different diseases. MRI had a very similar problem. So, a case was studied as a sciatic neuropathy and the other was identified as oculomotor neuropathy. Although in both cases the BL was already disseminated, MRI was normal. Contrast media was not administered because of lack of suspicion for neoplastic disease. The key was the lymphocytic pleocytosis and atypia in CSF. Although sciatic affectation could be secondary to arachnoiditis, however, pINO, an infrequent sign, pointed a mesencephalic-pontine lesion, a parenchymatous damage not shown in MRI. In our experience, and excluding primary central nervous system lymphoma, only Burkitt lymphoma developed CNS infiltration. Clinical data, laboratory test, pictures/filmations and neuroimaging of both cases are presented.

## Ischemic stroke and the "hidden" atrial fibrillation

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**Objective:** To determine the possible relationship and prevalence of combination of ischemic stroke with transient atrial fibrillation (AF).

**Material and Methods:** We observed 74 patients with acute ischemic stroke (46 men, 28 women, average age 71.4 years old). All the patients at admission had sinus rhythm on ECG. On the first day of observation the Holter ECG monitoring was performed. AF was considered as "hidden" in case of registration of one or more episodes of AF with at least 20 minutes duration.

**Results:** 40 (53%) patients had from one to eight episodes of AF with duration between 22 minutes and 2.2 hours. AF episodes were observed mainly at night and early morning hours. The average age of the patients with number of AF episodes from 1 to 4 (Group 1) was 66.6, years, and with the number of episodes from 5 to 8 (Group 2) - 77.2 years (p <0.05). Average duration of essential hypertension in group 1 was 12.6 years, in the 2nd group - 17.6 years (p <0.05). The prevalence of diabetes type 2 in group 2 was on 36% higher than in the 1st group.

**Conclusions:** The findings suggest high frequency of the combination of ischemic stroke with episodes of AF lasting more than 20 minutes on the background of original sinus rhythm. It was also found that the number of transient AF episodes in these patients increases according to age, duration of essential hypertension and presence of diabetes mellitus type 2.

## An unusual cause of abdominal pain

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**Case report:** A 48 years old male engineer (non-toxic working environment), with a history of pulmonary TB in 2011, presented with marked fatigue, weight loss of 4 kg, and severe muscle weakness. These symptoms started 5 days earlier and worsened progressively. One month before presentation, the patient had an episode of continuous low abdominal pain, accompanied by bilious vomiting. After 2 days, the pain disappeared, but the patient continued to have frequent abdominal belching and constipation for a few days. He presented to a hospital, and had a panel of normal investigations: abdominal ultrasound, CT examination of the chest, abdomen and pelvis. However, blood work revealed normocytic normochromic moderate anemia and colonoscopy was unsuccessful after three trials- possibly because of onset of dynamic ileus. When he presented to our clinic, he was in poor general condition, with skin pallor, no superficial palpable lymph nodes, muscular hypotonia and marked hypokinesia, BP 140/80 mmHg, HR 110 bpm, rhythmical, distended painless abdomen, abolished reflexes in the lower limbs and diminished reflexes in upper limbs, no signs of meningeal irritation, no apparent cognitive impairment, hoarseness, dysphagia for liquids, severe symmetrical motor deficit in both upper and lower limbs (flaccid tetraparesis) but with normal sensitivity, plantar cutaneous flexion reflex and no focal neurological signs. Laboratory tests showed moderate normochromic normocytic anemia, biologic inflammatory syndrome, a direct negative Coombs test, increased ferritin, marked reticulocytosis on the blood smear (66%), normal LDH levels, elevated indirect bilirubin, negative hepatitis B and C, and HIV serology. Bone marrow aspirate showed frequent erythroblasts with basophil staining. Both the plain abdominal radiography and abdominal

ultrasound showed significant flatulence. Given all these data, we tested the patient for inflammatory conditions and heavy metal poisoning, which showed increased lead levels in blood and urine (2xULN). He was started on lead chelating therapy and his condition improved.

**Discussion:** Although difficult to illicit at first and a reason for delayed diagnosis and treatment in this patient, we were able to identify the cause of lead poisoning: home-made alcohol (in Romania most installations for alcohol distillation are made of lead).

## Cardioembolic severe cerebellar infarction

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**Introduction:** The connection between stroke and cardiac disease is well known. Around 15-30% of ischemic strokes are due to embolism of cardiac origin. These events are usually severe, with multiplicity of site and time, involving both cerebral circulations. Left ventricle (LV) mural thrombus accounts for almost a third of the cardioembolic strokes. Around 26% of patients with an ischemic stroke present an intracardiac thrombus. LV dysfunction is an independent predictor of intracardiac thrombus and the presence of a thrombus is associated with more advanced systolic dysfunction and extense myocardial scarring. Patients with protruding, mobile, large thrombus are at increased risk of embolization and should be anticoagulated. Ischemic cerebellar stroke may prove difficult to diagnose due to its elusive, nonspecific symptoms. However, cerebellar swelling may compress the pons, resulting in fourth ventricle obstruction, acute hydrocephalus, and neurological deterioration.

**Case report:** 60 years old, male, Caucasian, medicated with bisoprolol and nifedipine for hypertension, and metformine, gliclazide and insulin for mellitus diabetes. The patient resorted to the urgency department due to vertigo and vomiting since the day before, together with asthenia, orthopnea and effort dyspnea with 1 month of evolution. Computed tomography (CT) scan showed large infarction zone in the right cerebellar hemisphere with mass effect over the fourth ventricle. Echocardiogram revealed a dilated cardiomyopathy, with severe left ventricular dysfunction and a 34x26mm protruding thrombus on the apex. The patient was admitted in, and, after multidisciplinary discussion, began anticoagulation with enoxaparin. At the first day, there was a severe deterioration of the neurologic status of the patient. The new CT scan revealed increased mass effect and ventricular dilation. After unsuccessful osmotherapy, decompressive craniectomy ensued, with progressive but partial resolution of the neurological deficits.

**Discussion:** Cardioembolism is a very important cause of ischemic stroke and the echocardiogram still is the most accessible, feasible exam to undergo in the urgency setting. The pitfalls of the cerebellar stroke diagnosis are many, but its evolution might be dramatic. The management of brain infarction with neurological deterioration requires a multidisciplinary discussion, in which the Internist plays a central role in accessing the risks and benefits for the patient.

## Call-Fleming syndrome: reversible cerebral vasoconstriction syndrome

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**Introduction:** We report a case of Call-Fleming syndrome or reversible cerebral vasoconstriction syndrome (RCVS).

**Case report:** A 19 years old and 41-weeks pregnant woman was admitted because of prodromal labor clinic, thunderclap headache, alteration of behavior and spatial disorientation, accompanied by nausea, vomiting and malaise. Later she presented 2 episodes of generalized tonic-clonic epileptic crisis with fetal hypodynamia for which emergency cesarean section was performed. Physical examination was normal. Results of laboratory test were normal. Cranial-CT showed 3 subcortical hypodense focal lesions in frontal and left parietal lobe (1 cm, well delimited, rounded, without significant mass effect and no peripheral edema, without enhancement, without calcifications and without intracranial hemorrhage). Phenytoin was started and she was admitted to intensive care unit. Differential diagnosis was made with patient clinic and image test, between subarachnoid hemorrhage (SAH), infection (tuberculosis, toxoplasma, neurocysticercosis), tumor, demyelinating disease, vasculitis and thrombosis among others. Lumbar puncture for CSF showed unaltered cytochemical, with cultivation and negative pathology. PCR for virus in CSF and serology had negative results. Autoimmunity was also negative. Transcranial doppler ultrasound showed a small area of stenosis at level of middle cerebral artery (>50%). Cranial-MR showed 3 lesions with same characteristics. Cranial-CT control was requested 12 days later with disappearance of the subcortical hypodense lesions. At 17 days, cerebral angiography had normal results. Patient remained asymptomatic. That case might be a RCVS taking into account pregnancy to term, debut with epilepsy and thunderclap headache, having ruled out as causes bleeding, infectious, tumoral, demyelinating and ischemic; however absence of diagnostic criteria for areas of vasospasm on angiography could be explained by delay in its realization and reversible nature of it, which was presented in transcranial Doppler ultrasound. Final diagnosis: RCVS or Call-Fleming syndrome.

**Discussion:** RCVS is a rare entity, which presents with thunderclap headache, reversible, and can be associated or not focal neurological deficit to non-aneurismal SAH. Due to possibility of neurological complications such as ischemic or hemorrhagic stroke, cerebral edema, cortical involvement, and arterial dissection will be important to discard it.

## Stroke by an unexpected cause

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**Introduction:** Ischemic stroke is a high burden to our society. Thrombus within the carotid artery (CA) can be an embolic source

of stroke. Risk factors for carotid artery thrombus formation in the absence of atherosclerosis are not well understood, however, there are few case reports suggesting that anemia and thrombocytosis may be related.

**Case report:** A 46 years old woman with no relevant past or familial medical history besides anemia of unknown cause diagnosed 2 months earlier, presented to the emergency department with acute onset of right-sided motor deficit. On neurological examination right hemiparesis, global aphasia and right hemianopia were noted. Brain computer tomography (CT) and later magnetic resonance imaging showed signs of acute ischemia in the left middle cerebral artery territory. Cervical ultrasound revealed a partially adherent mural thrombus in the left common CA with embolic potential. Laboratory workup was remarkable for microcytic hypochromic anemia (6.8 g/dL), decreased folate level and borderline vitamin B12. All other exams such as electrocardiogram, 24-hour Holter, transthoracic and transesophageal echocardiograms were normal and the comprehensive study of rare causes of stroke excluded autoimmune, infectious and coagulation disorders. As for the study of anemia, she performed thoracic-abdominal-pelvic CT, endoscopy and colonoscopy. The only positive finding was a uterine myoma. We concluded that anemia was probably due to increased vaginal blood loss and nutritional deficiencies. She was started on anticoagulant therapy and follow-up ultrasound 1 week later demonstrated partial resolution of the thrombus.

**Discussion:** Severe iron-deficiency anemia may be a risk factor for CA thrombus formation. As a precautionary measure it is important to study and treat the anemia. Due to its high prevalence, especially in young females, correction of the anemia may avoid stroke in these patients. Medical management with anticoagulation therapy is a reasonable approach for thrombus resolution.

## Neuroleptic malignant syndrome - characterization of a population

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**Objectives:** The neuroleptic malignant syndrome (NMS), a neurological emergency, is a rare idiosyncratic reaction related to the introduction of anti-psychotic drugs or the interruption of dopaminergic medication. It usually presents as a change in mental status, hyperthermia, muscular rigidity and dysautonomia associated to rhabdomyolysis. The mortality is high, the diagnosis requires a high index of suspicion and the prognosis depends on the prompt initiation of therapy. The aim of this study was characterizing a population of patients with NMS in terms of epidemiology, clinical presentation, drugs involved, therapeutic approach and outcome.

**Methods:** We retrospectively reviewed all patients with a diagnosis of NMS admitted to our center between 2000 and 2014.

**Results:** 15 patients were included, with a median age of 52 years. 60% were female. 80% had a previous psychiatric/neurological history. The most frequent symptom was hypertension (86.7%) followed by hyperthermia (80%), change in mental status (66.7%), tremor (46.7%) and symptoms of dysautonomia (40%). The drugs

most frequently involved were haloperidol (40%), risperidone (33.3%) and metoclopramide (20%), with a history of introduction of a new drug in 53.3% of the cases. 50% of patients had a creatine kinase value at presentation of 200-2000 U/L and 42% of >2000 U/L. Regarding treatment, the most frequently used drug was bromocriptine (60%), followed by dantrolene (40%) and benzodiazepines (33.3%), with 20% of patients treated only with fluids and discontinuation of the neuroleptic. In terms of outcome, 20% were admitted to an intensive care unit, 93.3% improved without sequelae and there was 1 case of recurrence. Mortality was 0%.

**Conclusions:** Although most of our findings are consistent with the existing literature, some of our data (female predominance, mortality) is not. Due to its low incidence and extensive list of differential diagnosis, NMS is likely an underdiagnosed condition, making the study of its presentation in clinical practice of the uttermost relevance.

## Postural orthostatic tachycardia syndrome – case report and brief review

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**Introduction:** Postural orthostatic tachycardia syndrome (POTS) is a heterogeneous group of disorders that result from disturbances in autonomic function. It is a subset of orthostatic intolerance that is associated with the presence of excessive tachycardia upon standing, accompanied with palpitations, exercise intolerance, fatigue, lightheadedness, nausea, tremor or syncope. Although the etiology is unknown, an autoimmune hypothesis seems likely. It can be primary (partial dysautonomic or hyperadrenergic forms) or secondary to drugs, diabetes mellitus or auto-immune disorders, among others. The diagnosis is based on history and the finding on physical examination of a heart rate increase of 30 beats per minute (bpm) or more within the first 10 minutes of standing. Treatment consists of hydration, increase in salt intake, physical reconditioning and, in non-responders, pharmacotherapy. The prognosis in most cases seems to be good.

**Case report:** We report a case of a 20 years old previously healthy woman that presented with a 6 month history of several episodes per week of light headedness and syncope or near-syncope upon standing up, with full recovery within some minutes of lying down. She also complained of a non-pulsatile bilateral temporal headache that was frequently related to the episodes. She had a normal physical examination except for an increase in heart rate of 30 bpm after standing up (80 bpm at rest and 110 bpm after 10 minutes standing), with no hypotension. The brain computed tomography, brain magnetic resonance imaging, electrocardiogram, electroencephalogram and blood tests (including an autoimmunity panel) were unremarkable. She was diagnosed with POTS. The treatment included general measures for avoidance of orthostatic intolerance and venlafaxine for a comorbid anxiety disorder, with good outcome.

**Discussion:** Since POTS is a poorly known entity with limited data available, with this case report we intend to highlight a disorder that may be more prevalent in the general population

than previously reported. A simple bedside test is sufficient to establish the diagnosis and provide treatment that may substantially improve the patient's quality of life.

## Behind the Horner's syndrome. A case report

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**Introduction:** The Horner syndrome, described by Johann Friedrich Horner in 1929, classically presents with ipsilateral ptosis, miosis, and anhidrosis. It results from an interruption of the oculosympathetic pathway. The causes include: stroke, artery (carotid or subclavian) aneurysm, iatrogenic causes, traumatic injuries and tumors such as schwannoma, carotid body tumor, thyroid cancer, lung cancer, sarcoma, metastasis and Hodgkin lymphoma, which has been less frequently reported in the literature. The aim of this report is call attention of the physicians about a rare presentation of a malignant tumor in a young man.

**Case report:** A 17 years old man, presented with a complaints of right arm weakness, right ptosis and size reduction of his right pupil. He had a neck trauma at a Taekwondo practice, without important personal information. At the physical exam were found: partial right ptosis, miosis in the right pupil with normal light reaction, distal right arm weakness with hypoesthesia cubital. The blood tests were normal, the chest X-ray was normal, cerebral magnetic resonance was normal and cervical magnetic resonance showed a 9x5 cm paravertebral mass that arises from the 6th and 7th vertebral junction's hole and extends to right upper pulmonary lobe. A biopsy was performed and it showed a classic lymphoma Hodgkin. Now the patient is under chemotherapy.

**Discussion:** Classic signs of a Horner's syndrome include miosis, ptosis, and anhidrosis. The miosis is typically mild, associated with a dilation lag and most prominent in dim light. The ptosis is also mild and also involves the lower lid. This patient did not present anhidrosis so the lesion must to be at the post ganglionic level in this level the most frequent causes are: carotid dissection, followed by neck and upper chest traumatic lesions. Although exists a clear history of trauma, the imaging studies should be required in order to avoid the misdiagnosis of potentially malignant entities. In this case the early diagnose can radically change the prognosis and illness natural history.

## Takotsubo cardiomyopathy and seizures: a rare association

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**Introduction:** Takotsubo cardiomyopathy is an acute syndrome characterized by wall motion abnormalities with transient left

ventricular dysfunction, absence of significant angiographic evidence of obstructive coronary disease or acute plaque rupture, presence of new electrocardiogram (ECG) abnormalities or modest troponin elevation. It is triggered by a medical illness (including seizures) or by intense emotional or physical stress. Although the pathogenesis is not fully understood, mechanisms like catecholamine excess levels, multivessel coronary artery spasm and microvascular dysfunction were associated. The clinical presentation can be similar to an acute myocardial infarction. Takotsubo after seizures are rarely reported in literature.

**Case report:** A 70 years old women with history of hypertension, diabetes mellitus, dyslipidemia, obesity and epilepsy taking levetiracetam 1000 mg/day was admitted to the emergency room after three generalized tonic-clonic seizures at home, with motor activity ceased after 10 mg of intravenous diazepam. On physical examination she was tachycardic but haemodynamically stable, with consciousness impaired but without neurological deficits. The serum troponin level was 0.375 ng/ml and the ECG showed ventricular extrasystoles and a right branch bundle block with nonspecific repolarization changes. Brain computed tomography (TC) didn't show acute lesions. An echocardiogram showed a decreased left ventricular ejection fraction with moderate depression with akinesis of the mid and apical segments. On day 2 of admission there was persistent elevation of troponin serum levels (0.777 ng/ml) and the ECG showed negative T waves in I, II, III, aVL, AVF, V3-V6 leads and the patient was admitted to the coronary care unit. Coronary angiography didn't show significant disease.

**Discussion:** Takotsubo cardiomyopathy should be considered in the differential diagnosis of acute cardiac events in patients with seizures since the consequences can be fatal. This cardiomyopathy predisposes to serious complications like embolism, cardiogenic shock, heart failure, arrhythmias and sudden death. In this patient, the authors emphasizes the association between seizures as a trigger for this pathology and the difficulty in the diagnosis in a patient with multiple cardiovascular risk factors in which a coronary syndrome could be the only diagnosis proposed.

## Deaths by cerebrovascular diseases in Europe

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**Objectives:** 1) Describe long term mortality time series controlling for population dynamics (age, sex) and time trends; 2) Identify patterns in terms of level and trends by country; 3) Forecast the impact in number of deaths for these countries.

**Methods:** We used JoinPoint analysis methods to identify patterns in trends of standardized cause-specific mortality rates for countries with available data and then performed multiple negative binomial regression models by trend-period constrained to exposed population and controlling for age group and sex. These regression coefficients by country were used to estimate the number of deaths according to previously

published population projections. Data source: WHO Mortality Database, UN Population Projections.

**Results:** The incidence increases with age and is higher among men. Most European countries have a downward trend in recent years. These aspects vary in magnitude and there are some exceptions.

**Conclusions:** Although the comparability of this indicator might be harmed by different death registration and coding procedures there are some consistent patterns and the estimates were stratified by country. The anticipated population ageing exerts an influence towards the increase of the burden of this cause of death which is counterweighted by the downward trend in mortality.

### Primary pituitary cancer – a rare presentation

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**Introduction:** The primary pituitary cancer is an extremely rare entity (<1% of pituitary tumors) and has a very poor prognosis.

**Case report:** We report the case of a 51 years old woman with complaints of frontal headache, left ptosis, left brachial palsy with left central facial palsy and hypoesthesia of the left side of the face that lasted for 24 hours. She also referred anorexia with significant weight loss in 1 month (>10% BMI). CT/MRI-CE showed bone erosion of the sella turcica filled with a bulky mass that is intertwined with the pituitary gland, and extended to both sphenoid and cavernous sinus, also contacting with the optic chiasm on the left. Laboratory studies showed hyponatremia, decreased serum cortisol and hypothyroidism. The diagnosis of pituitary macroadenoma was assumed with pituitary apoplexy and therefore replacement therapy was initiated along with a transsphenoidal excision of the mass. Later, an improvement of the headache complaints was observed but left cranial nerve III palsy persisted. At the same time, we watched a rapid deterioration of her general status with polyuria, frontal/orbital disabling headache, uncontrollable vomiting, bilateral ptosis, right mydriasis, bilateral ophthalmoplegia, and left facial hypoesthesia. The patient started treatment with desmopressin for insipid diabetes and anti-edematous measures as the neurological worsening was interpreted in the context of intracranial hypertension (ICH). CT/Angio MRI-CE revealed increased dimensions of the expansive sella and suprasellar lesion, reduced gauge pre-pontine cistern without compression of the brain stem, and cavernous sinus involvement. Histological examination was compatible with carcinoma and immunohistochemistry (primary versus secondary) was inconclusive, hence requiring further diagnostic studies to exclude a hidden neoplasia with pituitary metastasis. Finally, the patient underwent emergency radiation therapy to decrease the HIC component and, later, surgical treatment. However, the patient clinical outcome was not good, culminating in death.

### Effect of lipoic acid on serum asymmetric dimethyl arginine level in multiple sclerosis patients: a double blind randomized clinical trial

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**Objective:** Multiple sclerosis (MS) is a progressive neurological disease. Nitric oxide (NO) and other reactive nitrogen species play crucial roles in the pathogenesis of disease. Endogenous Asymmetric dimethylarginine (ADMA) is a serum biomarker, competitively inhibits the enzyme NO synthase to reduce the NO level. The aim of this study was to evaluate the effect of lipoic acid (LA) supplementation as an anti-oxidant on the serum ADMA level in MS patients.

**Methods:** 52 patients with definite MS diagnosis were enrolled in the study. They were randomly assigned to two groups: LA (n=26) and placebo (n=26) to receive either LA (1200 mg/day) or placebo capsules for 12weeks. Fasting blood samples were collected before the first dose and 12 hours after last administrated dose to evaluate the serum ADMA level.

**Results:** The results showed that LA group had serum LA concentration of 1 to 15µg/dL after 3 months of supplementation. LA treatment significantly reduced ADMA from 32.2±8.3 mmol/l to 27.6±7.8 mmol/l (p<0.05) in LA group compared with the control group.

**Conclusion:** LA supplementation had positive effects in reducing the nitroxative stress in multiple sclerosis patients. It could improve antioxidant status thus it can be regarded as a helpful antioxidant in the treatment of MS patients.

### Painkillers that make you tremble

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**Introduction:** Parkinsonism refers to a clinical syndrome characterized by rest tremor, bradykinesia or akinesia, cogwheel rigidity and postural instability. Within the rubric of parkinsonism, there are a myriad of disorders, ranging from Parkinson's disease itself to some unclassified states. Drug-induced parkinsonism (DIP) is a common clinical condition observed in certain types of drugs, such as antipsychotics, however, occurrence with opioid drugs like fentanyl are poorly described in literature (up to 0.1% cases with transdermal patch [TD], according to the FDA).

**Case report:** A 68-year-old man with previous medical history of chronic articular pain, mild in severity initially, and severe over time, was admitted in the emergency department due to neurological status deterioration. Two weeks prior to admission, he had initiated fentanyl for the pain, in an ascending posology (maximum 75 mg, tid). He also reported articular rigidity and rest tremor over the past two months, having experienced aggravation in the last two weeks, making him in full dependence of daily life activities by then. Physical examination was normal except for neurological

exam, which revealed disorientation, a severe generalized rigidity, bradykinesia, hypomimia and a postural and resting bilateral tremor. Laboratory tests and brain CT scan performed were unremarkable. The clinical case was discussed with a neurologist and it was assumed the diagnosis of fentanyl-induced parkinsonism in a previously predisposed patient. Fentanyl was suspended and he started on levodopa-carbidopa with improvement of the symptoms.

**Discussion:** Differentiating between Parkinson's disease itself and other parkinsonic conditions can be clinically challenging, especially in the early stages. This distinction has crucial implications in management and prognosis, once in the drug-induced disease, the mainstay of treatment is suspension of the drug. There are some cases, however, where the two situations overlap and even potentiate each other. Our clinical experience showed that dopaminomimetic drugs remain, thus, an excellent therapeutic resource.

## Cannabis induced ischemic stroke. A case report and review of the literature

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**Introduction:** The objective of this case report is to demonstrate a case of a middle age male, who was diagnosed with ischemic stroke after cannabis use and to review the current literature for this association. The diagnosis was confirmed after thorough medical workup in our clinic. Moreover, all the other possible causes of ischemic stroke were ruled out.

**Case report:** A 52 years old Caucasian male presented to the emergency department of our clinic with a sudden weakness on the right limb with an approximate duration of 5 hours. The patient admitted that he was smoking cigars filled with cannabis when the symptoms occurred. Patient was alert and oriented, vital signs were normal and physical examination disclosed muscle strength 0/5 in the right lower limb and 4/4 reflexes in the same limb. Laboratory findings were within normal values and all the other illegal substances were excluded with urine toxicology. ECG, echocardiograph, carotid artery triplex revealed nothing abnormal. Computed tomography brain scan showed no abnormalities. The magnetic resonance test that followed revealed a recent ischemic type injury in the left parietal lobe. After 4 days of uneventful hospitalization patient was discharged with the appropriate medication. He was also strongly advised to discontinue the use of cannabis. Unfortunately, he did not appear in his follow up appointments for further consultation.

**Discussion:** Available experimental evidence regarding this association and the underlying mechanisms is limited. Possible mechanisms include hypotension, vasospasm, reversible cerebral vasoconstriction syndrome, cardioembolism and vasculopathy. The results from 2 observational studies as well as the most recent review have shed more light suggesting that there is an association between cannabis use and ischemic stroke. In clinical practice there are significant questions that remain unanswered, such as the initial screening of cannabis along with the other illicit drug in patients presenting with ischemic stroke. What remains to be investigated further from large observational and experimental studies is the exact role of cannabis as a causative factor in ischemic strokes.

## Cases of bilateral thalamic stroke due to occlusion of the artery of Percheron

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**Introduction:** Strokes affecting both thalamic territories are unusual and limited cases has been reported, they result from a combination of predisposing factors and anatomic variations. Clinical and image findings of bilateral symmetric paramedian thalamic of these uncommon form of posterior circulation infarct may lead to a suspicion of an occlusion of the artery of Percheron, characterized by a single arterial trunk that irrigates both paramedian thalamic regions and can be occluded as a result of embolic diseases. Two cases are reported along.

**Case reports:** Case one: A 62 years old woman with previous history of hypertension and dyslipidemia was admitted to hospital after suddenly had had an acute confusional syndrome without abnormalities on the physical and complete neurological examinations. Cranial magnetic resonance showed a bilateral thalamic stroke probably to variant thalamus irrigation: artery of Percheron. Further evaluations including electrocardiogram, Holter, echocardiogram and vascular duplex ultrasound as well as laboratory tests (complete blood cell count, platelets, cholesterol profile, anti-beta-2 glycoprotein I antibodies, anticardiolipin, immunoglobulins G and M, activated partial thromboplastin time, venereal diseases research tests, factor V Leiden, activated protein C and S tests) didn't reveal abnormalities or were all negative in order to define the etiology of the infarction. Case two: A 72 years old man with medical history of coronary artery disease, hypertension, dyslipidemia, diabetes mellitus and chronic renal failure admitted to the emergency department after he was found in a deep stupor. On admission his vital signs were normal (blood pressure 131/60 mmHg, breath rate 18/minute, heart rate 81/minute, axillary temperature 36.9°C). On neurologic examination we found bilateral palpebral ptosis, arreflexive mydriasis, symmetric facial responses and withdrawal of both arms and legs to painful stimuli. All brainstem reflexes were patent and Babinski reflexes were negative on both sides without other abnormalities on the physical. An urgent magnetic resonance was performed, it revealed symmetric bilateral hyperintense paramedian thalamic lesions consistent with acute ischemic events, the posterior circulation was normal including the top of the basilar artery and both posterior cerebral arteries, making the case compatible with occlusion of the artery of Percheron. Laboratory blood tests were all negative and further cardioembolism study including echocardiogram and artery duplex ultrasound showed no abnormalities.

**Discussion:** A careful evaluation of the patient's history, clinical presentation together with imaging findings facilitates in making the correct diagnosis of occlusion of artery of Percheron that must be considered when bilateral symmetric paramedian thalamic infarcts are revealed on image studies in the context of a patent basilar artery and posterior cerebral arteries. The most common cause is cardioembolism.

## An unusual cause of ischemic stroke

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**Introduction:** Make the audience aware of a not-so-common cause of sudden neurological deficits.

**Case report:** 41 years old Caucasian male was admitted to the emergency department with right-sided arm weakness and hypoesthesia, and right-sided central face paralysis of sudden onset. In the past medical history the patient had arterial hypertension and arteriovenous malformation (AVM) within the territory of the left middle cerebral artery (MCA), which underwent stereotactic radiosurgery one year before the event. The computerized tomography (CT) scan of the brain revealed an ischemic stroke in the territory of the left MCA. Due to the young age of the patient, possible involvement of the previously known AVM and to help to clarify the etiology of the ischemic event, a magnetic resonance imaging (MRI) of the brain was ordered. The MRI showed sparing of the brain cortex, denying an ischemic stroke of arterial origin. A multidisciplinary discussion of the case between internal medicine, neurosurgery and neuroradiology was taken and it was possible to attribute the cause of the neurological deficits to a long-term side-effect of radiosurgery. The patient was admitted to the stroke unit of the hospital, received treatment with dexamethasone and showed progressive improvement of the neurological deficits.

**Discussion:** Stereotactic radiosurgery is an important and useful technique to treat AVM but possible late effects include radiation necrosis and vascular injury. It is important to have this present when these patients present with late new neurological deficits. The internist played an integrative role in this case, putting all parts of the history together and managing the multidisciplinary discussion between internal medicine, neurosurgery and neuroradiology.

## Ischemic stroke with internal carotid artery dissection after blunt trauma

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**Introduction:** The internal carotid artery dissection (ICAD) is a rare cause of ischemic stroke accounting for 20% of patients less than 50 years old. The extracranial location is more common than the intracranial one. The incidence of traumatic ICAD is unknown but thought to be around 0,08%. ICAD is a potentially life-threatening condition and carries a substantial risk of disabling stroke that may present non-specific symptoms as headache.

**Case report:** 52 years old male, with a recent diagnosed hypertension. In the morning, he suffered blunt trauma to the periorbicular region with a pitchfork that caused hyperextension of the neck, followed by syncope. 30 minutes after the trauma, he started head aching, difficulty in the execution of rapid movements of the right upper arm, disequilibrium and numbness to the right hemiface and ear. Later was observed at the hospital, with a normal cranial computerized tomography (CT) and later on discharge. He was last time seen with no neurological deficits at 23 pm by his wife. At 2 am he aroused anxious with inability to speak, right hemiparesis and deviation of labial commissure. At time of hospital admission the neurological examination showed severe speech and comprehension aphasia, right homonymous hemianopsia, oculocephalic deviation to the right hand side but crossing the median line, severe right face palsy, right arm and leg hemiparesis and weak gag reflex (NIHSS 21). The initial angio-CT showed occlusion of the cervical segment of the left internal carotid artery and an ischemic lesion of the medial cerebral artery territory. At this time, he filled no clinical criteria for thrombolysis or intra-arterial intervention. He was transferred to a specialized unit where it was than started both antiedema and anti-aggregation therapies. The magnetic resonance image showed a complete proximal occlusion of the artery with bifid aspect prolonged by a linear image characteristic of a dissection. Echocardiogram, electroencephalogram and laboratory tests were normal. It was assumed an ischemic stroke in the context of an internal carotid artery dissection due to traumatic cervical hyperextension. After clinical stabilization it became possible to initiate daily physical and language therapy. The patient was transferred to a physical recovery Centre with a NIHSS of 17.

**Discussion:** The authors report a case of traumatic ICAD with subsequent ischemic stroke, pretending to draw attention to this rare cause of stroke in young people.

## A strange cause of hypocalcemia

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**Introduction:** Even though there are many potential causes of hypocalcemia, impaired PTH and vitamin D production are the most common etiologies. In adults, hypoparathyroidism most commonly results from inadvertent damage to all four glands during thyroid or parathyroid gland surgery, but can be a sign of an autoimmune endocrinopathy or an infiltrative disease such as sarcoidosis. Reduced PTH secretion may be caused by magnesium deficiency or to activating mutations in the CaSR, which suppress PTH. Vitamin D deficiency, impaired 1,25(OH)<sub>2</sub>D production or vitamin D resistance also cause hypocalcemia. However, the degree of hypocalcemia in these disorders is generally not as severe as that seen with hypoparathyroidism because the parathyroids are capable of mounting a compensatory increase in PTH secretion. The authors describe a case of hypoparathyroidism due to parathyroid ischemia secondary to cervical trauma with a life threatening condition.

**Case report:** A 67 years old Caucasian woman, with previous diagnosis of diabetes type 2, arterial hypertension, status post myocardial infarction, minor thrombophilia, Parkinson disease, car accident 3 years ago with cranial-encephalic and cervical trauma was transferred to our hospital from other health institution where she was intubated (endotracheal) due to a post-ictal state (tonic clonic seizure). At the physical examination: GCS 6, opening eyes spontaneously, no verbal or motor response, without focal neurological signs. The patient initiated an anticonvulsant and was admitted to the ICU where after some blood work: calcium 4.4 mg/dL, phosphorus 6.9 mg/dL, magnesium 1.3 mg/dL, PTH 18 pg/ml, decreasing to 9.2 pg/ml after administration of magnesium. The rest of the investigation did not reveal any alteration. After correction of electrolytic alterations, the patient recovered the level of consciousness and after a while, she was discharged home.

**Discussion:** After all the investigation, the authors got to the diagnosis of primary hypoparathyroidism due to an ischemic event, related to a car accident that happened 3 years ago and probably due to trauma. The patient was discharged with calcium, vitamin D and magnesium supplements and until date, there was no more seizures or disturbances of electrolytic balance.

## A case of bilateral medullar infarction

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**Introduction:** Medullar cerebrovascular events accounts for <1% of vertebrobasilar strokes. For their rarity, the diagnosis of bilateral medullar infarctions can be imperceptible and therefore influence the functional prognosis. The progressive neurological involvement combined with typical brain resonance (MRI) features, expand the diagnostic accuracy.

**Case report:** An 85 years old woman with hypertension, diabetes and dyslipidemia presented to the emergency department with sudden onset dysarthria and left hemiparesis. A cerebral tomography was made and showed old lacunar infarctions. She was admitted in a stroke unit. On the day of admission, worsening weakness on the left side with plegia of upper limb and noted paresis of the right arm. A repeat brain scan showed no new changes. On the 4th day, progression to tetraparesis and aggravated signs of bulbar palsy (dysarthria and dysphagia), were noted. In this setting, brain MRI was done which demonstrated acute bilateral anterior-medial medullar infarction affecting anterior spinal artery territory. Duplex ultrasonography of extracranial vessels detected no flow in the vertebral arteries. Neurological stabilization in the rest of hospital stay. At 14th day, the patient was discharged to a physical rehabilitation centre.

**Discussion:** The rare occurrence of bilateral medullar infarction is due its blood supply. Since, the absence of imaging translation on cerebral tomography is universal, the performance of brain MRI it's essential for an early diagnosis. In some cases, due to the anatomical location and neurological extent, the outcome is reserved.

## Prognostic value of markers of hemostasis in patients undergoing cardioembolic stroke with atrial fibrillation

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**Background:** Despite advances in diagnosis and treatment of stroke, the incidence of and mortality from this disease in the Russian Federation, as well as around the world remain high. It requires modern technology aimed at implementing mechanisms to facilitate the prevention, both primary and repeated, acute cerebrovascular accident. Achieving results is possible not only at the level of a common methodological approach to stroke prevention, but not least, at the choice of methods of correction based on the type of ischemic stroke (IS). To date, highly relevant is to determine the tactics of antithrombotic therapy in patients with atrial fibrillation (AF) undergoing cardioembolic stroke (CS). In these patients, the issue should be considered primarily in terms of the possibility of using anticoagulant therapy, taking into account changes in the rheological properties of blood and hemostasis in acute and early recovery period.

**Objective:** To study features of hemostasis in patients undergoing AF CS.

**Material and Methods:** The study included 350 patients (227 women and 123 men) who underwent carotid CS in non-valvular AF. The patients were divided into 3 groups according to the severity of the stroke indices criterion on a scale NIHSS. We are pursuing a comprehensive clinical and instrumental examination at entry, 3, 6 months and 1 year of observation, including estimated figures plasma hemostasis (fibrinogen, D-dimer, SFMC, antithrombin III) and indicators of vascular-platelet hemostasis (factor von Willebrand, platelet aggregation). Statistical analysis was performed using the standard c program Microsoft Excel and statistical software package Statistica for Windows. The significance of differences was calculated using the Student t-test, correlation coefficients - for Spearman. Results were considered significant at  $p < 0,05$ .

**Results:** In all patients, a history of hypertension, 96% had comorbidities: diabetes - 77%, rheumatoid arthritis - 7.1%, chronic kidney disease - 16.6%. A long history of AF in 252 people (72%) ranged from 1 year to 10 years ( $6,7 \pm 3,4$ ), in 28% cases of AF were diagnosed for the first time in acute stroke. At the time of incorporation is set hyperfibrinogenemia in all groups (fibrinogen  $5,3 \pm 1,54$  g/L), regardless of the severity of the neurological deficit and the volume of the AI outbreak. In group III, the fibrinogen component -  $5,6 \pm 1,72$  g/l, on the scale NIHSS -  $14,5 \pm 1,8$  points, pronounced neurological motor deficit, 34.6% of patients with a score of  $\geq 3$  for HAS-BLED, which limited the appointment of anticoagulants. In this group at 3 months was significantly compared with those groups I and II deteriorated all indicators of hemostasis: SFMC -  $4,3 \pm 2,9$  mg%; antithrombin III -  $90,2 \pm 3,7\%$ ; D-dimer -  $0,44 \pm 0,21$ ; It draws attention to the high values of spontaneous aggregation of platelets -  $1,80 \pm 0,83$  standard units

**Conclusions:** Within 3 months after suffering a CS observed marked changes in the coagulation and vascular-platelet hemostasis, especially in patients with severe motor and aphasic disorders. Further research is needed to examine the relationship of the markers of hemostasis with the severity of neurological deficit, risk of bleeding and the possibility of rational use of anticoagulants in stroke recovery period against the background of AF.



## **Pleural effusion: two clinical cases of less frequent underlying malignancy**

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**Introduction:** Pleural effusions can have multiple pathophysiological mechanisms. Exudates are particularly challenging to diagnose. Malignancy is one of the main causes of exudates. Carcinomas of the lung and breast and lymphoma are responsible for 75% of malignant pleural effusions. In 10% of cases, the primary tumor is not identified.

**Case reports:** Patient 1 was 80 years old, female. She sought the emergency department complaining of worsening fatigue lasting two weeks. She also mentioned anorexia and significant weight loss during the previous 3 months. She had no other complaints and the only significant finding in the physical examination was the absence of breath sounds on auscultation of the lower right hemithorax. Chest radiography was consistent with pleural effusion. Pleural fluid chemistry was consistent with an exudate. She was admitted for etiological study and was diagnosed with pancreatic carcinoma with pulmonary, pleural, hepatic and soft tissue metastatic disease. During her stay at the hospital, she complained of pain in her left gluteal region which was explained by nervous compression by a soft tissue metastatic mass. The patient was offered palliative care. She died one month after diagnosis. Patient 2 was 62 years old, female. She sought medical help because of sudden onset pleuritic right sided chest pain. She had had fatigue, dyspnea and cough for the last 3 days. She also mentioned early satiety and vomiting during the two previous weeks. She denied anorexia or weight loss. The only objective finding was the absence of breath sounds on auscultation of most of the right hemithorax. Computed tomography (CT) excluded pulmonary embolism and confirmed the presence of a large right pleural effusion and mediastinal lymphadenomegalies. Pleural fluid chemistry was consistent with an exudate and the patient was admitted for study. She had extensive imaging study that consistently demonstrated peritoneal carcinomatosis but failed to identify the primary tumor. CT scanning of the abdomen suggested a gynecological process. A Pap smear was positive for adenocarcinoma and endometrial biopsy documented endometrial adenocarcinoma. The patient's clinical status worsened rapidly and she died before treatment was considered.

**Discussion:** Up to 50% of patients with a variety of metastatic malignancies develop pleural effusions. The median survival is 4 months after recognition of a malignant pleural effusion.

## **An extremely rare presentation of metastatic small-cell lung carcinoma**

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**Introduction:** Intramedullary tumors are extremely rare, reaching 0.1-0.3% of cancer patients, and those of metastatic origin are even rarer, accounting for 8.5% of all metastasis of central nervous system (CNS). Approximately 50% of intramedullary metastases are of pulmonary origin, with particular emphasis on small cell lung carcinoma (SCLC).

**Case report:** 56 years old female diagnosed with a stage III B SCLC, who underwent chemotherapy, local radiation therapy and prophylactic holocranial radiotherapy without evidence of disease progression for 6 months after treatment. Later on, the patient showed up with right hemiparesis accompanied by intense neck pain, which worsened with Valsalva maneuvers and neck flexion. Neurological examination revealed muscle atrophy of the right hand and forearm and loss of pain and temperature sensation on the left side of the body. Subsequent evaluation exhibited progressive deterioration, with right hand function loss and limitation of motion. Although pain and neurological abnormalities favored bone metastasis with medullary compression, both sides involvement aroused the hypothesis of medullary malignancy. Magnetic resonance imaging of cervical and dorsal medulla showed "expansive intramedullary lesion to the spinal cord at C7 level and evidence of swelling extending from C2 to D3". Given this information it was assumed the diagnosis of metastatic SCLC, considering to be less likely a synchronous primary tumor of the medulla. The patient initiated steroid therapy and underwent emergent radiation therapy. 2 months after therapy she keeps the described deficits, with a slight improvement in the degree of strength and no evidence of disease progression.

**Discussion:** The SCLC is a tumor with high metastasis rate, and two thirds of the patients have secondary deposits at the time of diagnosis. The CNS, with particular emphasis on the brain, is one of the preferred sites of metastasis, as well as bone, liver and adrenal glands. Though extremely rare, the differential diagnosis of new neurological findings in patients with SCLC must include the possibility of spinal metastasis.

## **Hypercalcemia: while treatments do not respond**

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**Introduction:** Hypercalcemia associated with malignancies is reported in up to 20 to 30% of patients with cancer during the course of the disease, and points to a poor prognosis. Symptoms related to the central nervous system, as progressive mental impairment, stupor and coma predominate. Cancer-induced hypercalcemia may be classified as: 1) local osteolytic hypercalcemia (LOH), due to marked increase in osteoclastic bone resorption in areas surrounding the malignant cells within the marrow space; 2) humoral hypercalcemia of malignancy, caused by the secretion of parathyroid hormone-related protein (PTHrP) by the malignant tumor; 3) ectopic

hyperparathyroidism; 4) 1,25(OH)<sub>2</sub>D-secreting tumors. Adequate control of hypercalcemia is necessary to give the patient time to respond to anticancer therapy. Intravenous bisphosphonates are the most effective agents to control hypercalcemia, as they block osteoclastic osteolysis and also have antitumoral effects, decreasing bone metastasis.

**Case report:** Female patient, 55 years old, refers to the emergency department with a history of nausea, vomiting and malaise. We conducted an analytical study and abdominal ultrasound that revealed suspicious lesions of liver metastasis. She was hospitalized for hypercalcemia in context to study cancer with liver metastasis. She presented mental confusion and hypercalcemia 9.1 mEq/L, ALT 51 IU/L, AST 73 IU/L, the total CK 101 IU/L; urea 78 mg/dL, creatinine 1.1 mg/dL, potassium 3.0 mEq/L. No other relevant clinical or analytical changes. We performed the following tests: left breast biopsy: ductal carcinoma, grade 2, luminal B HER2. Bone scintigraphy: no evidence of metastasis. Biopsy liver damage: morphological findings and immunohistochemical profile compatible with breast carcinoma metastasis. In the hospital she had poor response to therapy instituted, having made fluid therapy, bisphosphonates and corticosteroids. We made complementary unfavorable study the bone metastasis or parathyroid adenoma as the cause of hypercalcemia. PTHrp production was assumed or (1.25) dihydroxyvitamin D by the tumor as the cause of hypercalcemia.

**Discussion:** We conducted chemotherapy with epirubicin and cyclophosphamide with improved values of serum calcium (5.1 mEq/L) and resolution of confusion board. Despite the bisphosphonates is the most effective therapy in the treatment of hypercalcemia the patient has not responded, and only improved with chemotherapy.

## Lymphoma nodal marginal zone

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**Introduction:** Lymphoma nodal marginal zone is a rare disease, found mainly in older women. It affects the lymph nodes but bone marrow may be involved. This tends to be a slow-growing lymphoma (although not usually as slow as MALT), and many are cured if diagnosed at an early stage.

**Case report:** Female, 74 years old, with a history of alcoholic consumption and osteoporosis. She refers to the emergency department with ascites high volume. After analytical study she was hospitalized in the internal medicine service for spontaneous bacterial peritonitis. It had already done 6 months before an abdominal ultrasound that revealed a liver with criteria chronic liver disease, steatosis and ascites. She also held at the time one endoscopy which revealed stigmata of portal hypertension and a colonoscopy that revealed angiodysplasia of the small and sigmoid colon polyp (high-grade dysplasia). During hospitalization she held an abdominal CT scan that detected some adenopathies in the mediastinum, most 16 mm, and the celiac trunk, most also with 16 mm. To study she performed a biopsy of mediastinal lymphadenopathy with histopathological diagnosis of morphology compatible with lymphoma.

**Discussion:** The patient was oriented oncology consultation, no indication for treatment. This patient never showed constitutional

symptoms type B or other specific complaints. It was found in the staging of chronic liver disease that has lead to a diagnosis. She keeps then in internal medicine consultation and alcoholic abstinence.

## More than just a sore back

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**Introduction:** Plasmacytoma is a malignant tumor that originates from irreversible and autonomous proliferation of plasma cells, which may present as circumscribed or diffuse infiltration. The solitary bone plasmacytoma is rare. Although age of patients is variable, it is uncommon before 30 years old. It is predominant in males in a 3:1 proportion and its main location is the spine. In solitary plasmacytoma, electrophoresis of serum proteins, the bone marrow examination and laboratory and radiological tests show no evidence of systemic disease.

**Case report:** Female, 75 years old, came to the emergency departments by intense episode of low back pain with 3 days of evolution. She was already medicated by the family doctor with non-steroidal anti-inflammatory drugs without clinical improvement. In emergency departments she performed radiograph and column CT for suspected lumbar fracture: osteolytic lesion to engage the vertebral body of L2, with disruption of the posterior wall fractures of the vertebral platforms, with sinking. On suspicion of secondary infiltrative lesion/plasmacytoma was admitted to proceed study. It was performed a nuclear magnetic resonance that revealed change in L2 vertebral body by secondary oral bone infiltration or plasmacytoma etiology. Bone scintigraphy showed bone metastases in L2 and the lesser trochanter of the left femur. Endoscopy and colonoscopy, the thoraco-abdominal-pelvic CT, ultrasound thyroid and breast revealed no change. FDG PET showed an enhancing lesion in L2. Analytically the only change relief is a monoclonal peak region range of 1,3 g/dL. She performed a L2 injury biopsy that was compatible with plasmacytoma. The patient started radiation therapy with improvement of pain and mobility. She remains to be followed in consultation.

**Discussion:** Chronic low back pain (CLBP) is one that affects the lumbar spine, preventing its normal mobility, lasting more than three months, and is a frequent reason for consultation in primary care and emergency departments. Although in most cases has a mechanical nature, persists in 10% at 6 months, and 1-5% is made constant, intense and desperate, increasing at rest and preventing night's sleep, which warns of a neoplastic possible.

## Symptomatic devaluation: a hidden diagnosis

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**Introduction:** The sarcomatoid subtype accounts for 1-13% of cases of renal cell carcinoma (RCC), generally carrying poor

prognosis at presentation, mainly because of the late diagnosis. **Case report:** We report the case of a 58 years old male patient, a former fireman and still active smoker. He presented to the emergency room with pelvic pain, constipation, urinary retention and recent worsening of sensomotor function of the lower limbs. The patient also mentioned constitutional symptoms and worsening of chronic low back pain for the last 2 months. He had a medical history of previous lumbar spine surgery (herniated disc), gallstones and left kidney stones. The physical examination revealed a palpable bladder, flaccid paraplegia of the lower extremities with abolition of sensitivity and osteotendinous reflexes. An abdominopelvic computed tomography (CT) scan identified expansive bone lesions at the lumbar spine with invasion of the spinal channel as well as a lesion in the left kidney suggestive of malignancy. Lung, pleural and bone metastasis were suspected on thoracic CT. In the absence of neurosurgical criteria, the patient underwent on palliative radiation of the dorsolumbar spine and supportive medical therapy. In order to clarify the diagnosis, a bone biopsy of the left femur was performed, guided by CT scan. At the 8th day of hospitalization, the patient presented severe clinical worsening culminating in his sudden death. The histological results obtained post mortem revealed the diagnosis of RCC of sarcomatoid subtype.

**Discussion:** This case demonstrates the importance of recognizing early symptoms and the need of a high index of suspicion in order to timely diagnose an aggressive and potentially fatal disease.

## Mantle cell lymphoma: unexpected developments

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**Introduction:** Mantle cell lymphoma account for 7-9% of all non-Hodgkin lymphomas in Europe. Although considered an indolent lymphoma, it may behave as an aggressive disease. The survival rate of these patients is approximately 4 years. Complete remission rates of 20-40% can be achieved with combination chemotherapy, however long-term remission or cure are unlikely. The disease-free survival might reach 18-44 months. Therefore this disease is known for a sequential path between remission and frequent relapses.

**Case report:** We report the case of a 67 years old male patient, who at age 55 was diagnosed of mantle cell lymphoma (non-Hodgkin's lymphoma, lymphoma type B with phenotype CD20 and L26+) after having been hospitalized for weight loss and anorexia of 12 month's evolution, and hepatosplenomegaly. After the diagnosis, splenectomy was performed and followed by 6 cycles of chemotherapy with cyclophosphamide, vincristine and prednisolone, with good clinical, analytical and histological response. The patient has remained in surveillance and with an expectant clinical conduct, with no recurrence ever since.

**Discussion:** It is considered that the mantle cell lymphoma may present a variable evolution, and some cases may have a slow evolution, according to various prognostic factors. This case is representative of those situations in which, upon surgical and medical therapy, the patient has remained in remission throughout the 17 years of evolution.

## Refractory hypokalemia and toxic epidermal necrolysis: a case report of adrenocortical carcinoma

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**Introduction:** Adrenocortical carcinomas (AC) are uncommon malignancies and the majority of cases are metastatic at the time of diagnosis. Hormonally active variants of AC constitute approximately 60% of the cases, 30-40% of which present with Cushing syndrome, while 20-30% present with virilization signs. We present a case of adrenocortical carcinoma presenting with severe hypokalemia and toxic epidermal necrolysis.

**Case report:** A 54 years old woman with a history of diabetes mellitus and adrenal mass histologically benign with 3 cm, diagnosed 5 years ago. She underwent resection of the suprarenal, with further surgery 2 years later for pancreatic fistula which revealed recurrence of the mass, histologically correspondent with macronodular hyperplasia. She had several admissions for refractory hypokalemia. This time she was admitted to the emergency department with profound weakness, hirsutism and ileus with 2 week's duration. One month prior to presentation, she had noticed diminished appetite and weight loss. Physical examination revealed round face, buffalo-hump fat distribution and bullous skin lesions in the chest abdomen and limbs that were histologically compatible with toxic epidermal necrolysis. Biochemical parameters revealed hypokalemia (potassium levels 2 meq/l) and normal renal function. Estradiol, T3, T4, TSH, FSH and 24 h urinary metanephrine were within normal limits. Testosterone and serum cortisol were elevated. Contrast-enhanced computed tomography of the abdomen and pelvis showed a new adrenal mass (53x44 mm diameter) and hepatic lesions suggestive of metastatic nodules with 30 mm. A positron emission tomography scan and magnetic resonance imaging revealed right femoral lesions compatible with bone metastasis. She was submitted to adrenalectomy along with splenectomy and nephrectomy. Immunohistochemistry was consistent with primary AC.

**Discussion:** Only 1 in 1500 incidentalomas represent malignancies. This case reflects that close monitoring and early detection of tumors is crucial for curative resection and even with total resection, recurrence may occur 10 years after surgery. Cushing syndrome, autonomous adrenocortical hormonal production and cutaneous paraneoplastic syndromes warn further search for recurrence.

## ST-segment elevation: not always acute coronary syndrome

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**Introduction:** The electrocardiogram (ECG) is one of the most commonly used medical tests and is essential in evaluating any chest pain; however it can also be misleading sometimes. Not all ST-segment elevations are caused by coronary syndromes,

many other conditions, such as normal variants, left bundle-branch block, pericarditis, hyperkalemia or pulmonary embolism can mimic this ECG pattern.

**Case report:** A 79 years old woman with a history of undifferentiated big cell lung cancer with 8 years of evolution and in palliative care sought medical attention because of a 3 day progressive shortness of breath and dorsal right pain. On examination, the patient was alert and fully oriented. The temperature was 36.7°C, the blood pressure 111/84 mmHg, the pulse 155 beats per minute and the oxygen saturation was 94% while the patient was breathing ambient air. In the cardiopulmonary auscultation the first and second heart sounds were diminished with no murmur, respiratory sounds were symmetrical and basal crackles were identified. Blood biochemistry was normal except for a slight elevation of the cardiac lesion markers. ECG revealed a supraventricular tachycardia with a marked ST-segment elevation in leads I, II, aVL and V5-V6 in the absence of a Q wave. Reciprocal change of the ST depression was also noted at leads III, aVR and V1-V3. The hemodynamic laboratory was contacted to schedule an emergency cardiac catheterization. In the meantime, a transthoracic echocardiography was performed, revealing a mass localized in the lateral and inferolateral walls with a maximum thickness of 25 mm, as well as a generalized akinesia of the remaining walls and a depressed ventricular function. These findings were confirmed through chest computed tomography, as well as the presence of a small pericardium effusion and the destruction of the right rib cage. The patient stayed under careful observation for 24 hours in which no cardiac enzymatic rise was documented. After that, she was admitted to the infirmary for symptomatic relieve and a cardiac magnetic resonance imaging was ordered to better delineate the mass and define a treatment approach. The ST-segment remained elevated through the entire admission. The patient's clinical condition gradually deteriorated due to the disease's natural evolution and she passed away 2 weeks after.

## New method for biomarkers determination using a mass spectrometry-based electronic nose in saliva samples of patients with cancer

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**Objective:** We propose a rapid, simple and sensitive method based on a headspace sampler (HS), a programmed temperature vaporizer (PTV) and a mass spectrometer (MS) that could be applied to a huge number of patients with good precision and accuracy for the detection of cancer biomarkers in saliva samples.

**Material and Methods:** Unstimulated saliva samples were obtained from healthy volunteers and patients. The method used (HS-PTV/MS) has the advantage of being a non separative technique which it is faster than the gas chromatography (GC)-based standard method (HS-PTV-GC/MS). All the samples in

which the biomarkers were found with the screening method were analyzed by GC for confirmatory purposes. Eight biomarkers mainly related to lung cancer (benzene, 3-methyl-1-butanol, toluene, styrene, o-xylene, propylbenzene, 1,2,4-trimethylbenzene and 2-ethyl-1-hexanol) were selected to check the applicability of the proposed methodology. Patients with cancer were defined by pathological analysis of primary or metastatic lesion.

**Results:** 30 samples: 18 from healthy volunteers and 12 from patients with different types of pathologies were analyzed. None of the biomarkers studied were detected in the samples corresponding to the healthy volunteers. Among the patients with different diseases, 2-ethyl-1-hexanol was found in the saliva samples corresponding to 4 patients (1 with lung cancer, 1 with breast cancer and 2 with non-oncology gastrointestinal diseases) and 3-methyl-1-butanol was found in the saliva sample corresponding to 1 patient with lung cancer. The results obtained were in agreement with those of the pathological diagnoses in all cases except in 2 patients (those with non-oncology gastrointestinal diseases). All the samples in which biomarkers were found with the screening method were analyzed by GC for confirmatory purpose providing the same results.

**Conclusions:** The proposed methodology, with headspace sampling, does not required prior sample treatment, which reduces the errors associated with this step of the analysis. In addition, the method is fast, has good precision, accuracy and sensitivity, and in view of the results it could be considered as a suitable first option for determining volatile biomarkers in a large number of patients. After screening, GC/MS could be only used for positive samples for confirmatory purposes. The limitation of the study fall on small number of cancer patient samples measured. Nowadays we are working in a large study to enhance cancer disease patients' branch and in the next future new results about the specificity of these biomarkers will be provided.

## Bone lytic lesions: what's it all about?

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**Introduction:** Lytic bone lesions are usually a diagnostic challenge. Multiple myeloma and metastatic carcinoma should always be considered.

**Case report:** An obese 50 year-old woman, with history of hormonal fertility treatments 10 years before, presented cervical and lumbar mechanical pain that was partially controlled with analgesics and muscle relaxants in the first 4 months. Later, pain got more intense and extended to the left thigh and chest. She had already performed several ancillary exams. Magnetic resonance imaging (MRI) showed multiple lumbar and sacral spine lesions, as well as iliac lesions, with signs of Th12 vertebrae pathologic fracture, but no cord compression. Chest, abdominal and pelvic computed tomography (CT) scan revealed pathologic fractures in the 2nd and 3rd right chest arches and multiple axillary and mediastinal adenopathies; liver and spleen were slightly increased; no pulmonary lesions were

present. Cranial CT scan had multiple skull lytic lesions, mainly in the right parietal bone. PET scan revealed foci of increased FDG uptake throughout the axial and appendicular skeleton, as well as in multiple cervical and axillary lymph nodes and in the internal quadrants of the right breast. When she presented to our medical attention she was sudoretic and in pain. She had no fever and vital signs were normal. A non-tender retroareolar mass of undefined margins was palpable on the right breast. She had normochromic and normocytic anemia (hemoglobin 11.4 g/dL), leukocytes and platelets were normal. Erythrocyte sedimentation rate was increased (84 mm/h). Thyroid function, renal function and liver panel were normal, including alkaline phosphatase. She had hypercalcemia (Ca<sup>2+</sup> 1.68 mmol/L), hyperuricemia (9.9 mg/dL) and increased total plasma proteins (89 g/L). Protein electrophoresis revealed a non-monoclonal component, with 3230 mg/dL IgG1. Serum κ/λ ratio was increased (3.42). Urine had no light chains and serum and urine immunofixation detected no monoclonal protein. Breast ultrasound showed hyperechoic retroareolar mass of 3.9 cm maximum size. Breast and axillary lymph node biopsies confirmed invasive breast carcinoma of no special type: ER/PR+ (100%/40%), HER2-. Primary chemotherapy was programmed.

**Discussion:** The diagnostic approach of bone lesions is complex. Even when a malignant neoplasia is found elsewhere, doubts can persist concerning the true nature of the bone lesions.

## And it keeps on coming back: recurrence of hepatocellular carcinoma after liver transplant

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**Introduction:** Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and occurs predominantly in patients with underlying chronic liver disease and cirrhosis. Its pathophysiology is clearly multifactorial and some of the risk factors include HBV or HBC infection and alcohol consumption, among others. The treatment of HCC covers for more than one strategy and includes nonsurgical and surgical therapies. HCC recurs in 50-80% of patients following resection, the majority of which occurs within 2 years. Among patients undergoing liver transplantation, the rate of recurrence is dependent upon the characteristics of the tumor in the explanted liver. The majority of these recurrences occur within 14 months after transplantation.

**Case report:** 68 years old man with a medical history of HCV (hepatitis C virus) and HBV (hepatitis B virus) infection and pulmonary tuberculosis submitted to a sequential liver transplant for a HCC. The explant revealed HCC, confirmed histologically. After 11 years the patient is re-transplanted for paramyloidosis. After 24 month follow up the CT scanning reveals a "transplanted liver with normal dimensions, with altered margins due to a tumor mass with 7x5,5 cm, matching a local relapse" and a body positron emission tomography (PET) tracing a hepatic lesion related with primary neoplasm. A liver biopsy was proceed leading to a carcinoma "de novo" diagnosis. One year later a liver biopsy is repeated diagnosing a poorly differentiated carcinoma, concluding a recurrent HCC on an second liver

transplant. Given patient age and medical complications, the patient was no longer candidate for a third liver transplant. It was performed an imaging and symptomatic care follow up. The actual medical status stands only for palliative care.

**Discussion:** There is no established management proven to be beneficial for treatment of HCC recurrence after liver transplantation. More important, the necessity of immunosuppression to prevent allograft rejection makes many medical professionals hesitate to administer systemic chemotherapy. Currently, the most realistic approach in prolonging survival after resection of HCC is early detection and aggressive management of recurrence by a "all eyes on patient" protocol.

## Body mass index may predict the long-term outcomes of advanced gastric cancer

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**Objectives:** Radical gastrectomy followed by adjuvant chemotherapy for advanced gastric cancer brings about serious nutritional impairment. Recent studies have shown an association between body mass index (BMI) and perioperative outcomes of gastric cancer. However, little is known about the association between BMI and long-term outcomes of advanced gastric cancer. Our study evaluated the clinical impact of BMI on the long-term outcomes of gastric cancer staged at II and III, treated by radical gastrectomy followed by adjuvant chemotherapy.

**Methods:** We analyzed a total of 211 cases of advanced gastric cancer stage II and III between January 2005 and December 2010 at Chung-Ang University Hospital. The patients were divided into 4 groups according to BMI; underweight, normal, overweight, and obese. In addition, they were divided into two groups (BMI-High vs BMI-Low). We assessed age, sex, tumor location, lymph node involvement, operation method, initial cancer stage, recurrence, and survival (overall survival and disease free survival) between two groups.

**Results:** There was no difference in overall survival between normal, overweight, and obese group. However, there was significant difference between underweight group and the other groups. As for disease free survival, similar findings were observed. Among 211 patients, 154 patients (72.9%) were included in BMI-L (body mass index <25), whereas 57 patients (27.1%) in BMI-H (body mass index ≥25). There was no difference in age, sex, tumor location, stage, lymph node involvement, operation method, recurrence, and cancer-related death between two groups. When classified into 4 groups as stage II in BMI-H, stage II in BMI-L, stage III in BMI-H, and stage III in BMI-L, overall survival showed significant difference in stage, however, no difference between BMI-H and BMI-L. Disease free survival showed no significant difference in stage and BMI, especially, no significant difference between stage II in BMI-L and stage III in BMI-H.

**Conclusion:** Our findings suggest that preoperative BMI may predict the long term outcomes of advanced gastric cancer after radical surgery and chemotherapy.

## Ewing's sarcoma in a department of internal medicine

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**Introduction:** Ewing's sarcoma is an aggressive malignant tumor and the second most common primary bone cancer of childhood. Primary bone tumors are exceptionally rare and account for 0.2% of all malignant tumors. Ewing's sarcoma accounts for approximately 10% of malignant bone neoplasms. It can affect all bones, but it has predilection for the trunk and long bones. Ewing's sarcoma that affects the skull accounts for only 1 to 6% of total cases. We report a case of a 17 years old patient with metastatic Ewing sarcoma.

**Case report:** A 17 years old boy presented with one-month history of fever up to 39°C, sore throat, frontal headache, low back pain and lower chest pain. His general practitioner had prescribed amoxicillin, without improvement, thus he was referred to our department. He owned a dog and he reported ingestion of unpasteurized dairy products. Physical examination revealed palpable liver and tenderness of the lower left ribs. Blood studies revealed anemia, elevated serum LDH, erythrocyte sedimentation rate and C-reactive protein levels. After excluding infectious and autoimmune diseases, a computed tomography scan was performed and revealed osteolytic lesions of the ilium and spine. Bone scintigraphy 99m Tc-MDP demonstrated multiple focal lesions of increased radionuclide uptake in the skull, sternum, ribs, spine, ilium and sacroiliac joints. The patient underwent bone marrow aspirate and biopsy. The histopathological examination showed small blue round cell tumor and immunohistochemistry for CD99 marker was positive, findings consistent with Ewing/PNET (primitive neuroectodermal tumor) sarcoma. The patient was referred to a pediatric oncologist unit for further treatment.

**Discussion:** Ewing's sarcoma is a malignant, small, round cell tumor arising from bone and primarily affects children and adolescents. Most cases (85%) are the result of a translocation between chromosomes 11 and 22. Clinically it presents as localized pain and a palpable mass. Systemic manifestations include fever, fatigue and weight loss. Diagnosis requires a histomorphologic, immunohistochemical, cytogenetic and molecular examination. Patients hospitalized in internal medicine departments are mainly adults and primary bone malignancies are extremely rare among them. Neoplastic bone involvement in adults is usually due to hematologic or solid organ malignancies. Clinicians should maintain high suspicion for primary bone tumors when evaluating adolescent patients.

## Lung cancer simulating pulmonary tuberculosis

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**Introduction:** Through the description of a clinical case, the authors intend to review the differential diagnoses in the presence of cavitary lung disease.

**Case report:** Male, 67 years. Former smoker. He presented to the family doctor with a 3-month history of cough, blood-tinged sputum, weight loss (8 kg), anorexia and excessive sweating night. He has felt febrile at times during the previous days but has not measured his temperature. He denied history of pulmonary tuberculosis (TB) or TB exposure. The chest X-ray showed cavitary lesion in the right upper lobe (RUL) and positive acid fast bacteria (AFB) smear (4 bacilli/40 fields). The patient initiated treatment with isoniazid, rifampicin, ethambutol and pyrazinamide while awaiting culture results for drug susceptibility testing. He was re-evaluated after 1 month. He presented persistent symptoms and the three sputum cultures were negative for growth of Mycobacteria, so he was referred to the pulmonology consult to study eventual cancer. Bronchoscopy showed inflammatory signs at the level of the anterior segment of the right superior lobar bronchus with acid fast bacteria (AFB) smear and polymerase chain reaction negative for mycobacterium tuberculosis in bronchial aspirate and negative cytology for malignancy. Transthoracic needle biopsy (TTNB) was negative for acid fast bacteria (AFB) smear. Scheduled appointment to review and determine the histological and cultural results. The patient kept antibiatic therapy. For worsening symptoms, he presented to the emergency department. Laboratory results revealed increased inflammatory parameters and type I respiratory failure. Chest X-ray showed overlapping cavitated lesion in RUL. He was hospitalized. Started antibiotic treatment with clindamycin and ceftriaxone, but with persistence of symptoms and imaging worsening. Collected blood cultures (negative) and changed antibiotic to piperacillin-tazobactam, improving clinical, analytical and imaging. TTNB histological results consistent with squamous cell carcinoma (SCC). It was requested complementary tests for cancer staging. Outstanding cultural were negative for Mycobacteria. It was suspended antituberculosis drugs.

**Discussion:** It is described in the literature the presence of false positive smear in patients with SCC. The authors intend attention to this possibility, which can delay the diagnosis and treatment of lung cancer.

## Belaboring the obvious? Hypercalcemia due to primary hyperparathyroidism in cancer patients

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**Objectives:** Hypercalcemia of malignancy is a well-known entity, usually diagnosed when high levels of calcium are detected in routine biochemistry results and are attributed to either lytic cancer lesions or to paraneoplastic phenomenon. In the general population, hypercalcemia work-up would include measurement of parathyroid hormone (PTH) and a broad differential diagnosis. In cancer patients, usually an empiric treatment with bisphosphonates is given without any further work-up. We present five cases of hypercalcemia in cancer patients due to parathyroid adenomas.

**Methods:** We performed a retrospective chart review of 5 cases of cancer patients with parathyroid adenomas. The

diagnosis of hypercalcemia was based on albumin-adjusted total serum calcium concentrations and the diagnosis of primary hyperparathyroidism and parathyroid adenoma was based on parathyroid hormone levels, sestamibi scan and ultrasound of the thyroid and parathyroid glands. PTH, 25-hydroxy-vitamin D, phosphorus, alkaline phosphatase levels were also measured. Urinary calcium levels were measured in two patients. DEXA scan was obtained in four patients. This study was performed in accordance with the policies and procedures of the Hygeia Hospital. Informed consent was obtained from the patients.

**Results:** Records of 2 male and 3 female patients were reviewed. Patients' mean age was 70.8 years old. 2 patients have breast cancer, 1 has renal cell carcinoma, and 2 have more than one cancer, specifically prostate cancer and melanoma and prostate cancer and renal cell carcinoma, respectively. Initial mean calcium level was 10.9 mg/dL (8.5-10.1), mean PTH level 192.2 pg/dL (14-72), mean 25-OH-vitamin D levels 25 ng/dL (30-80), mean phosphorus level 3.05 mg/dL (2.5-4.9), mean ALP is 88.8 U/L (46-116). 1 patient had bone metastatic disease at the time of the primary hyperparathyroidism diagnosis. 3 patients had osteopenia according to the DEXA scan and one had osteoporosis. Urinary calcium in 2 patients was 209 and 250 ng/dL respectively (50-250). As part of the treatment 1 patient underwent parathyroidectomy. One patient received cinacalcet daily and all patients receive vitamin D and calcium supplementation.

**Conclusions:** Hypercalcemia in cancer patients is not always due to the malignancy, especially when very persistent and relatively mild. A full work-up should be done in cancer patients as meticulously as in the general population.

## Carcinoid syndrome and occult neoplasm: a case report

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**Introduction:** Most causes of acute diarrhea are infectious in origin. Still, in rare cases, there is a different underlying condition that should warrant prompt investigation. One of those cases is carcinoid syndrome, a very rare entity that may be the first presentation of an occult neuroendocrine tumor (NET).

**Case report:** An 81 years old female presenting with profuse diarrhea and a maculopapular rash with a 2 day evolution. Known asthma, medicated with tiotropium bromide and a leukotriene inhibitor, without recent crisis. At admission she was dehydrated and in severe shock, with need for aminergic support, had bronchospasm and crackles on the right hemithorax, non-tender abdomen without palpable masses, and a generalized rash. From the study: creatinine 3.15 mg/dL, Na 127 mmol/l, K 3.9 mmol/l, Cl 93 mmol/l, leukocytes 12x10<sup>9</sup>/l, C-reactive protein 6.96 mg/dL and ESR 27 mm/h. Arterial blood gases showed metabolic acidosis. Assumed to be in septic shock due to acute gastroenteritis and started on ciprofloxacin, changed to piperacillin/tazobactam and metronidazole due to lack of response. Further study discarded infectious origin, since blood and urine cultures and search for parasites, *Clostridium difficile*

and leukocytes on stool were all negative. The persistency of diarrhea, in addition to rash and bronchospasm raised suspicion on a carcinoid syndrome, supported by high chromogranin A (15 (<6)), urinary serotonin + 5-hydroxytryptophan (43.7 (<8.0)) and serum 5-HIAA (6.24 (<6)). Imaging studies couldn't identify metastasis or primary origin. Despite support therapy with fluid and electrolytes, this patient deteriorated rapidly, and its clinical condition didn't allow undergoing further study. She died 2 weeks after the beginning of the diarrhea. The family refused an autopsy.

**Discussion:** NET of unknown primary origin and carcinoid syndrome are both highly aggressive. In the first, the median survival without treatment is 11 weeks. In the latter, failure to manage the fluid and electrolyte imbalance and to identify a primary origin are both associated with severe morbidity and mortality. One should be highly aware and promptly recognize these two entities, since the adequate management can, eventually, improve survival and quality of life of these patients.

## Protective effects of curcumin and amifostine against gamma radiation-induced gastric mucosal damage: a light and electron microscopic study

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**Objectives:** Although gamma radiation is known to have metabolic and structural effects on various systems, studies done to determine its effects on stomach are limited. There is limited information on the pathogenesis of the effects of radiation on stomach; however in the previous studies it was found that oxidative stress has a role on this effect. Antioxidant elements are claimed to have positive effects against radiation damage.

**Methods:** In this study, which was done on rats; it was aimed to examine the possible protective effects of curcumin and amifostine against damages formed on the stomach mucosa caused by gamma radiation at different doses, at light and electron microscopic levels. The rats were divided into 5 groups, one which was the control, one of which was the sham, and 3 of which were the experimental groups. All the rats except for the control and the sham group were exposed to 15 Gy of gamma rays on their abdominal areas. In order to prevent radiation damage, the IVth experimental group was given 100 mg/kg of curcumin dissolved in dimethylsulfoxide via intragastric way starting 10 days before the radiation until sacrifice; the Vth experimental group was given 200 mg/kg of amifostine i.v. 30 minutes before the radiation. Stomach biopsy materials taken from all subjects under anesthesia on the 4th day after radiation were prepared for light and electron microscopic examinations.

**Results:** It was observed in our study that 15 Gy of gamma radiation caused damage on the stomach mucosa and it caused misformation and mislocation of the stomach mucosal cells. Ulcerative areas were observed to be formed on the mucosa

because of the loss in the epital cells of the surface layer. Especially the loss in the flat tubular stomach glands on the mucous neck cells was observed to be serious. At the electron microscopic level, it was determined that there were damages on the secretion granules, microvilluses and nucleuses of the cells, and erasements on the cristas of the mitochondrias, and also dilatations occurred particularly on the granular endoplasmic reticulum cisterns.

**Conclusions:** Amifostine, which was the only radioprotective agent used in clinic was observed to provide an efficient protection in preventing the damage on the stomach mucosa caused by high gamma radiation. On the other hand, curcumin was determined to partly prevent the mucosal damage. As a result; antioxidant elements were considered to have positive effects in protection of the normal tissues during radiotherapy.

### **Against cisplatin-induced rat testes tissue damage, the protective effects of amifostine, curcumin and cafeic acid phenethyl ester levels of light and electron microscopic examination**

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**Objectives:** Cisplatin is an effective antineoplastic agents commonly used in the treatment of many types of cancers. One of the most important side effects of in use cisplatin on testis tissue damage is indicated as the cause of infertility. By increasing the formation of oxygen free radicals that of cisplatin in testicular tissue has been reported to cause damage through oxidative stress. Based on this basic idea of study known as the antioxidant properties of oxidative stress caused by the use of cisplatin in rats.

**Methods:** In our study, the control rats, Cis, Cis + Amp, Cis + Cur, Cis + CAPE were divided into 5 groups (n = 6). No application was made outside of the control group. In our study, a single dose of cisplatin group ip way 5 mg / kg will be cisplatin. Starting 24 hours before the cisplatin injection Cisplatin + Amf group, for 7 days after intraperitoneal injection of cisplatin injection of amifostine apply. Cis+Cur, starting 24 hours before the cisplatin injection curcumin set up to cut after the cisplatin injection orally for 7 days, curcumin (sigma), DMSO dissolving, intragastric of the road. Cis + CAPE group was started 24 hours before cisplatin intraperitoneal injection of CAPE 10 µmol/kg/day, was administered for 7 days up to cut.

**Results:** The cisplatin study spermatogonia in the seminiferous tubules of the germinal epithelium in other non-germ line cells, Sertoli cells and leads to damage to the connective tissue; we show cell damage in the NF-kB/p65, we found that t by Caspase-3 and 8-OHdG to increase the cytoplasmic expression. However, the all protective agents in, we found that the expression of NF-kB/p65, Caspase-3 and 8-OHdG

especially amifostine reduced maximum decrease in the group.

**Conclusions:** Leydig cells in the germinal epithelium and the damage caused by cisplatin, amifostine prevents curcumin and CAPE. However only amifostine protects the integrity of the membrane of the seminiferous tubule epithelial cells.

### **Thrombotic thrombocytopenic purpura related to occult disseminated malignancy**

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**Introduction:** Thrombotic thrombocytopenic purpura (TTP) is a rare entity, and it may be idiopathic or associated with many entities, including cancer. It was originally characterized by the pentad thrombocytopenia, microangiopathic hemolytic anemia (MAHA), fever and neurological and renal disorders, but in the current diagnosis criteria, in the presence of thrombocytopenia and MAHA the diagnosis should be considered.

**Case report:** The authors describe a case of a 61 years old man, with previous history of mesangioproliferative glomerulonephritis, who went to the emergency department with a persistent lumbar pain with a month of evolution, associated to nocturnal sweating, weight loss of 4kg and dyspepsia. He was treated with proton pump inhibitors and an antibiotic to urinary tract infection. No changes in laboratory exams and ultrasound. He realized an abdominal computed tomography that showed multiple retroperitoneal lymph nodes suggesting metastatic cancer and two nodular lesions in the right adrenal gland. He performed upper and lower endoscopy, immunological study and prostatic, scrotal and pelvic ultrasound, with no changes; an adrenal magnetic resonance scan and laboratory exam which excluded pheochromocytoma and concluded that it was a non-functioning adrenal incidentaloma. A retroperitoneal lymph node CT-guided biopsy was performed too. The patient remained hemodynamically and analytically stable, only with complaints of lumbar pain. The laboratory blood count at day 15 in hospital revealed a little decrease in hemoglobin and platelets, with no visible blood loss. Later, the patient started with mental and behavioral changes, with sudden drop in hemoglobin and platelets, laboratory changes consistent with hemolysis and schistocytes in peripheral blood smear. For the suspicion of TTP the patient was transferred to intermediate care unit and started plasmapheresis and steroids. Histology of retroperitoneal lymph node revealed undifferentiated carcinoma of unknown primary. Given the clinical severity in a patient with TTP related to cancer, we decided to start palliative chemotherapy. The patient had an unfavorable evolution, without answer to treatment, and died.

**Discussion:** TTP is an entity difficult to diagnose, a medical emergency with poor prognosis. In TTP related to cancer, the treatment involves treating the underlying malignancy and plasmapheresis doesn't have benefit. Without treatment, TTP has a mortality rate reaching 90%.



## Simultaneous presentation of tuberculosis and diffuse large B-cell lymphoma in an immunocompetent patient

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**Introduction:** The number of patients with tuberculosis and cancer has increased in recent years. There is an increased risk of tuberculosis in patients with cancer, or by immunosuppressive treatments, either by immune dysfunction caused by cancer.

**Case report:** The authors present a case of an 83 years old woman, non-HIV, without diseases, who went to the emergency department with asthenia, anorexia with half a year of evolution and progressive dyspnea. A large left sided pleural effusion was documented, not present in a previous X-ray in the same year. The study showed: pleural effusion was an exudates, with increased adenosine deaminase (ADA) (91 U/L) and negative cytology for malignant cells; pleural biopsy with reactive inflammation without malignancy and chest computed tomography (CT) with two suspected nodules, whose histology revealed granulomatous process, negative to malignant cells. Noteworthy, bacteriological, micobacteriological and Mycobacterium tuberculosis PCR were persistently negative in pleural fluid, bronchoalveolar lavage and pulmonary nodules. The pleural fluid immunophenotyping revealed monoclonal B lymphocytes gammopathy. The case was discussed in a multidisciplinary meeting: for the presence of granulomas on biopsy, increased ADA in pleural effusion and immunophenotyping with atypical lymphocytosis, which excluded most of lymphomas; the patient was oriented to Hematology consultation for further study and started treatment for tuberculosis. Because of the general health deterioration, new hospitalization was decided for diagnostic review. She performed cervical, thoracic, abdominal and pelvic CT that showed new multiple adenopathies. Thus, we performed cervical lymph node biopsy, which immunophenotyping was compatible with lymphoma, with monoclonal population of large cells (91%), CD5+, CD20+, IgM phenotype and histology diagnosed diffuse large B-cell lymphoma. Tuberculosis and lymphoma were two different diagnoses and as granuloma decreased in size with treatment for tuberculosis, in a new multidisciplinary meeting we decided to maintain this treatment and started treatment with cyclophosphamide and prednisolone. The patient continues in consultation with frank improvement of her general status.

**Discussion:** Pleural effusion secondary to tuberculosis and lymphoma are two entities with similar clinical, laboratory and radiological characteristics, making the diagnosis a challenge. Thus, the clinicians need to be aware in the presence of tuberculosis with atypical features, which can be overlapping with a malignancy.

## A case of acute lymphoblastic leukemia presented with pathologic fractures

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**Introduction:** Acute lymphoblastic leukemia (ALL) occurs in both children and adults – its incidence peaking between 2 and 5 years of age – 60% of cases occur in younger than 20 years. It is multifactorial with exogenous, endogenous exposures and genetic susceptibility playing a role. Although ALL is primarily a disease of bone marrow (BM) and peripheral blood, any other organ may be infiltrated by leukemic cells. Different skeletal abnormalities have been described in this disease, including osteoporosis, periosteal reaction, reactive sclerosis, lytic defects and vertebral compression fractures. These mostly involve the spine, associated with osteoporosis, with occasional peripheral locations.

**Case report:** A 73 years old woman, suffering from back pain was referred to the hospital after documentation of spontaneous compressive fracture of D5 and D6. Also she reported anorexia, asthenia, pallor and loss of weight within the last 2 months. In physical examination were remarkable pain at the spinal articular joint and hepatomegaly. The value of hemoglobin was 9.8 g/dL, normocytic, normochromic and leukocytes 3.400 /uL, with normal formula. Protein electrophoresis, renal and hepatic function were normal, B2-microglobulin 2731 ng/ml and LDH 341 U/L. Chest and abdominal CT revealed homogeneous hepatomegaly and diverticulosis of the sigmoid. Bone mineral densitometry was normal. Bone scintigraphy showed fixation of D5, D6, D12, humeral head, hip joint and femoral proximal shaft, bilaterally. BM aspiration revealed hypercellularity, with immature cells infiltration. BM biopsy demonstrate diffuse infiltration of lymphoproliferative process, and immunophenotyping was CD45+, CD20+, CD3- and TdT +, showing B-cell ALL. Karyotyping revealed normal findings.

**Discussion:** ALL may cause alterations in bone metabolism and defective mineralization. Leukemic infiltration and expansion of the BM spaces leading to destruction of spongiosa, as well as the factors secreted by the leukemic cells such as osteoblast inhibiting factor and PTH-related peptide, might contribute to bone loss in ALL. Additionally, local hemorrhage and osteonecrosis of the adjacent bone give rise to osteolytic lesions. In conclusion, orthopedic conditions, including multiple bone fractures may be the first manifestation of acute leukemia and it is important for the physicians to recognize the skeletal manifestations of acute leukemia in adulthood.

## Cardiac epithelioid hemangioendothelioma: unusual clinical presentation mimicking a systemic vasculitis

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**Introduction:** Primary cardiac tumors, particularly atrial myxoma and less frequently cardiac hemangioendothelioma may be confused with systemic vasculitis. Therefore, even if rare, they should be considered in the differential diagnosis.

**Case report:** We describe a 74 years old woman admitted to our hospital for severe bone pain. 7 months earlier a preoperative chest X-ray for knee arthroplasty revealed a single lung nodule with malignant features. She underwent lobectomy and the histology showed perivascular infiltration by lymphomonocytic

cells resembling the aspects of a granulomatous disease with myointimal fibrosis. She was then referred to our department with the diagnosis of vasculitis, in particular granulomatosis with polyangiitis (formerly Wegener's disease). Physical examination revealed shoulder and hip girdle tenderness and a palpable breast lump, while blood tests showed inflammation. Radiological investigations confirmed a malignant mammary nodule and demonstrated multiple bone, subcutaneous and pulmonary lesions, some with vasculitis-like aspects, and an infiltrative necrotic lesion of the left ventricle wall (about 5 cm) with neoplastic features. The histological and immunohistochemical findings of the mammary nodule were suggestive for epithelioid hemangioendothelioma. Because of the characteristics of the metastatic nodules and, above all, the systemic spread of the disease, we finally concluded for a primitive cardiac hemangioendothelioma with multiple metastases and pulmonary pseudovasculitis. Anyway, in the present case we were able only to provide supportive medical care, because it was not possible to treat the tumor for the large extent of the disease at diagnosis.

**Discussion:** Hemangioendothelioma is one of the rarest primary cardiac tumors, with about 20 cases described. It represents an intermediate variant within the family of vascular tumors. Nonetheless, the frequent occurrence of systemic metastases leads to the conclusion that this tumor should be better managed as a fully malignant rather than borderline neoplasm. The prognosis is unpredictable but a life expectancy ranging from 1 to 20 years has been described. In most reports, patients with hemangioendothelioma have a favorable outcome after surgical radical resection, while chemotherapy and radiation therapy have limited effect. Recent data about the efficacy of pazopanib (tyrosin-kinases inhibitor) in metastatic disease appear promising.

## Hypercalcemia in a cancer patient – the importance of the diagnostic approach

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**Introduction:** Relatively common in cancer patients (20-30%), hypercalcemia is mainly caused by osteolytic metastasis with local release of cytokines, tumor secretion of parathyroid hormone-related protein and tumor production of 1,25-dihydroxyvitamin D. Moreover primary hyperparathyroidism is more common in oncologic patients.

**Case report:** We report a case of a 45 years old female referred to oncology consultation with a cT2N0 luminal B breast cancer, otherwise healthy, with a family history of a dead father (45 years old) with hypercalcemia stated in the context of a lung cancer. In the initial workup hypercalcemia was found, so the staging was completed with a bone scan that showed no osteoblastic metastasis. Chest CT showed no osteolytic metastasis, but found a lung nodule which was biopsied and diagnosed as a neuroendocrine tumor, T1N0. Parathyroid hormone was elevated and the ultrasound showed nodularity suggestive of

parathyroid adenomas, supporting the diagnosis of primary hyperparathyroidism. The patient was treated with: dose-dense neoadjuvant breast cancer chemotherapy followed by quadrantectomy and sentinel node biopsy, after which she started adjuvant hormone therapy and radiotherapy; atypical lung resection; and partial parathyroidectomy. Genetic counseling found no hereditary cancer syndrome. The patient is presently in follow up, with no evidence of recurrence.

**Discussion:** The correct approach to hypercalcemia in oncologic patients is of great importance. In this case it allowed not only an accurate breast cancer staging, but also the diagnosis and treatment of a second neoplasia and primary hyperparathyroidism.

## Clinical report: esophageal cancer. A silent enemy

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**Introduction:** Alert on physicians esophagus adenocarcinoma, even though is an uncommon neoplasm, is also extremely lethal by which we must familiarize more with this entity and diagnose it on early stages to be able to make an effective treatment.

**Case report:** Male patient, 69 years old, Caucasian, went to ER because a month of abdominal pain and weight loss. Medical background: smoking, prostatism. Physical examination: cachexia, dehydration, hepatomegaly, tenderness to abdominal touching. Chest X-ray: default fibrotic-interstitial. Blood tests: slight leukocytosis, slight increase of LDH and alkaline phosphatase. Tumor markers positive Ca125 683.8, Ca19.9 196.6, Ca72,4 >300, CEA 4890, AFP 8.9, CYFRA21.1 233.10. Upon the results of the analysis was requested chest TAC that revealed multiple adenopathies, pleural effusion, hepatomegaly with nodular images, esophagus wall thickening without cleavage within sub-carina. Therefore, it was decided to request an upper endoscopy that reveals: multiple lesions from 25 cm in Rosary's shape, longitudinal, around the entire circumference, easily bleeding and hypervascularized metastases, intraabdominal lymphadenopathies. Biopsy: adenocarcinoma T1N2M3. The patient had an unfavorable evolution due to the advanced stage of the disease when it was diagnosed. He accepted to be treated with QT but did not get a good response and then, given palliative treatment. Subsequently, he developed intra-hospital pneumonia and passed away.

**Discussion:** Esophagus adenocarcinoma is uncommon and silent during initial stages. Its diagnosis and treatment are usually performed too late to be treated effectively. That is why it is important to assess people with risk factors such as nutritional deficiencies associated with alcoholism and smoking or with clinic pattern of progressive dysphagia, odynophagia, retrosternal discomfort, epigastric pain, nausea and anorexia. We should suspect and call for evidence to detect the disease on early stages. It is also fundamental to have a multidisciplinary teamwork with the goal to reduce morbidity and mortality of this pathology increasingly frequent in society.

## Primitive neuroectodermal tumor in the spinal canal: a case report

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**Introduction:** Primitive neuroectodermal tumors (PNETs) are rare tumors of uncertain histogenesis, which concept has been controversial for over a decade, as diagnosis remains difficult and no effective treatment has been identified. PNETs are rapidly growing soft tissue masses, which cause symptoms of nerve compression and pain. The annual incidence of this condition is estimated to range from 0.2–0.4 cases per 100,000, and occur predominantly in children and young adults. PNETs have a high rate of relapse and poor prognosis. The 5-year survival rate is 30–40% and has not altered significantly over the last 30 years.

**Case report:** A healthy 48 years old man, presenting with a 2 month history of lower back pain, irradiating to the left leg and with increasingly need of analgesic medication. He also referred paresthesia and mild weakness in the left leg over the past 2 weeks. On physical examination, hypoesthesia, an abolished patellar reflex and a positive Lasegue sign (35°) was found in his left leg. He also had cervical lymphadenopathy. He performed a lumbar magnetic resonance which revealed tumor infiltration in L4-L5 with L4 roots compression, aspects suggestive of lymphoma. Laboratory tests showed no changes including complete blood count and lactate dehydrogenase. Computed tomography scan found multiple cervical, thoracic and abdominal lymphadenopathies, compatible with lymphoma. Bone marrow biopsy showed absence of neoplastic involvement. Histopathological examination of excised cervical node revealed large neoplastic cells with high mitotic indices and immunohistochemical CD99/Mic2 characteristic reactivity on the tumor cell membranes, suggestive of PNET.

**Discussion:** PNETs are highly malignant and invasive tumors that can occur in unusual locations. As this case shows, the clinical and imaging features of peripheral PNET are non-specific, making differential diagnosis often difficult and tissue diagnosis essential.

## Acute kidney injury by deposition of bilirubin in a patient with fulminant cholangiocarcinoma

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**Introduction:** Cholangiocarcinoma corresponds to 10–25% of hepatobiliary malignancies and 3% of all cancer deaths. Is more prevalent in men between 50–70 years and acute onset jaundice is a common presentation in 90% of cases. It can be extrahepatic (40%), perihilar (50%) or intrahepatic (10%). The major causes of death are liver failure and infectious complications.

**Case report:** A 69 years old male patient was admitted with a 4 days history of jaundice, pruritus and nausea and choluria, acholia and 15% of body weight loss in 3 months. On initial

observation the patient was icteric, afebrile, hypertensive and eupneic. The abdominal examination revealed hepatomegaly. The rest of the physical findings were unremarkable. Blood test revealed a total bilirubin of 11.5 mg/dL, alanine transaminase 298 U/L, aspartate transaminase 143 U/L, gamma glutamyl transpeptidase 789 UI/L and creatinine (Cr) 1.3 mg/dL. The computerized tomography documented multiple solid lesions in both hepatic lobes and adjacent to the hilum with concomitant dilation of the intrahepatic bile ducts and lymphadenopathies in the territory of the celiac trunk and paraaortic. In just 18 days it evolved to hyperbilirubinemia of 42 mg/dL and to renal failure (Cr 6.8 mg/dL). Biliary shunt prosthesis was placed in this context with no success. Liver biopsy showed a poorly differentiated adenocarcinoma and the exfoliative cytology of the bile ducts adenocarcinoma cells with high degree cytological atypia. The diagnosis of cholangiocarcinoma was assumed. The situation progressed to terminal kidney failure with anuria and the need for dialysis. The patient died 28 days after admission.

**Discussion:** This case reports a rapidly progressive cholangiocarcinoma with fatal acute kidney injury (AKI) probably in the context of tubular necrosis by deposition of bilirubin. There is growing evidence that the constituents of the bile do not play a direct nephrotoxic effect. However, retention of bile in cholestatic jaundice has deleterious effects on cardiovascular function and vascular volume. Thus, there is an increased susceptibility to pre-renal failure and acute tubular necrosis in post-intervention patients with obstructive jaundice. Severe AKI is a major factor for mortality in these patients.

## Sensibility and specificity of tumor markers in patients with unintentional weight loss, asthenia and anorexia

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**Objectives:** Unintentional weight loss associated or not to asthenia and anorexia (constitutional symptoms) are frequent at an internal medicine consult. The utility of tumor markers to diagnose is not well established. In this study we investigated the frequency of unintentional weight loss with or without constitutional symptoms, and the utility of tumor markers, especially CAE and CA 19.9, to diagnose colorectal cancer (CRC) and pancreas cancer (PC).

**Material and Methods:** Retrospective, cohort study of 234 patients studied in a internal medicine consult, with unintentional weight loss associated or not to asthenia and anorexia (constitutional symptoms) from 2008 to 2012 in a tertiary-care level teaching hospital in Spain, including only those whose physician suspected malignancy tumor and order TM as a diagnostic method.

**Results:** During the study period, 234 patients had unintentional weight loss and their physician suspected malignancy as a possible cause and ordered TM (CA 19.9 to 219 patients and CEA to 227 patients). 55% were males, 45% female. The median age was 74 years old (range 27–96). Cancer was found in 38% of the cohort (91 patients). PC represents 12% (11 patients) and CRC – 31% (28 patients). In our cohort, the sensibility of CA 19.9 for PC was 90% and specificity 78% (normal range 0–40 U/ml), but if we enlarge the range 2 times its normal value we can get more

specificity not losing that much sensibility, (normal range 0-80 U/ml) – sensibility 90%, specificity 88%. The sensibility of CEA for CRC is 68% and the specificity 69% (normal range 0-5 U/ml).

**Conclusions:** CEA is a TM that can be elevated in many neoplastic diseases as in non-neoplastic diseases and in our cohort is not a good marker in the moment of the diagnostic, but a necessary proof when the diagnosis is made. CA 19.9 is useful at the initial study of unintentional weight loss and can give us reliable information, although we don't recommend it as a screening test.

## Tumor markers – shall we use it in clinical practice?

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**Background:** Tumor markers are derived from neoplastic cells and have the ability to reflect their growth and activity. Currently its role is well defined, since it may be useful to monitoring patients with malignancies, but they are not useful for the diagnosis.

**Objective and methods:** To review the usefulness of tumor markers in clinical practice based on the guidelines released by experts in the theme.

**Results:** Only  $\beta$ -hcg and alpha feta protein are validated to make the diagnosis of cancer in specific cases, i.e. hepatocellular carcinoma and germ cells tumor. Both CA 19.9 and CEA are not useful for the diagnosis, but they are extremely useful in the follow up of patients with pancreatic and colon/rectum neoplasms, especially for patients with high values pre-operatively. The role of CA125 for the diagnosis of ovarian cancer is not yet fully defined, it is very important in the follow up patients and it can be very useful when read in conjunction with gynecological ultrasound. For breast cancer, CA 15.3 and CA 27-29 are helpful in monitoring early recurrences and during the follow up of advanced disease. The same could be admitted for NSE and CYFRA 21 in cancer of the lung. Finally, the most widely used in clinical practice is PSA, which is specific to the prostate but is not synonymous of malignancy. The major indication for prescription is the determination in prostate cancer patients after treatment and to prevent one death due this type of cancer, 140 patients would be required to track and from those we would need to treat 48.

**Conclusions:** The authors pretend to emphasis that tumor markers alone have no value in the diagnostic and can not replace histological examination of the primary tumor. There are several benign medical conditions which may simulate false positives, so its main function is related to the follow up.

## A metastatic lung cancer case diagnosed due to postoperative hyponatremia

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**Introduction:** We here present a small cell lung cancer (SCLC) case diagnosed with inappropriate anti-diuretic hormone

secretion syndrome (SIADH) triggered with a hernia repair operation.

**Case report:** A 64-year-old male patient was admitted to our hospital for diaphragmatic hernia repair. Perioperative laboratory values were within normal limits (Na 142 mEq/l). Serum Na levels dropped to 124 mEq/l on the postoperative 2nd day. The physical examination was unremarkable; without nausea, vomiting, polyuria and polydipsia. Renal and liver insufficiency, congestive heart failure, volume depletion, diuretic use, hypoadrenalism, and hypothyroidism were not detected. Patients' fluid therapy and medications were controlled. Treatment of metamizole 4x1 IM was stopped. Because IV contrast was used during the preoperative tests performed, 2000 ml 0.9% NaCl and 1500 ml/day 0.45% NaCl with 5% dextrose were administered after the surgery. Hydration with 1500 cc/day with 0.9% NaCl according fluid balance was suggested. Patients' hyponatremia (hNa) during follow-up did not respond to 0.9% NaCl. In the 6th day to 110 mEq/l, 3% NaCl was initiated. In the hemodynamically stable patient, severe hNa findings including mental changes, headache, nausea and vomiting were not observed. Serum Na raised following the addition of 3% NaCl to the treatment. Following the interruption of 3% NaCl, hNa was re-observed (Na125 mEq/l). Further reasons to explain this clinic were investigated. Urinary analysis revealed hematuria, ketosis and mild proteinuria. Acute interstitial nephritis secondary to contrast and metamizole was thought as differential diagnosis. Increased IgA, creatinine and eosinophilia were not found. In our laboratory urinary N-acetyl- $\beta$ -glucosaminidase and  $\beta$ 2-microglobulin tests could not be evaluated. Fever, rash, acid-base imbalance, potassium abnormalities were not observed. USG revealed "normal renal parenchymal echogenicity and thickness with multiple metastatic lesions in the liver". Furthermore, hNa and serum hypoosmolality (235 mOsm/kg) were accompanied by increased urine osmolality (475 mOsm/kg). Patient was being examined for malignancy with the treatment of fluid restriction. Serum Na reached 137 mEq/l within a few days. Patient was diagnosed with metastatic SCLC and referred to oncology.

**Discussion:** Several causes can induce hNa in hospitalized patients for major surgical procedures. During the management of hNa, especially in treatment-resistant patients other reasons must also be revised.

## Carcinoma of unknown primary... always a difficult challenge

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**Introduction:** Carcinoma of unknown primary (CUP) is a rare disease in which malignant cells are found in the body but the place where the cancer began is unknown. Data for the European countries and the USA indicate that 2-7% of malignancy diagnoses are due to CUP, but it is believed that the prevalence of the disease is underestimated.

**Case report:** A 72 years man with benign prostatic hyperplasia, without other relevant medical background, was admitted at the hospital for fatigue and anorexia for 2 months. The patient remained clinically stable during hospitalization, but

keeping complaints of postprandial fullness and anorexia. A large analytical study was performed. Of relevance, there was anemia (Hb 10.5 g/dL), increased sedimentation rate, and increased expression of protein Ca 15.3 (1576 U/mL, with normal values below 32). Other tumor markers were within normal range. Endoscopy showed atrophic gastritis without dysplasia and the colonoscopy was normal. The chest, abdominal and pelvic tomography revealed a bulky mass adjacent to the gastric antrum with 8.5 cm in the axial plane, surrounding the vena cava and extending to the right paracardiac region; there was another lump in small gastric curvature with approximately 3.5 cm. Other masses were observed in the peritoneal cavity. It was decided to make positron emission tomography (PET) scan that showed uptake of the radiopharmaceutical in right paracardiac mass that extends to the abdomen and multiple dispersed nodes compatible with malignant pathology. Then, an ultrasound guided biopsy was performed and identified undifferentiated carcinoma impossible to distinguish between gastric or lung origin. The patient was oriented to Internal Medicine and Oncology consultation. He underwent several cycles of chemotherapy but the disease progressed unresponsive to treatment, getting palliative care and died one year later.

**Discussion:** CUP is represented by a heterogeneous group of diseases all of which have presented with metastasis as the primary manifestation and remains a major challenge for doctors and patients. Although only a minority of patients will have curable disease or a disease for which there is substantial palliative benefit, the appropriate use of special diagnostic pathology and selected radiologic studies will identify patients for whom directed therapy will provide the best possible chance for response.

## Pericardial and pleural effusion in an oncologic patient: a diagnostic challenge

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**Case report:** A 68 years old woman was admitted to medicine department for the etiologic study of a pleural and pericardial effusion. She had an history of breast cancer (pT2N1M0) submitted in 1995 to mastectomy, chemotherapy and radiotherapy, cardiovascular disease with an acute coronary syndrome in April 2014, heart failure (NYHA class II), dyslipidemia, arterial hypertension and thyroid nodular disease. One month before, she had already been admitted, for the same reason. The study was negative for malignancy and was discharged to cardiology consultation. Since then she was complaining of increasing dyspnea, edemas, persistent cough, asthenia and anorexia. She had a normal hemogram and renal function, BNP 475.5 pg/ml and a discrete elevation of hepatic markers. The pleural effusion was a sero-hematic, exudate. The echocardiogram showed a medium volume pericardial effusion (without tamponade), an ovoid echogenic mass (18x11 mm) in the parietal pericardium, pulmonary hypertension and LVEF in the inferior normal limit. Biopsy was negative for pleural malignant cells. CT-scan showed noduliform areas in the pericardium, mediastinal adenomegalies and captant milimetric nodularities in the liver.

At D5 of admission, she complained of increased dyspnoea and was admitted in the intermedial care unit where was done a diagnostic pericardiocentesis. Once again it presented a sero-hematic liquid, negative for malignant cells. At D20 of admission, she had a sudden cardiorespiratory arrest. The echocardiogram showed a large volume effusion, no signs of cardiac tamponade and no contractility of the left ventricle. It was done pericardiocentesis with drainage of 100 mL of hematic liquid, without hemodynamic recover and resuscitation maneuvers where suspended.

**Discussion:** This case shows the diagnostic difficulty in these patients, with a history of neoplasia. The differential diagnosis of pleural and pericardial exudative effusions includes malignancy (particularly lung and breast cancer, leukemia and lymphoma), but in 50% of the cases are not associated with an oncologic condition (infections, radiotherapy, drug-induced disease, hypothyroidism). Development of malignant pleural and pericardial effusions is associated with a very poor prognosis, with median survival of four months. Although all the results were negative, how can we be sure that a patient treated for cancer 20 years ago does not have a malignant effusion? How to manage the patient and family's expectations?

## Lytic bone lesions: an unfortunate and atypical first presentation of thyroid cancer

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**Introduction:** Lytic bone lesions or metastases are due to a large variety of primary tumors. Diagnosis is established by correlating clinical suspicion with imaging. When in presence of distant metastases from differentiated thyroid carcinoma, there may be severe reduction of the quality of life causing pain, fractures, spinal cord compression and the 10-year survival of patients decreases by 50%.

**Case report:** A 53-year-old woman was admitted to the ER with severe left arm pain. A meticulous physical inquiry revealed that the pain had started in the previous 2 months, but was, initially, easily controlled by applying local pressure and oral analgesia. Her general practitioner had solicited an arm X-ray, due to pain worsening, which bared "bone demineralization and a highlighted bulky image loss of bone density in the proximal/middle third of the (left) humerus, which seems to inflate the cortical component". An appropriate follow-up by Orthopedics was requested and, subsequently a whole-body CT scan, whole-body magnetic resonance imaging (MRI) as well as a skeletal scintigraphy were performed. CT scan was negative, but the MRI "identified on the left humerus shaft, a nodule, central and aggressive lesion", skeletal scintigraphy presented an "increased uptake lesion in the middle one-third of the left humeral shaft and cortical bone deformities with increased risk of fracture; focal uptake of the radiopharmaceutical in the left iliac crest". At this point, the patient started being followed by internal medicine, for investigation of the primary tumor localization. Laboratory tests, bone turnover and tumor markers were unremarkable, though a recent outpatient regime

mammography revealed a suspicious lesion, which lead us to presume breast carcinoma as a diagnostic hypothesis. Bone biopsy revealed a primary follicular thyroid cancer, and so, the patient was immediately referred to the Portuguese institute of Oncology for appropriate treatment.

**Discussion:** Patients with differentiated thyroid carcinoma have a 10-year survival rate of 80–95%. However, when distant bone metastases are present, especially in follicular thyroid cancer, this dramatically alters the prognosis: 10-year survival rate is drastically decreased to 40%. It's crucial to refer the importance of a multidisciplinary team management of oncological patients.

### Thirty-four cases of intrahepatic cholangiocarcinoma: the experience of an internal medicine department

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**Objectives:** Intrahepatic cholangiocarcinoma (iCC) is the second most common primary cancer of the liver. The incidence has increased and is currently estimated at 2.1/100.000/year in western countries. Mortality is high, with a 2-years survival rate of just 12.8%. The primary goal was to characterize consecutive cases of iCC admitted to the Internal medicine department of a single centre, between 2001-2013.

**Methods:** A retrospective study. Statistical analysis was made with SPSS v20.0, Kaplan Meier survival curves and log-rank test were used.

**Results:** From a total of 72 cases of cholangiocarcinoma, 34 had intrahepatic location. The sample was composed by 61.8% men and had a mean age of 68±10 years, with an incidence of 2.6 cases/year. 47% had advanced disease at the time of diagnosis. The most common symptoms were abdominal pain (32.8%), followed by weight loss (31%), jaundice (15.5%), fever (15.5%) and ascites (5.2%); 8.8% were asymptomatic. Analytically: the median GGT was 4.5x the upper normal limit (UNL), AST 1.5xUNL, Alk. phosphatase 1.5xUNL, LDH 1.1xUNL, CRP 6.3xUNL and CA19.9 10.6xUNL. 71% did not undergo invasive therapy, 17.6% placed biliary stent and 11.8% underwent surgery with curative intent. The median survival was 6 months, with only 23.5% of the patients lived more than 1 year. Chemotherapy and invasive treatment did not statistically correlate with better outcomes ( $p=0.42$  and  $p=0.079$ , respectively) and higher CRP values ( $\geq 3$  mg/dL) correlated with mortality ( $p=0.005$ ). Among the risk factors alcohol consumption was the most prevalent (46.7%), followed by diabetes mellitus (30%), tobacco (16.7%), chronic B hepatitis (3.3%) and liver cirrhosis (3.3%).

**Conclusions:** This series is in accordance to what is described in the literature, regarding the higher prevalence of the male gender, age >50 years, presenting symptoms and risk factors. The relation between higher CRP values and a worse outcome is described in the literature and our sample reinforces this relationship. Given the morbidity and mortality of this kind of

tumor, early diagnosis represents the most important element for the survival of these patients.

### mRNA gene expression of surviving, PDGFA, PDGFB, PDGFRA and PDGFRB in lung cancer cell lines

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**Objectives:** Lung cancer is one of the leading causes of death worldwide, with an increasing incidence and poor prognosis. Angiogenesis, the process of forming new blood vessels, as well as apoptosis evasion and imbalanced cell cycle regulation resulting in cell proliferation, are hallmarks in the pathology of cancer. Proto-oncogene SURVIVIN is a member of the IAP (inhibitor-of-apoptosis) family of proteins. SURVIVIN has dual function on inhibition of apoptosis and regulation on cell cycle (phase G2/M). SURVIVIN is overexpressed in various cancers, and has been suggested to be involved in cancer development, progression and resistance to treatment. PDGF/PDGFR signaling has been recognized to have a major role in angiogenesis. Activation of platelet-derived growth factor receptors (PDGF) by ligand-induced dimerization, leading to autophosphorylation on specific tyrosine residues promotes cell growth, survival, and migration. Pathway's overactivity or mutations of PDGF receptors is seen in tumor cells and malignancies. Controversial studies show the expression of SURVIVIN, PDGFA, PDGFB, PDGFRA and PDGFRB in cancer lung cell lines. In this study SURVIVIN, PDGFA, PDGFB, PDGFRA and PDGFRB expression was quantified in cell lines with small and non small lung cancer (SCLC and NSCLC) compared to normal lung fibroblasts.

**Methods:** Total RNA was isolated from the A549, NCI-H1299, NCI-H460 (NSCLC) and NCI-H69, DMS-114 (SCLC), as well as the MRC-5 normal lung fibroblasts cell line. Then cDNA synthesis and Real-time PCR was used to quantify mRNA gene expression of PDGF-A, PDGF-B, PDGFR-A, PDGFR-B and Survivin by mean of SYBR green detection (CFX96, Biorad) and hybridization probes (LightCycler, Roche). Results were compared to lung fibroblasts and analyzed by using t-test. There are expressed as: mean value±SEM ( $p<0,05$ ).

**Results:** Increased mRNA levels of SURVIVIN, PDGFA and PDGFB have been expressed in all cell lines compared to normal lung fibroblasts, while of PDGFRA and PDGFRB were minimally expressed. However, the SURVIVIN, PDGFA and PDGFB increased expression is in accordance with experimental data of two-pathway synergy and paracrine interaction with tumor cell microenvironment.

**Conclusions:** The increased mRNA levels SURVIVIN, PDGF and PDGF B have a very important role in tumorigenesis and angiogenesis. They could be useful biomarkers for monitoring patients with cancer. Further investigation is needed to improve understanding disease appearance and progression.

## Hyperventilation syndrome in patients with essential hypertension

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**Objectives:** Dyspnea is the result of the necessity to force breath; subjective component is always present in this phenomenon, but detection of its objective signs is by no means always possible. However definite group of patients has a distressing feeling of dyspnea with absence of its any internal manifestations. In 80s-90s of the 20th century dyspnea during hyperventilation syndrome (HVS) began to be studied actively. The aim of this investigation was the study the peculiarities of the syndrome of dyspnea in patients with essential hypertension (EH) of stages I and II.

**Material and methods:** 80 patients with EH with the syndrome of dyspnea at the age from 35 to 62 (average age  $45,8 \pm 1,7$ ) were examined. 35 (43,8%) of them had stage I of EH (15 men and 20 women); 45 (56,2%) – stage II (15 men and 30 women). The peculiarity of this group was that besides complaints, typical of EH, patients noticed dyspnea, intensity of which didn't correspond to the degree of functional changes of the cardiovascular system. Examination of functional condition of the cardiovascular and respiratory systems, including ECG, ultrasound of the heart, spirometry, assessment of gas and acid-base balance of blood, capnography was carried out to all patients. Capnographic examination was carried out with the usage of quick-response gas analyzer "Normocap-200-OXY" (Datex, Finland). Psycho-physiological assessment of the degree of dyspnea was carried out with the use of Borg scale and visual analogue scale. For detection of hyperventilation conditions and determination of degree of their severity psychological inquirer of the department of pulmonology of Naimigen university (the Netherlands, 1987) with the method of questioning with assessment of symptoms according to 4-scored scale was used.

**Results:** In 41 patients with EH (26 patients with stage I, 15 – with stage II) with hypocapnic type of ventilation complaints of dyspnea were noticed, dyspnea intensified during physical exercise, it was characterized by patients as "feeling of lack of air", "breathing discomfort", "restraint in the chest", yawning and frequent "dreary sighs" (gasps), dry cough. Hypercapnic type of breathing disorders in patients with EH was diagnosed in 12 patients. Lability of ventilation types at different moments of investigation was marked in 7 patients with EH of stage II. Normocapnic type of ventilation with various breathing disorders was marked in 4 patients with EH of stage I and in 16 – of stage II.

**Conclusion:** According to the results of the investigation presence of HVS is clinically and instrumentally detected in 50% of patients with EH.

## Receptor for advanced glycation end-products serves a protective role during Klebsiella pneumonia

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**Objectives:** Klebsiella (K.) species is a commonly isolated Gram-negative organism in sepsis and a frequent causative pathogen in pneumonia. It is associated with considerable morbidity and mortality. The receptor for advanced glycation end products (RAGE) plays a key role in diverse inflammatory responses. High mobility group box 1 (HMGB1) is a high-affinity ligand of RAGE. The objective of our study was to investigate the role of RAGE in the host response during Klebsiella pneumonia.

**Methods:** We investigated the role of RAGE in the host response during K. pneumoniae pneumonia by intranasal inoculation of  $1 \times 10^4$  colony forming units of viable Klebsiella bacteria in rage gene deficient (RAGE<sup>-/-</sup>) and normal wild-type (Wt) mice (n=8-10 mice per genotype for each time point and n=14 for survival studies). Mice were either euthanized at predefined time points or (in survival studies) monitored for 2 weeks. In a separate experiment, RAGE<sup>-/-</sup> and Wt mice intranasal received 100 µg highly pure lipopolysaccharide (LPS) derived from Klebsiella.

**Results:** K. pneumoniae pneumonia resulted in an increased pulmonary expression of RAGE and its high-affinity ligand HMGB1 compared to healthy, uninfected mice. RAGE deficiency impaired host defense as reflected by a worsened survival, increased bacterial outgrowth and dissemination in RAGE deficient mice. RAGE<sup>-/-</sup> neutrophils showed a diminished phagocytosing capacity of live K. pneumoniae in vitro. RAGE<sup>-/-</sup> mice displayed an unaltered response to intranasally instilled Klebsiella LPS.

**Conclusions:** The current study is the first to establish that RAGE is important for antibacterial defense against Klebsiella pneumonia. We here show that RAGE plays a protective role during respiratory tract infection by a common Gram-negative causative pathogen, K. pneumoniae, by improving antibacterial defense in the lungs and reducing bacterial dissemination. This could at least in part be explained by a better phagocytosis capacity of neutrophils in the presence of RAGE. Moreover, our results document that RAGE is not essential for the induction of excessive lung inflammation and injury.

## Ventilator-associated pneumonia in a Portuguese intensive care unit – a one year retrospective study

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**Methods:** The authors retrospectively analyzed the data of all patients admitted to the intensive care unit (ICU) in the past year, who were diagnosed with ventilator-associated pneumonia (VAP) during their stay. Clinical findings, laboratory data and microbiology results were registered and evaluated,

as well as clinical evolution. VAP was differentiated from ventilator-associated tracheobronchitis (VAT) by the presence of radiographic pulmonary infiltrates.

**Results:** The majority of VAP were found to be caused by Gram-negative organisms (*Pseudomonas aeruginosa*) and methicillin-resistant *Staphylococcus aureus*. Major risk factors for the development of VAP were prolonged hospital stay and prolonged mechanical ventilation. The continuous use of corticoid treatment in patients with acute respiratory distress syndrome also seems to favor the development of VAP.

**Conclusions:** VAP is a high-mortality condition, with well known risk factors and almost always caused by pulmonary infection with multidrug resistant organisms. Although the diagnostic criteria are not fully standardized, a high clinical suspicion should lead to its early management and treatment, which has shown to improve prognosis.

## Cancer in patients with pulmonary embolism

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**Objectives:** The interplay between cancer and venous thromboembolic disease is well-known with an increased risk for both cancer in patients with pulmonary embolism (PE) and for PE in patients with cancer. Our aim was to explore the incidence of new cancer after an episode of PE.

**Methods:** From a cohort of 629 patients admitted to hospitalization with symptomatic PE, we studied the new cancers diagnosed at follow-up, the timing of diagnosis as well as the histological type and the organ of origin. We also determined the type of cancer diagnosed in the index episode vs. those diagnosed later. We compared the clinical characteristics of patients in who a cancer was diagnosed with those of patients without cancer.

**Results:** At follow-up, 60 (11%) patients had a diagnosis of cancer in a median time of 17 IQR 35 months. The main histological type was adenocarcinoma in 36 (60%) patients. The most frequent diagnosed cancer were lung cancer in 7 (12%) patients, breast cancer in 6 (10%) patients, colorectal cancer in 6 (10%) patients, bladder cancer in 6 (10%) patients, prostate cancer in 6 (10%) patients, myeloproliferative malignancies in 4 (7%) patients and ovarian cancer in 4 (7%) patients, being the rest miscellaneous. In patients with a subsequent diagnosis of cancer, the PE was more frequently an unprovoked PE (57 vs. 34%,  $p < 0.001$ , CI 95% 0.08-0.36), they had a higher proportion of clinically evident venous thrombosis of the limbs (48 vs. 32%,  $p < 0.05$ , CI 95% 0.02-0.31) and a higher rate of death (60 vs. 30%,  $p < 0.001$ , CI 95% 0.16-0.44). The severity of PE was similar in patients with and without subsequent cancer. The most frequent cancer diagnosed in the index hospitalization was ovarian cancer (3 over 4 [75%]). The longer time to diagnosis was for gastric cancer (44±15 months), gallbladder cancer (29±34 months), myeloproliferative malignancies (24±11 months), bladder cancer (22 IQR 21) months, and prostate cancer 13.5 IQR 53 months.

**Conclusions:** The percentage of patients with PE who subsequently is diagnosed with a cancer remains stable in most statistics, around 10%. Patients with subsequent diagnosed

cancer have more frequently unprovoked PE, deep venous thrombosis and a higher mortality. The surveillance for idiopathic PE should be extended longer in anticipation of the emergence of a new malignance. The timing of diagnosis depends on the biology of every type of cancer.

## Surveillance of pulmonary embolism in the elderly

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**Objectives:** Elderly patients with pulmonary embolism (PE) seem to have a worst prognosis than younger patients with higher rates of bleeding and showing difficulties in prediction with sPESI and troponin T. We evaluated the differences in severity and mortality in patients older and younger 75 years old.

**Methods:** Consecutive patients diagnosed with symptomatic PE in our unit of internal medicine were prospectively put on surveillance with the recording system of clinical episodes of the health service of our community. Patients were grouped in those older than 75 years as elderly patients (278 patients) and younger 75 years (245 patients). Clot burden was calculated from the Qanadli equation.

**Results:** Elderly patients were in higher proportion women (65 vs. 43%,  $p < 0.001$ , CI 95% 0.13-0.30), had a higher overall mortality rate (45 vs. 19%,  $p < 0.001$ , CI 95% 0.17-0.33), a greater clot burden (37.5 IQR 25 vs. 25 IQR 32.5,  $p < 0.01$ ), an increased proportion of PE provoked by mobility impairment (70% vs. 54%  $p < 0.001$  CI 95% 0.01-0.18), a higher rate of bleeding (15 patients vs. 4 patients, two-tails Fisher 0.03) and greater levels of plasma NT-proBNP ( $p < 0.001$ ), troponin I ( $p < 0.001$ ), D-dimer ( $p < 0.01$ ) and alveolar to arterial oxygen gradient ( $p < 0.01$ ), while they had a lower proportion of time in therapeutic range (74.75 IQR 25 vs. 77.35 IQR 38,  $p < 0.05$ ). Significant causes of death in the elderly patients as compared with the younger were new PE, cardiovascular related death, fatal bleeding, pneumonia and sepsis. The time up to death was 27±29.9 months in elderly patients and 29.4±29.3 months in younger patients ( $p$  non significant). The analysis of survival up to 96 months from the initial episode did not show differences between both groups.

**Conclusion:** Despite a higher late mortality in the elderly as compared with younger patients the survival up to 96 months after the initial episode were similar taking away nihilism in the treatment of PE of the elderly.

## Chylothorax and chylous ascites: the same etiology for two different conditions

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**Introduction:** Chylous pleural effusions result from disruption/obstruction of the thoracic duct. Chylous ascites is due to



an interruption in the lymphatic system. Simultaneous accumulation of chyle in multiple cavities, in non-traumatic etiologies, is rare. The authors present the case of a patient with a non-traumatic chylothorax and chylous ascites.

**Case report:** A 90 years old man was admitted in the emergency department complaining of progressive breathlessness, dry cough, asthenia and abdominal distension over the last 8 days. He denied fever, anorexia and weight loss. He was no past of smoking habits and his past medical history was not relevant, besides history of hypertension. General physical examination showed a pale male, emaciated, with breath sounds absent in left basal area with stony dull percussion note. Per abdomen, shifting dullness was present. Routine blood investigations revealed macrocytic anemia, elevation on C-reactive protein of 3,6 mg/dL (normal value <0,5 mg/dL), erythrocyte sedimentation rate of 105 mm/h (normal value <15 mm/h), creatinine of 2,02 mg/dL (normal value 0,6-1,20 mg/dL). The chest X-ray was suggestive of left pleural effusion. Thoracocentesis and paracentesis were performed with drainage of milky fluid. Pleural fluid examination revealed: >1000 cells/mm<sup>3</sup>, mostly lymphocytes, glucose 71,9 mg/dL, protein 3 g/dL, triglyceride 506 mg/dL, cholesterol 45 mg/dL, adenosine deaminase (ADA) 17,2 UI/L. Peritoneal fluid was also examined: >1000 cells/mm<sup>3</sup>, mostly lymphocytes, glucose 69,2 mg/dL, protein 3,2 g/dL, triglyceride 489 mg/dL, cholesterol 48 mg/dL, ADA 8,9 UI/L. Serum triglyceride and cholesterol were 122 mg/dL and 106 mg/dL, respectively. Pleural and peritoneal fluid analysis did not reveal any abnormal cell and cultures were sterile. A chest computed tomography was performed showing a large solid, nodular mass surrounding the aorta, with 14x11 cm. Flow cytometry revealed non-Hodgkin lymphoma. He responded to treatment with corticosteroid and a diet of medium chain triglyceride oil.

**Discussion:** Lymphomas are one of the main non-traumatic causes of chylothorax and chylous ascites. Treatment is the same as that of the hematologic malignancy. A pleural/ascitic fluid triglyceride level greater than 110 mg/dL is an accurate marker for the presence of chylothorax/chylous ascites.

## A case of achalasia mimicking pulmonary thromboembolism and causing aspiration pneumonia

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**Introduction:** Achalasia is a rare disease that can mimic respiratory symptoms. In the absence of radiological suspicion of achalasia, a patient may initially be managed for respiratory or cardiac conditions with subsequent development of complications, leading to a diagnostic delay. Therefore, this case presentation aims at contributing to clinicians' awareness regarding this condition.

**Case report:** A 36 years old female patients presented with right pleuritic pain and high fever. Despite an initial suspicion of pulmonary thromboembolism, a contrast enhanced computed tomography suggested achalasia. Achalasia was confirmed and

treated endoscopically. Treatment for aspiration pneumonia resulted in clinical and radiological improvement.

**Discussion:** A possible diagnosis of achalasia should be borne in mind by pulmonologists in the differential diagnosis of patients presenting with respiratory symptoms.

## Smoking addiction in youth: the opportunities of an educational "check point"

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**Objectives:** The smoking habit is one of the biggest worldwide health problem and major risk factors in the development of cancer, cardiovascular and respiratory diseases. According to the Italian Ministry of Health, between 15 and 24 years old 20.9% of males and 16% females are smokers. The aim of this work was to set preventive interventions among young people and to assess their effectiveness.

**Methods:** 377 students aged between 14 and 18, 155 male and 199 female (23 did not declare their gender), from Institute "Oberdan" of Treviso, Italy, were involved with psycho-educational intervention on smoke damage, the mechanisms of smoking addiction and cessation strategies. Self-administered anonymous questionnaire about possible smoking habits (before and after 2 weeks from intervention) was administered. The intervention consisted in a psycho-educational single meeting with a psychologist and a pulmonologist.

**Results:** In the questionnaire administered before intervention, 108/377 (29%) students among which 61/199 female (31%) and 47/155 male (30%) claimed to be regular smokers; 237/377 (63%) students declared to smoke sometimes "just to try". The declared mean age of onset of smoking habit was 13,3 years old. The average number of smoked cigarettes in die declared has been 5,7. Concerning the risk factors, 126/377 (33%) affirmed to live with smokers. In the self-administered questionnaire after intervention, 49/108 smokers declared to have changed smoking habits: specifically, 20/108 (18%) declared to smoke less than before, 10/108 (9%) to have stopped.

**Conclusions:** Compared to epidemiological data reported in literature, our sample revealed a higher percentage of female smokers. This difference could be explained by the data collection method (self-administered anonymous questionnaire) or reflect a real different data prevalence. Our intervention highlighted 9% of smoking cessation and 18% of quit attempts, in line with the percentages reported in the literature for intervention of the same type. Interventions targeted on adolescents must include appropriate issues to key developmental differences typical of youth. Peer influences and motivation for change are important considerations for any adolescent-focused smoking cessation intervention. Family influences are significant, particularly in the earlier stages of smoking and our data confirm as living with smokers is a well known risk factor for youth onset of smoking habit.

## The silent giant: solitary fibrous tumor of the pleura

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**Introduction:** Solitary fibrous tumors of the pleura (SFTP) are very rare mesenchymal tumors, accounting for less than 5% of all primary pleural tumors and affecting mostly patients in the 6th and 7th decade. The etiology is unknown, hematogenous metastatic dissemination is mostly the cause of death. The number of reported cases is limited, as is our knowledge about SFTP pathophysiology. The neoplasm is presenting as an asymptomatic mass in over 50% of all patients. SFTP can reach surprisingly large sizes before becoming clinically symptomatic. The basic frame of diagnostics includes a chest imaging and a biopsy with histological sections' staining and check for immunohistochemical marker expression. A surgical resection in toto is the corner stone of the management, followed by regular postoperative care and follow up.

**Case report:** We present a 46 years old male smoker with very mild respiratory complains. Computed tomography imaging revealed a large solid mass in the right hemithorax measuring 15x20x16 cm). The mass presented well circumscribed, homogenous and compressing the right upper and middle lobe, vena cava superior. CT guided needle biopsy confirmed the diagnosis immunohistologically. Complete en bloc surgical resection has been performed as the preferred treatment of benign (about 80% of all SFTPs), but also the malignant types.

**Discussion:** Clinicians should be aware of the SFTP and include it as a differential diagnosis, next to bronchogenic tumors, consolidated inflammation, empyema, fibrosarcoma or tuberculosis since they often remain clinically silent until they reach large dimensions and to proceed with curative resection without delay. It is essential to follow up patients for a long period of time as recurrence may occur. Additionally, a retrospective look on previous plain films of a patient might be wise, as it has been reported recently that SFTPs are being ignored for long periods due to ignorance of small mass changes on X-ray. It is especially important, as some SFTP seems to spontaneously expand and rapidly grow after a long-year follow up.

## Pulmonary alveolar proteinosis: a differential diagnosis for thorax X-ray alterations

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**Introduction:** Pulmonary alveolar proteinosis (PAP) is a rare disease (about 1 case per 100'000) of unknown etiology. Approximately 30% of affected individuals are asymptomatic, and many times the diagnosis is suggested by alteration in an occasional thoracic X-ray.

**Case report:** A 58 years old male, with a past medical history of type 2 diabetes mellitus, hypertension, obesity, acute myocardial infarction and humerus plate osteosynthesis after

a professional accident. He worked as a mason in a rock extraction company for 2 years. He came to the ER with fever and malaise since the previous day, associated with painful, swollen and hot right arm. Additionally he mentioned a long history of dry cough without dyspnea. The objective exam revealed 38°C, 160/90 mmHg blood pressure, 95 bpm heart rate; he presented with rough respiratory sounds without adventitious sounds; there were clear inflammatory signs in the scar of the right arm; the investigation in the ER revealed normal blood gas analysis, leukocytosis, neutrophilia and high PCR. An X-ray of the right arm didn't show signs of osteomyelitis and a thoracic X-ray show demonstrated bilateral pulmonary infiltrates with "cannonball" appearance. He was admitted in the wards to start empirical e.v. antibiotherapy and additional diagnostic investigation. Additional studies revealed negative hemocultures; negative HIV and TORCH group serologies; the CT scan revealed pretracheal, prevascular and periaortic nodes, with some calcifications, multiple opacities in ground glass appearance without broncovascular distortion and with thickening of interlobar septa representing a probable infectious process; normal DLO in the respiratory function tests; fiberoptic bronchoscopy with BAL revealed no structural, biochemical or microbiological alterations; bronchial secretions were positive for *Pneumocystis jirovecii* and the patient was started on sulphametoxazol-trimetropim. The patient was asymptomatic at discharge, but maintained the radiologic alterations. An elective transthoracic pulmonary biopsy identified PAP, and the PAS coloration and LBA were positive reinforcing the diagnosis. He presented very mild symptoms (longstanding dry cough) and a history of exposure to silica, considered a risk factor for alveolar proteinosis.

**Discussion:** The etiologic evaluation of occasional findings of the chest radiography is mandatory to diagnose diseases that in spite a silent beginning may have unfavorable clinical outcome if not treated as promptly as possible.

## An association between idiopathic pulmonary fibrosis and pancreatic tumor markers

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**Introduction:** The aim is to illustrate a clinical case of a patient diagnosed in our hospital of pulmonary fibrosis and high CA19.9 markers without evidence of digestive illness.

**Case report:** A 77 years old man, Scottish, lived in a nursing home. Medical background: idiopathic pulmonary fibrosis, alcohol consumption. Treatment: inhalers. He went back to the emergency room for coughing and fever. At physical examination rales and crackles bilaterally. Blood test normal, tumor markers: Ca125 – 431 U/ml, Ca19.9 – 1254 U/ml, CEA – 21.1 ng/ml, CYFRA21.1 – 7.1 ng/ml, NSE – 39.6 ng/ml. Chest CT scan: panacinar emphysema, bronco-vascular thickness and sub-pleural fibrosis with reticular pattern mainly in the underside,

lingula medium lobes. Abdomen CT scan: normal. There was a progressive impairment of respiratory function that took the patient to pass away.

**Discussion:** CA19.9 tumor marker might be elevated in several benign and malign processes, being higher in neoplastic syndromes. However, there are few revisions where has been reported an association of idiopathic pulmonary fibrosis and CA19.9 marker levels. Immunohistochemically, this antigen expresses in mucous cells of bronchial glands and epithelium cells of bronchiolar mucosa. It is believed that metaplastic changes in fibrotic lungs might provoke a higher release of that antigen. Additionally, these levels seem to correlate more with the grade of pulmonary architecture destruction than with the grade of activity of the disease and their increase matches strongly with poor prognosis in short term, having the patient life expectation lower than six months if level of CA19.9 tumor marker is above 1000. The correlation between tumor markers concentration and tumor active mass is a valuable tool for prognosis, follow up, and monitoring of oncology treatment. However, it cannot be used for screening, because it does not have absolute organ specificity. It has to be taken into account the poorly documented relationship between these antigens and other processes, which would help to establish a diagnosis, therapy and prognostic on an early stage.

## Interstitial lung diseases: a needle lost in the haystack

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**Introduction:** Interstitial lung disease (ILD) includes a heterogeneous group of entities that result from cells' infiltration, extracellular matrix deposition or various substances in the airspaces distal to the terminal bronchioles. Its clinical and radiological presentation is monomorphic, which results in a great difficulty in specific diagnosis. The authors wish to draw the attention to the importance of an early diagnosis in this type of diseases.

**Case report:** 52 years old woman, with active smoking habits, and a history of bone marrow aplasia, paving stone intraepithelial lesions of high-grade cervical and multinodular goiter. Hospitalized for respiratory infection with 3 days of evolution, corresponding to a severe bilateral pneumonia. The analysis presented elevated inflammatory parameters, negative autoimmune study and infectious serology. In the microbiological tests performed it was isolated, in the sputum, a multidrug-resistant *Enterococcus faecalis*. In the computed tomography (CT) of the thorax it was observed bilateral opacities "in ground glass" and septal thickening in the lung apex. Despite the treatment with broad-spectrum antibiotics, antifungal and prednisolone, the clinical condition worsened, and required non-invasive ventilation. Presence of ILD suspected, hypothesis corroborated by pulmonologist, the choice was the association of cyclophosphamin. The bronchoalveolar lavage or biopsy that could have allowed a more targeted treatment was not possible. The patient died after several days of hospitalization. The post mortem examination revealed a diagnosis of alveolar proteinosis.

**Discussion:** The frames compatible with ILD, especially if refractory and with a tendency to progression, require high suspicion and precocity of research, especially when is considered the hypothesis of a treatable interstitial disease. In this case, the overall pulmonary lavage could have saved the patient from an unnecessary death.

## Obstructive sleep apnea, type 2 diabetes, non-invasive ventilation therapy and cardiovascular risk factors according to polysomnography analysis

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**Objectives:** Obstructive sleep apnea (OSA) is the most prevalent sleep-disordered-breathing, characterized by episodes of upper airway collapses and sleep fragmentation. OSA is independently associated with cardiovascular (CV) diseases: hypertension (HT), acute myocardial infarction (AMI), type 2 diabetes (T2DM) and cerebrovascular disease (CD). The aim of our research was to estimate the prevalence of the link between T2DM and cardiovascular risk factors (CRF) in patients with OSA and non-invasive ventilation (NIV) therapy.

**Methods:** Retrospective analysis of polysomnographies (PSG) performed in our hospital from 2009 onward. Anthropometric rates, PSG parameters, T2DM diagnosis (plasma glucose criteria or A1C  $\geq 6.5\%$ ), CRF and NIV therapy were recorded. Multivariate statistical analysis SPSSv20.0.  $p < 0.05$  significance.

**Results:** The matter of study were 867 PSG of which 644 were diagnosed of OSA (25% mild, 20.6% moderate and 54% severe). 74% of them were men, with a mean age of 61 years, body mass index (BMI) of 31 kg/m<sup>2</sup>, waist circumference (WC) of 110 cm and neck circumference (NC) 41.4 cm. NIV was prescribed to 77% of them, 408 continuous positive airway pressure (CPAP) and 91 bi-level positive airway pressure (BIPAP). 35.4% suffered from T2DM and showed worse PSG outcomes, opposite to non-T2DM patients (apnea-hypopnea index: 46.6 versus (vs) 41.6,  $p = 0.07$ , oxygen desaturation index: 48.2 vs 39.5,  $p < 0.01$ , saturation below 90%: 19.9 vs 11.2,  $p < 0.01$ ). They also displayed: elderly age (66.3 vs 58.4,  $p < 0.05$ ), worse anthropometric variables (BMI 32.7 vs 30.2 kg/m<sup>2</sup>,  $p < 0.05$ , WC 115.4 vs 107.5 cm,  $p < 0.05$ , NC 42.3 vs 40.9 cm,  $p < 0.05$ ) and higher prevalence of CRF (CD 20 vs 8.8%,  $p = 0.032$ , AMI 24 vs 11.9%,  $p < 0.01$  and HT 93% vs 77%,  $p < 0.05$ ). NIV was needed in  $> 85\%$  T2DM patients with OSA ( $p = 0.001$ ): 51.7% with BIPAP and 34.6% with CPAP (opposite to 48% and 65% respectively, of them without T2DM  $p = 0.002$ ). Subgroup analysis was performed in T2DM patients with NIV: higher prevalence of AMI was observed in CPAP therapy ( $p = 0.045$ ), with a similar prevalence of other CV events.

**Conclusions:** In this statistically representative sample of our sanitary area, T2DM patients with OSA demonstrate: older, with worse anthropometric variables and severity of sleep apnea and highest prevalence of CRF. BIPAP therapy was needed more frequently in T2DM patients and they had a lower prevalence of AMI opposite to T2DM patients with CPAP therapy.

## High flow oxygen through nasal cannula in acute hypoxemic respiratory failure: experience of an intermediate care unit

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**Objective:** To evaluate the usefulness of high-flow oxygen through nasal cannula (HFNC) in patients with hypoxemic respiratory failure despite conventional oxygen therapy.

**Methods:** Prospective observational study conducted in intermediate care unit (IMCU). 28 patients were treated with HFNC. Patients with PaCO<sub>2</sub> >50 mmHg or pH <7.28 were excluded, as well as those with indication for immediate endotracheal intubation. Changes in clinical parameters (heart rate and respiratory rate) and arterial blood gases (saturation, PaO<sub>2</sub>, PCO<sub>2</sub> and pH) were measured.

**Results:** 14 men and 14 women were studied. The median age was 82 years, with an APACHE score of 16 (14-18). The etiology of heart failure was respiratory failure (11), respiratory infection (11), asthma (3) and miscellaneous (3). 2 patients (7.1%) died, 4 patients (14.2%) required admission to the intensive care unit, and 22 patients (78.5%) were discharged from the unit. Respiratory rate increased from 30 to 22 breaths/min ( $p < 0.001$ ), oxygen saturation decreased from 86.5 to 98 ( $p < 0.001$ ). Changes in PaCO<sub>2</sub> and pH were not significant.

**Conclusions:** HFNC improves oxygenation in patients with acute hypoxemic respiratory failure despite conventional oxygen therapy, without affecting pH or PaCO<sub>2</sub>.

## Necrotizing pneumonia to Staphylococcus aureus. A complicated case of cavitated lung lesions

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**Introduction:** The differential diagnosis of pulmonary nodules cavitation is a challenge in clinical practice, imaging and laboratory could direct us to the main etiologies: infectious, neoplastic, rheumatologic.

**Case report:** We present the case of a patient of 63 years with polyarthralgia history; HTA; hiatus hernia, frequent intake of NSAIDs that 4 days before admission had resorted to emergency room by the right sciatica. After evaluation was discharged treated with diclofenac 75 mg (injectable vials) and neurobion. For persistent pain, malaise, asthenia appealed again to the US and was hospitalized. Objectively on admission stood out mucocutaneous pallor and pain mobilization of right hip. A laboratory evaluation revealed iron deficiency anemia (Hb 10,1 g/dL), leukocytosis (17,500), neutrophils 93%, CRP 32.6 mg/l, urea 203 mg/dL, creatinine 4.8 mg/dL. Chest radiography: normal. It was admitted to the medical service with diagnosis of pneumonia and renal failure. From D3 found if fever (38°C) evening despite ongoing antibiotic

therapy with ceftriaxone, intensification of inflammatory parameters. Thoracic CT showed the presence of multiple pulmonary nodules cavitation. To exclude septic embolization was performed echocardiogram showed no vegetation. The bacteriological examination of bronchial secretions collected by bronchoscopy was positive for Staphylococcus aureus and also positive blood cultures for the same agent. Abdominal/pelvic CT revealed that two subcutaneous collections in gluteal regions associated with citoesteanecrose. After antibiotic-up for meropenem and vancomycin, fluid there has been progressive improvement of infectious frame, progressive resumption of diuresis, normalization of renal function and decrease in inflammatory parameters.

**Discussion:** In the evaluation of cavitated lung lesions, we have to keep in mind the characteristics of the lesion and other associated findings that may be objectified, the CT being a very useful diagnostic tool for it. Moreover we have to correlate the findings with clinic context, disease history and previous information, to establish an approximate diagnosis and/or priorities the most likely differential diagnoses that will guide the subsequent management of these cavitated lesions.

## Remodeling features of the left and the right heart in patients with chronic obstructive pulmonary disease

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**Objective:** To evaluate systolic and diastolic function of the LV and RV myocardium, pulmonary hemodynamics in patients with chronic obstructive pulmonary disease (COPD).

**Material and methods:** Patients (n=119; 87 are males, mean age is 62,5±14,8 years) with mild (I – n=43) and moderate (II – n=76) severity of COPD (GOLD, 2013) were observed. EchoCG was conducted at all patients with assessing LVEF (Simpson method), LV relative wall thickness, LA volume, LV diastolic function, and grading of LVDD as recommended by the ASE and EAE.

**Results:** All patients with COPD were revealed disturbances such as a RV diastolic dysfunction (E/e' TV = 11,7±3,3 и 16,1±2,9; of the I and the II groups respectively) and LV (E/e' MV=12,8±3,7 and 17,1±3,5; all  $p < 0.05$ ), which confirms the presence of heart failure. At patients with E/e' = 8-15 were revealed in 19% and 33% of patients, NT-proBNP was 223,8±27,5 pg/mL and 317,4±31,8 pg/mL. In 47% of patients of the II Group ( $p < 0.05$ ) were restrictive type transtricuspid blood flow. RV hypertrophy has evolved at moderate severity of COPD (RVWT=5,21±1,01 mm, (E/e' TV=12,6±4,1), with the progression of LV diastolic dysfunction (E/e' TV=15,5±3,8). Severe LV hypertrophy was defined as LV mass  $\geq 122$  g/m<sup>2</sup> in women or  $\geq 149$  g/m<sup>2</sup> in men – at 46% and 61% ( $p < 0.04$ ), and concentric LV hypertrophy was determined as relative wall thickness  $> 0.42$  + LV mass  $\geq 96$  g/m<sup>2</sup> in women or relative wall thickness  $> 0.42$  + LV mass  $\geq 116$  g/m<sup>2</sup> in men – at 35% and 57% ( $p < 0.04$ ). Pulmonary hypertension in COPD patients of the I group was 22,4±4,7 mmHg.; at the II – 24,9±3,5 mmHg. The average value of the LA size with mild COPD was 39,7±5,6 mm, with moderate – 43,7±6,3 mm (all  $p < 0.05$ ).

**Conclusions:** Thus, in patients with COPD, even at mild degree of COPD RV and LV diastolic dysfunction and low pulmonary hypertension were developed. Further progression of hemodynamic disturbances associated with worsening of respiratory disorders.

### **Riser blood pressure pattern and sleep apnea-hypopnea syndrome: prevalence and comorbidity**

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**Objective:** Determine the prevalence and morbidity of sleep apnea-hypopnea syndrome (SAHS) in hypertensive patients with riser pattern.

**Methods:** Were selected the first 100 consecutive patients valued, from January 1 2013, into the hypertension doctor's office of three Spanish hospitals. Inclusion criteria: being hypertensive with a riser pattern at the ambulatory blood pressure monitoring (ABPM). The diagnosis of SAHS (apnea-hypopnea index >10) was performed by polysomnography in patients with riser pattern. As a comorbidity we considered: obesity, hypercholesterolemia, smoking, heart failure (echocardiography and/or ECG), ischemic heart disease, ischemic cerebrovascular disease (stroke, transient ischemic attack (TIA)), peripheral artery disease, and renal disease (microalbuminuria in at least 3 determinations). In the descriptive analysis, quantitative variables are expressed as means  $\pm$  SD and qualitative in frequencies and percentages. The inferential analysis, the Chi-square test or Fisher's exact test was applied.

**Results:** We reviewed a total of 897 hypertensive patients until arrived to the first 100 patients with a riser pattern. Of them: SAHS – 83, mean age:  $71 \pm 16.7$ , men – 75. Years of evolution of hypertension – 8.4. Body mass index – 29 (27.6-31). Total cholesterol – 236 (213-254). Smokers – 32%. Comorbidity (72%): dyslipidemia 60%, type 2 diabetes mellitus 32%, benign prostatic hyperplasia 24%, left ventricular hypertrophy 16%, microalbuminuria 13%, ischemic heart disease 12%, AIT 9%. Risk by SCORE: normal – 8%, light – 20%, moderate – 16%, high – 48%, very high – 8%. Erectile dysfunction – 36%.

**Conclusions:** We detected a prevalence of SAHS 5 times higher among hypertensive patients than in the general population and especially in patients with riser pattern. Those patients with hypertension and riser pattern have been associated higher incidence of cardiovascular effects. We can say that maintaining a high suspicion of SAHS, will lead to an early diagnosis and therefore better treatment of hypertension. The existence of SAHS entails greater comorbidity, SAHS is considered as a independent vascular factor risk for angina and peripheral artery disease. Therefore maintaining a high suspicion of this disease would lead to early treatment to prevent the onset of these cardiovascular events.

### **The orphan disease: knowing what we mean, meaning what we say about bronchiectasis**

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**Introduction:** Bronchiectasis (BE) has been considered an orphan disease, but recently has made its mark in the scientific community. Is a final common pathway for many diseases with diverse fundamental causes? Knowledge of the root cause of BE in a particular patient is more helpful for treatment than an understanding of the generic subject of bronchiectasis. Bronchiectasis can be congenital but is most often acquired. Why do we have to know what we mean about this disease? Because the diagnosis based on etiology changes both the approach and the treatment of BE within a relevant percentage of patients, with a consequent change in the prognosis.

**Case report:** 74 years old man was admitted to the hospital for persistent wet cough, dyspnea and weight loss for the last months. His medical history was hypertension and type 2 diabetes and several admissions for similar symptoms and respiratory tract infections. On his initial laboratory and imaging workup, the following values were obtained: anemia, elevated white blood cell count with an increased percentage of neutrophils and protein C reaction. Posterior-anterior and lateral chest radiographs were obtained and revealed increased pulmonary markings, honeycombing and computed tomography (CT) scanning shows cystic and varicose bronchiectasias on the posterior segment of superior right lobe and medium and apical inferior right lobe. The patient was admitted for sputum analysis, quantitative immunoglobulin levels and pulmonary function tests. We set a timeline of initial symptoms, family history, profession, recognized risk factors, infection predisposition, CT scanning and sputum and blood cultures in previous hospital admissions. The patient workup sums up negative smear sputum for Mycobacteria and fungi and positive for Pseudomonas species and typical CT scanning imaging. Autoimmune and quantitative serum alpha1-antitrypsin (AAT) levels were not performed by appropriate clinical setting. So, the patient was diagnosed for acute on chronic bronchiectasias (with systemic and pulmonary function impairment), integrated in a recurrent respiratory tract infection sequelae with no professional and genetic history.

**Discussion:** With this clinical case the authors pretend to alert physicians for this clinical entity and its importance in the clinical timeline of symptoms, familiar and professional history in order to establish a driven workup and provide the best treatment according to the etiology. Instead of being a disease on its way to extinction, BE has gradually increased in importance, ever since it became known that its presence aggravates the prognosis of the underlying disease, accelerates the loss of pulmonary function, increases mortality, and significantly reduces quality of life.

## Chronic respiratory failure in patients with neuromuscular disorders – follow-up in home ventilation

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**Objectives:** Despite the severity of respiratory complications described in neuromuscular diseases (NMD), data regarding long-term follow-up under home-ventilation is scarce. We aimed to characterize and evaluate the effect of home ventilation in a group of NMD patients.

**Methods:** Retrospective study (20 months) of NMD patients at a Non Invasive Respiratory Care Unit.

**Results:** 35 NMD patients (26 men, 74%); mean age 56.6±13.9 (beginning of non invasive ventilation – NIV). Diseases: post-polio syndrome (n=12; 34%); muscular dystrophies (n=4); diaphragmatic paresis (n=4); amyotrophic lateral sclerosis (n=3); multiple sclerosis (n=2); heterogeneous congenital/acquired NMD (n=10). 16 patients started NIV electively and 19 during an episode of acute respiratory failure. At baseline, the mean daytime arterial blood gas values: PaO<sub>2</sub> 68.4±10.3, PaCO<sub>2</sub> 50.8±7.2, HCO<sub>3</sub> 31.0±4.5. At the end of the follow-up period, there was a significant improvement (PaO<sub>2</sub> 76.1±11.2, PaCO<sub>2</sub> 45.3±4.9, HCO<sub>3</sub> 28.6±2.5) (p<0.0001). 25 patients showed functional stability (initial FVC% predicted: 41.4±15.3; final 42.5±14.8). The mean Nº of hospital admissions in the year pre-ventilation was 0.71±0.52 and that occurred during home-ventilation period was 0.03±0.05 per year (p<0.05). Oxygen supplementation: initial evaluation 16 patients (46%); last evaluation 5 patients. Last evaluation: 1 tracheostomy, 32 pressure support and 3 volume assured pressure support ventilators, 9 cough assist and 2 percutaneous gastrostomy.

**Conclusion:** For NMD patients with chronic respiratory failure, home ventilation was effective with a significant decrease in hospitalizations and an improvement of arterial blood gases.

## Rivaroxaban for the treatment of venous thromboembolism

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**Objectives:** Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). The usual treatment of VTE is heparin, overlapped with and then followed by vitamin K antagonist (VKAs). More recently, new anticoagulants have emerged as a therapeutic alternative to VKAs; of those, rivaroxaban, a direct inhibitor of the Xa factor that is administered orally, has shown non-inferiority to standard therapy in patients with VTE in the EINSTEIN-DVT and EINSTEIN-PE studies. Once rivaroxaban became available, was offered to patients with VTE at our institution. We aimed to describe our experience with rivaroxaban in the treatment of VTE.

**Methods:** Retrospective review of patients with VTE who were treated with rivaroxaban at our institution during the last 4 years. The diagnosis of VTE was established clinically with confirmation by Doppler ultrasonography (US) for DVT or chest-CT scan for PE. Rivaroxaban was administered at least 3 months. Prior to stopping rivaroxaban, D-dimer was determined, and US or chest-CT were repeated.

**Results:** From February 2011 to April 2015, 15 patients with VTE were treated with rivaroxaban. All were males (mean age 48±15 years). 2 patients had chronic lung disease. 8 patients (53%) had DVT: 7 located in lower limbs (5 proximal DVT, 2 distal DVT), and 1 in the upper extremity. 6 patients (40%) had PE. One patient (7%) had both DVT and PE. In 14 patients (93%), the VTE event was considered secondary to immobilization without surgery after minor trauma of lower limb (n=6) or polytrauma (n=3), or to orthopaedic surgery (3 discal hernias; 2 lower limb fractures). The upper extremity DVT was not catheter-related. All patients had normal renal function. Thrombophilia testing was positive in 3 of 9 patients studied (all had factor V Leiden mutation). One patient stopped rivaroxaban after 15 days due to gastrointestinal intolerance. Median duration of treatment was 3,6 months; 11 patients (73%) were treated with rivaroxaban from the beginning. At the end of therapy, D-dimer was negative in all cases, and the US or chest-CT showed thrombus resolution in all cases. During the study period there were no deaths, no VTE recurrence, nor bleeding.

**Conclusion:** In our study, rivaroxaban was effective, safe and well tolerated.

## Bupropion intoxication induced serotonin syndrome

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**Introduction:** Bupropion is an antidepressant and a smoking cessation aid that selectively inhibits the reuptake of dopamine and norepinephrine, and it may have an indirect effect on serotonergic receptors. However, there is some evidence that shows that in high enough concentrations bupropion and its metabolites lose their selectivity and may have an effect at other neuronal sites including serotonin receptors, therefore, bupropion may play a role in the development of serotonin syndrome.

**Case report:** We report here a quite unique case of a 30 years old female who was taken unconscious to the ER after a suicide attempt by drinking alcohol and ingesting an unknown type of pill. 24 hours after arrival she woke up, cooperated and was clinically stable and extubation was performed. Some 8 hours later she developed fever, became rigid and started to hallucinate. Further investigation with her family exposed the fact that she ingested approximately 84 pills of bupropion together with vodka. Presently, a Medline search of the English language literature demonstrated only 4 case reports of serotonin syndrome in conjugation with bupropion ingestion, only one of them was secondary to bupropion alone.

**Discussion:** Serotonin syndrome is a potentially life threatening adverse reaction that may occur even many hours

after ingestion of a wide variety of drugs or combination of drugs, even drugs which under normal circumstances don't act on serotonin receptors or serotonin reuptake mechanism. Certain algorithms have been developed to help establish the diagnosis of serotonin syndrome (the Hunter's criteria, Sternbach's criteria etc.) but they may not always be applicable in cases of an atypical drug involved. In the case of intentional ingestion one must not solely rely on the information received from the patient. A good computerized interface between the GP, the specialist from the community and the hospitals, holding a fully updated chart regarding the patient's medical problems and current medications in use, may be helpful in early diagnosis and treatment of patients after suicide attempts by ingesting an OD of their therapeutic drugs.

## Asthma and the condition of cardiovascular system in young male

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**Objectives:** The problems of co-existing of different diseases, including bronchial asthma (BA) and cardiovascular disorders are widely discussed in recent scientific publications. BA is not considered to be a risk factor of progressing atherosclerosis on one hand, but seems to interfere and remodel heart and vessels – on the other, especially according to the “metabolic syndrome concept”. The aim of the investigation – to evaluate some heart and vessel parameters, serum lipids, C-reactive protein, fibrinogen and complete blood count indices (CBC) in patients with different stages of bronchial asthma.

**Methods:** We investigated 18 male with intermittent asthma (aged  $18,9 \pm 1,1$  years, BMI –  $23,2 \pm 3,7$  kg/m<sup>2</sup>) and 16 male with moderate persistent asthma (aged  $21,8 \pm 7,4$  years, BMI –  $22,1 \pm 3,6$  kg/m<sup>2</sup>). There were no significant differences in age, BMI, asthma duration and heredity, smoking history in groups. Diabetes, neoplasms, acute infectious diseases were excluded. We performed heart ultrasonography and duplex scanning of extracranial vessels by “General Electric Vivid 7” with particular attention to the measuring of epicardial fat, intima-media and adventitia thickness. Laboratory tests included CBC, serum lipids, C-RP and fibrinogen. The comparative and correlative analysis were performed, the results are presented in  $M \pm \delta$  and consider to be significant if  $p < 0,05$ .

**Results:** The epicardial fat thickness was  $1,2 \pm 0,04$  mm in the 1st group and  $1,7 \pm 0,08$  mm – in the second ( $p = 0,11$ ). Intima-media thickness remained within normal in the 1st group ( $0,5 \pm 0,02$  mm) and was significantly higher in the second group ( $0,7 \pm 0,07$  mm,  $p = 0,04$ ). The adventitia thickness was  $0,4 \pm 0,02$  mm and  $0,5 \pm 0,01$  mm correspondingly ( $p = 0,04$ ). Besides, there was a direct correlation between the number of eosinophil cells and adventitia thickness in both groups ( $r = 0,61$ ,  $p = 0,03$  and  $r = 0,72$ ,  $p = 0,04$ ). All the laboratory tests remained within normal conditions, but the level of CRP, very low density lipoprotein (VLDL) and triglycerides

(TG) were significantly higher in the 2nd group. There were no significant differences in other echo-indices between patients from researched groups.

**Conclusions:** Considering higher adventitia and intima-media thickness in patients with persistent BA, we suggest that this remodeling depends on the severity of the obstruction. These findings, together with higher CRP, VLDL and TG levels, may indicate an early risk of carotid atherosclerosis in asthmatic patients.

## Hypotension, even an important clinical sign, is not associated with imagery severity in patients with acute pulmonary embolism

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**Objectives:** Hypotension is a frequent presentation of PE. Aim of the study was to evaluate if there is any correlation between hypotension and thrombus localization in different segments of pulmonary artery tree in patients with acute pulmonary embolism.

**Methods:** This is a prospective study of 47 patients with pulmonary embolism, aged 43-89 years old (31-females). All the patients were admitted at Mother Theresa University Hospital, Tirana, Albania, during 2012–2014, 12 of them presented with hypotension (25.5%). We evaluated the presence of hypotension ( $< 90/60$  mmHg) at admission in correlation with the thrombus localization in pulmonary artery tree. The patients were evaluated with contrast CT and divided in 4 groups: group 1 with hypotension and central pulmonary artery embolism with pulmonary infarction, group 2 with hypotension and secondary and tertiary pulmonary arteries embolism with pulmonary infarction, group 3 with central pulmonary artery embolism without pulmonary infarction and group 4 with hypotension and secondary and tertiary pulmonary arteries embolism without pulmonary infarction. Statistical analysis was performed through binary logistic regression analysis. For each variable was estimated odds ratio (OD) and confidence interval (CI) 95%.

**Results:** From all the patients, 12 pts (25,5%) presented with hypotension. Through binary logistic regression analysis, is not evidenced a statistically significant correlation between hypotension and PE central pulmonary artery with pulmonary infarction [OD 2.55, CI 95%: 0.95-13.22], PE of the secondary and tertiary pulmonary arteries with pulmonary infarction [OD 0.78, CI 95%: 0.047-13.22], PE of the central pulmonary artery (without pulmonary infarction) [OD 0.37, CI 95%: 0.10-1.34] and PE of the secondary and tertiary pulmonary arteries (without pulmonary infarction) [OD 0.94, CI 95%: 0.21-4.25].

**Conclusion:** Hypotension is a frequent presentation of the pulmonary embolism, but it does not correlate importantly with the localization of thrombus in different segments of pulmonary arteries.

## Syncope is correlated with systolic dysfunction of right ventricle in patients with acute pulmonary embolism

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**Objectives:** Syncope is not an uncommon clinical presentation of pulmonary embolism (PE). The aim of the study was to evaluate if there is any correlation between syncope (as clinical severity index) with right ventricle systolic dysfunction (as echocardiographic index of poor prognosis) and pulmonary systolic arterial pressure (PsAP) at the moment of diagnosis of acute PE.

**Methods:** A prospective evaluation of 47 patients, age 43-89 years old (31- women) diagnosed with acute pulmonary embolism. Patients were admitted at Mother Theresa University Hospital, Tirana, Albania during 2012-2014. Pulmonary embolism was diagnosed by clinical, echocardiographic and contrast CT. Data analysis was performed with SPSS statistical package, version 20 (Statistical Package for Social Sciences). It was considered significant values of  $p \leq 0.05$ .

**Results:** From 47 pts, 7 pts (15%) presented with syncope. In this group of patients, pulmonary systolic arterial pressure, right ventricle diameter (RVD) and TAPSE were analyzed. The medium value PsAP was  $(41.2 \pm 2.2 \text{ mmHg})$ , RVD –  $40.3 \pm 3.0 \text{ mm}$  and TAPSE –  $12.9 \pm 1.3$  in patients with syncope. It is seen an important statistical correlation between syncope and right ventricle systolic function (TAPSE) ( $p < 0.001$ ). Although there was no correlation of PsAP ( $r = 0.335$ ,  $p = 0.35$ ) and RVD ( $p = 0.82$ ) with the presence of syncope in the analyzed group, that was unacceptable result due to probably low systolic right ventricle function.

**Conclusions:** Syncope is a feared clinical sign of pulmonary embolism. Patients with acute PE and syncope are associated with a low right ventricle systolic function (low TAPSE values). Once again, demonstrating the importance of multimodality evaluation of clinical and echocardiographic signs of poor prognosis of patients with pulmonary embolism.

## Occurrence frequency and development peculiarities of chronic kidney disease at patients with chronic obstructive pulmonary disease

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**Objective:** To study the frequency of occurrence, reveal peculiarities of chronic kidney disease (CKD) in patients (pts) with chronic obstructive pulmonary disease (COPD).

**Material and Methods:** Researches with the study of renal function, ERF were conducted in 286 patients with COPD. According to criteria GOLD (2013) Group A was in 17.1%, Group B – in 45.1%, Group C – at 37.8% pts. Patient age was  $66,2 \pm 9,4$  years, including men – 68.9%. Exclusion criteria were: IHD, AH II-III degree, diabetes, heart defects, atrial

fibrillation, chronic pulmonary heart, decompensation stage CHF of FC III and IV.

**Results:** Due to the criteria of the National guidelines for CKD (2011) CKD was diagnosed in 69 (24.1%) pts. Creatinine level was  $109,4 \pm 9,8 \text{ mmol/l}$ . Significant impairment of renal excretory function of nitrogen – at 15%. A correlation between the duration of hospitalization and creatinine level detected ( $r = 0,32$ ;  $p < 0.001$ ). Glomerular filtration rate (GFR) (by CKD-EPI) was  $88,7 \pm 6,2 \text{ mL/min/1,73m}^2$ , sustained decrease of GFR  $< 60 \text{ mL/min/1,73m}^2$  were detected in 11,9% pts. At GFR over  $60 \text{ mL/min/1,73m}^2$  persistent proteinuria ( $> 30 \text{ mg/dL}$ ), revealed in a random urine samples doubly for 3 months and more, and increased echogenicity of the cortex (by ultrasound) were detected. CKD stage I – in 34.8% pts, II – in 20.3%, III – in 29%, IV – in 14.5%, V – in 1 patient.

**Conclusions:** Disturbances of functional condition of kidneys are detected in every fourth patient with COPD. Presence of the general pathogenesis (systemic inflammation, endothelial dysfunction) forms interactions aggravating impact of COPD on the urogenital system by detecting changes at prenosological stage that needs further study.

## Pulmonary complications in intravenous drug users

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**Objective:** To study the features of pulmonary complications in intravenous drug users (IDUs).

**Material and methods:** Among 72 IDUs (66 males, mean age  $33,6 \pm 4,9$  years) 60 (83,3%) were diagnosed with HIV, 58 (80,6%) – HCV and 18 (25%) – tuberculosis (TB). The main types of using drugs were opiates and amphetamine.

**Results:** More commonly were diagnosed: septic pulmonary embolism  $n = 23$  (31,9%), if there are signs of acute thrombophlebitis of the proximal veins, as evidenced by ultrasound and/or CT scan and febrile illness (86%); pleuritic chest pain (36%), 19/22 (86%) had bacteremia with staphylococcus aureus. All patients had peripheral nodular lesions on chest CT scan; systemic sepsis and severe pneumonia  $n = 21$  (29,2%), criteria for severe CAP IDSA/ATS and ARDS as manifestation of the multisystem organ failure syndrome; non-severe CAP,  $n = 17$  (23,6%) with HIV and  $\text{CD4}^+ > 500 \text{ cells}/\mu\text{l}$  and respiratory dysfunction to severely reduced DLCO of  $\leq 60\%$  ( $n = 11$ ); PCP,  $n = 11$  (15,3%) HIV infected with  $\text{CD4}^+ < 200 \text{ cells}/\mu\text{l}$ , copies of HIV RNA  $> 100,000$  per ml, leukopenia. The most frequent clinical manifestations were fever ( $n = 66$ ) and dyspnea ( $n = 62$ ). Chest CT showed multiple peripheral nodules in both lungs ( $n = 54$ ), cavitation ( $n = 48$ ), focal or wedge-shaped infiltrates ( $n = 34$ ) and pleural effusion ( $n = 28$ ). Echocardiography often revealed vegetations ( $n = 48$ ). Blood cultures grew methicillin-resistant Staphylococcus aureus (MRSA) ( $n = 12$ ) and Candida ( $n = 6$ ). 28 patients died.

**Conclusions:** In assessing pulmonary disease in IDUs should be considered: septic pulmonary embolism, severe sepsis-associated pneumonia, non-severe CAP, Pneumocystis pneumonia; a significant number of complications: HIV, hepatitis, tuberculosis, right-sided endocarditis.



## Complicated pneumonia – a clinical case of cryptogenic organizing pneumonia

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**Introduction:** Organizing pneumonia (OP) is defined histopathologically by intra-alveolar buds of granulation tissue. When no cause or underlying context is found for OP, COP is diagnosed.

**Case report:** We report the case of a 45 years old male, ex-smoker; without allergies, known diseases or chronic medication; admitted to the emergency department with high fever, malaise, dyspnea and dry cough. Chest radiography (CR) showed a discrete infiltrate of the left inferior lobe (LIB) and the patient was discharged with amoxicilin/clavulanate prescription. Three days later he returns to the hospital with respiratory failure and hemoptoic sputum; CR showed new infiltrates in the LIB and hilar regions and is hospitalized with CAP. Due to his progressive clinical and analytical worsening, thoracic tomography (CT) was performed, revealing multiple consolidations and ground glass opacities (GGO) more pronounced in the lower lobes, suggesting infectious process. Despite broad spectrum antibiotics and non invasive ventilation, the patient clinical condition deteriorated with admittance to the intensive care unit (ICU) due to extensive bilateral pneumonia with ARDS and severe respiratory failure. No vaporizable infectious agent was identified. Invasive ventilation was not needed. In all this process the patient completed course of broad spectrum penicillin, macrolid and linezolid with clinical improvement. Few days after ICU discharge, dyspnea complaints increased and hemoptoic sputum appeared. High-resolution contrasted CT excluded pulmonary embolism and showed multiple bilateral alveolar opacities, mostly in the lower lobes, some with air bronchogram and imagiological worsening of the GGO suggesting COP. Adequate COT was started with clinical improvement. The patient was discharged after 20 days and COT tapering was initiated. After 2 weeks a new onset of respiratory failure led to new hospitalization. TC showed scattered bilateral infiltrates and bronchiectasis and worsening of the inferior left lobe infiltrates albeit a global favorable evolution. COT was increased with improvement. 8 months later the patient was fully recovered and COT was suspended without relapse.

**Discussion:** It is of the outmost importance to avoid delays in the diagnosis of COP due to its resemblance with recurrent pneumonias with resulting elevated morbidity. Rapid clinical and imaging improvement is obtained with COT but relapses are common with tapering or stopping treatment.

## Obstructive sleep apnea and cardiovascular risk factors – characterization of a sample

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**Objectives:** Obstructive sleep apnea (OSA) is defined by the coexistence of excessive daytime sleepiness and at least 5

episodes of cessation of airflow (obstructive cause) per hour, during sleep. This disorder is quite prevalent, estimated to affect 4% of men and 2% of women in Portugal, and is associated with the increased prevalence of cardiovascular events and traffic accidents, among other consequences. The main objective was to carry out epidemiological and cardiovascular risk factors characterization of the patients followed in consulting of a central hospital.

**Methods:** Retrospective analysis, including 1 in each 3, of patients followed in sleep apnea respiratory medicine consultation of a central hospital during 4 months, September-December 2014.

**Results:** We evaluated a total of 143 patients, 110 males (76.9%) and 33 females (23.1%). The mean age was 58 years, ranging between 27 and 87 years, with a median of 59 years and a standard deviation of 11. The entire sample had confirmed diagnosis of OSA and 96 patients had indication for treatment with non-invasive ventilation. It was evaluated the prevalence of cardiovascular risk factors in the sample considered: 121 (84,6%) patients were obese (BMI > 30 kg/m<sup>2</sup>); 72 (50.3%) patients had arterial hypertension; 43 (30.1%) patients had metabolic syndrome; 40 (30%) patients had dyslipidemia; 28 (19.6%) patients had type 2 diabetes mellitus; 13 (9.1%) patients had cardiovascular disease and 2 patients had stroke. In many situations coexisted more than one comorbidity.

**Conclusions:** Most of the referred patients were male and had cardiovascular risk factors, corroborating described in recent literature. OSA is associated with significant morbidity and mortality largely attributed to risk factors so these should be identified early and treated improving the outcome of this disease. In contrast, the presence of cardiovascular risk factors can alert for suspected OSA and signs and symptoms of sleep disturbance should be investigated, and sleep study (if indicated) should be requested. In patients with persistent hypertension, OSA should be excluded.

## Persistent non-productive cough and hoarseness as the sole initial presentation of pulmonary tuberculosis

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**Introduction:** Pulmonary tuberculosis (TB) remains a major public health problem and it must be included in differential diagnoses even subtle clinical presentations.

**Case report:** Female, 52 years old, works as hospital cleaning assistant. She was initially observed by the family physician by nonproductive cough and hoarseness having been treated with antihistamine and proton pump inhibitor unsuccessfully. By persistence of symptoms for 6 months, she presented to the Emergency Service. She denied fever, weight loss, nocturnal excessive sweating, hemoptysis, dyspnea or chest pain. She described contact with a patient diagnosed TB in the previous year. At that time, she was called to screening that was negative. On examination the patient was febrile, with audible crackles at the apex of the right upper hemithorax by lung auscultation. Remaining physical examination it was normal. Laboratory results

revealed elevated inflammatory parameters. Radiologically there was extensive consolidation in the right upper lobe (RUL) with central cavitation areas, and several cavitated lesions in the upper segment of the right lower lobe (RLL) and smaller in posterior segment of the RLL and upper segment of the left lower lobe. It was observed micronodular centrilobular infiltrate like "tree-in-bud" and small scattered foci of consolidation. As there was an imagiologic suspicion of TB, a collection of sputum was performed for acid fast bacteria (AFB) smear and culture. AFB smear was positive and the patient initiated treatment with isoniazid, rifampicin, ethambutol and pyrazinamide while culture results for drug susceptibility testing.

**Conclusion:** In respect to subtle clinical presentations and cavitary pulmonary disease, clinicians must be aware of differential diagnosis with TB.

## Non-low risk pulmonary embolism patients' allocation

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**Background:** Non-low risk patients' allocation constitutes a difficult challenge in daily hospital management. The current approach to critical (high risk) patients implies their admission in Intensive Care Units (ICUs), associated with higher fund consumption. To overcome this problem, the concept of 'intermediate care', 'high-dependency', 'step-up/down' or 'progressive care' units appears, leading to the creation of units where patients with more severe conditions (needing more care/supervision than a General Ward [GE]) can be managed. Non-low risk pulmonary embolism (PE) constitutes a perfect example of patients that demand a higher level of care, non-necessarily driven in an ICU.

**Objectives:** Characterization of the patients admitted in an Intermediate Care Unit (IntCU) with the primary diagnosis of PE during a 30-month period; study the patients allocation flow during entire hospital stay; analyze the economical impact; document the mortality rates; characterize the patients submitted to thrombolysis.

**Methods:** A retrospective study of patients with acute PE consecutively and primary admitted into a Portuguese tertiary Medical Center IntCU. Period of inclusion located between June 2012 and December 2014. Student t-test was used in the comparison of continual/quantitative variables. The value of Chi-square test was applied in the comparative analysis of categorical/qualitative variables. A p value <0.05 was considered statistically significant. Overall survival times (after the diagnosis) were analyzed using Kaplan Meier method.

**Results:** Included 52 patients with the primary diagnosis of PE, being the majority female (60.4%, n=32) and the median age 68.0 years (CI 95%, 58.1-68.5 years). In terms of early mortality risk stratification there was a predominance of non-high risk events (n=41, 78.8%). Intravenous thrombolytic therapy was performed in 21 patients (40.4%). The hemorrhagic complication rate was 33.3% (n=7/21), almost all classified as minor complications. None of the cases needed to "step-

up" the level of care. Readmission after discharge (to a lower level of care) was not verified. The median length of stay in the IntCU was 2.0 days (CI 95%, 1.9-3.0 days). There were no differences in the median length of stay between the different early mortality risk groups (high-risk versus intermediate risk, p=0.324; intermediate risk versus low-risk, p=0.442) concerning EV thrombolysis. The median length of (total) hospital stay was 8.0 days (CI 95%, 7.9-10.2 days), without differences between the different early mortality risk groups. In-hospital mortality rate was 5.8% (n=3). Estimated direct fund saving was superior to 20.000€ (considering only hospitality expenses) during the study period.

**Conclusions:** IntCUs constitute a valuable resource in hospital management. PE was found to be a good example: there wasn't worst outcomes (in-hospital mortality rate was 5.8%), security/adequate care (no need to step-up the level of care) were observed and consequent direct fund saving potentiated.

## A retrospective study of tuberculous uveitis

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**Background:** Tuberculosis (TB) is a disease caused by infection of *Mycobacterium tuberculosis* (MT) that can occur in many organs, including the eye.

**Methods:** The authors report the results of a 3-year retrospective study where analyzed 7 cases of uveitis. 5 of these had criteria for possible TB uveitis: with anterior, intermediate or posterior uveitis and one of the following: positive IGRA (in immunocompetent) or positive TST and IGRA (in immunocompromised); evidence of sequelae or lesions suggestive of active TB in thorax radiography or computed tomography (CT); pulmonary or extrapulmonary TB (with positive direct exam or culture to MT), after exclusion of other causes, such as autoimmune diseases, sarcoidosis, infectious and neoplastic diseases.

**Results:** It was observed 9 unilateral and 4 bilateral uveitis. Anatomically 5 anterior, 4 intermediate and 3 posterior uveitis were observed. All cases initiated antibacilar treatment and were reassessed by ophthalmology after 2 months of treatment (3 patients were not treated with ethambutol because of the difficulty to differentiate between adverse events and progression of disease). All patients showed improvement of eye injuries and completed treatment. Two cases are still under treatment with isoniazid, rifampicin and pyrazinamide. There was only one case of non-tuberculous granulomatous uveitis, clinically with photophobia, red left eye and synechia, treated with only corticotherapy. 3 patients had sequelae or lesions suggestive of active TB on chest CT, but no patient had pulmonary TB confirmed.

**Discussion:** The disease can manifest itself at any age, ranging from 12 to 74 years, verifying a higher incidence above 70 years. Both genders were equally affected. Generally, ocular TB and pulmonary TB have the same treatment. In the setting of choroidal TB, lesions can resolve completely. Retinal TB is managed with antituberculous therapy together with systemic corticosteroids. In fact, in cases in which a lesion is present near the macula or optic disc, administration of concomitant steroids

is mandatory to save these delicate structures from rebound inflammation that may occur with antituberculous therapy alone. Development of neovascularization warrants photocoagulation of the retina. In present study, a presumed diagnosis of ocular TB is made and clinical response to antituberculous therapy further supports that, since isolation of bacilli from the ocular tissues was not achieved.

## Community-acquired necrotizing pneumonia caused by *Pneumococcus*: an unpredictably exuberant case

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**Introduction:** This case describes the diagnosis, evolution and treatment of a non-fatal case of necrotizing pneumonia due to community-acquired *Pneumococcus* (CAP) in a 59 years old male patient.

**Case report:** We present a case of a 59 years old male with a history of hypertension, diabetes mellitus, dyslipidemia and smoking habits. He was admitted to the emergency room with increasing dyspnea associated with wheezing, productive cough with purulent sputum and left pleuritic chest pain. Objectively he presented polypnea, hypertension, tachycardia and was subfebrile. In the pulmonary auscultation revealed scattered ronchi and increased expiratory time. Analysis revealed CRP 344 mg/dL, leukocytosis with neutrophilia and acute kidney injury. Chest X-ray showed a heterogeneous hypotransparency in the left hemithorax and urinary antigens were positive for *Pneumococcus*. Arterial blood gas test indicated hypoxemic respiratory failure and hyperlactacidemia. Once pneumococcal CAP was assumed, he began empirical antibiotic therapy with amoxicillin/clavulanic acid and azithromycin. Due to clinical worsening with multiple organ dysfunction (respiratory, neurological, renal, cardiovascular and hematological), he was transferred to intensive care unit, intubated and ventilated. Blood cultures isolated *Streptococcus pneumoniae*. Computed tomography image was compatible with necrotizing pneumonia with cavitary lesions and areas of pulmonary hepatization. Bronchoscopy had no macroscopic changes and bronchoalveolar lavage was non-recoverable. During his prolonged hospitalization antibiotic treatment required several adjustments based on antibiograms, completing 6 weeks of treatment. He had a favorable clinical evolution and was transferred to Intermediate Care Unit and then to internal medicine ward. At discharge, there was no hypoxemia, although with severe necrotizing sequelae. He was referred to Pulmonology and Thoracic Surgery evaluation and awaits decision for upper left lobectomy.

**Discussion:** Necrotizing pneumonia is a rare complication of CAP, characterized by the rapid development of the necrosis within infected lung tissue and rise of necrotic foci in consolidated areas. *S. pneumoniae* is one of the most common causative agents. This disease is clinically characterized by respiratory failure and rapid development to septic shock with high mortality rate.

## Effects on right ventricular size and function of riociguat administration in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

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**Objectives:** Riociguat is a soluble guanylate cyclase stimulator approved for pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTPEH). The aim of this study was to evaluate the change of right heart size and function assessed by echocardiography during long-term treatment with riociguat.

**Methods:** We assessed patients who started riociguat treatment (1.0-2.5 mg tid) within the trials PATENT, PATENTplus, EAS and CHEST and continued for 3-12 months. Echocardiography, 6-minute walking distance (6MWD) and further clinical parameters were analyzed at baseline, after 3, 6 and 12 months. Right heart catheterization was performed at baseline and after 3 months. For missing data we performed the last and baseline observation carried forward (LOCF, BOCF) method as sensitivity analyses.

**Results:** 39 patients (21 PAH, 18 CTPEH, mean pulmonary arterial pressure  $43 \pm 2$  mmHg, PVR  $600 \pm 43$  dynes/sec/cm<sup>-5</sup>, 56.4% treatment-naïve) were included. Mean right ventricular (RV) area significantly decreased after 3 ( $-2.1 \pm 3.9$  cm<sup>2</sup>, equals  $-7.4 \pm 15.3\%$ ,  $p=0.002$ ), 6 ( $-4.2 \pm 3.2$  cm<sup>2</sup>, equals  $-16.1 \pm 11.5\%$ ,  $p<0.001$ ) and 12 months ( $-5.9 \pm 4.6$  cm<sup>2</sup>, equals  $-22.1 \pm 14.2\%$ ,  $p<0.001$ ) compared to baseline. Right atrial area significantly decreased after 12 months ( $-3.5 \pm 4.1$  cm<sup>2</sup>, equals  $-16.8 \pm 19.2\%$ ,  $p<0.001$ ) and TAPSE significantly improved after 6 ( $2 \pm 4.7$ , equals  $12 \pm 25.8\%$ ,  $p=0.025$ ) and 12 months ( $3.6 \pm 5.4$ , equals  $21 \pm 29.6\%$ ,  $p=0.002$ ). Furthermore, RV wall thickness and 6MWD significantly improved after 3, 6 and 12 months ( $p<0.05$ ). Invasive hemodynamics significantly improved after 3 months. Both LOCF and BOCF showed similar significance and lower effect sizes.

**Conclusions:** Long-term treatment with riociguat significantly reduced right heart size and improved RV function in PAH and CTPEH. Further prospective studies are needed to confirm these results.

## Chylothorax – case report

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**Introduction:** Pleural effusions can develop as a result of many different pleuropulmonary or systemic disorders. Chylothorax is caused by disruption or obstruction of the thoracic duct or its tributaries that result in leakage of chyle into the pleural

space. The fluid typically has high triglyceride content and often a milky white appearance. The most common etiology is traumatic (surgery or trauma). The non-traumatic causes are malignancy, idiopathic (5 to 10%) and other.

**Case report:** 82 years old man, with history of arterial hypertension, prostate cancer (follow up after 1 year without disease) and alcoholic chronic liver disease, with portal hypertension and esophageal varices, Child-Pugh A. He was diagnosed with pleural effusion on October of 2014. At that time he referred dyspnea, without any other symptoms. The physical examination showed decreased breath sounds on the right and the chest radiograph revealed a hypotransparent image on the right hemithorax. Thoracentesis was performed and confirmed the presence of a milky fluid with high triglyceride content (366 mg/dL). There was no history of surgery or trauma. We excluded portal thrombosis, tuberculosis, heart failure, progression of prostate cancer and lymphoproliferative disease. Thorax and abdomen CT only revealed a pleural effusion and ascites. Liver biopsy showed chronic hepatitis and pleural biopsy showed fibrosis and chronic inflammation. The patient remained without triglyceride in his diet since November and still had high triglyceride content on pleural fluid. On December a lymphoscintigraphy was performed but didn't show any leakage. At this time the patient had a chest tube with a pleural drainage over 1000 cc/day. We presented the patient to the thoracic surgery center and they suggested a talc pleurodesis. So we started on parenteral nutrition. When the drainage was <100 cc/day we decided to do a talc pleurodesis without success. Once again we presented the patient to the thoracic surgery center and they decided to do a thoracic duct ligation. The chest tube was removed after 3 weeks. Two months later the patient is asymptomatic. Chest radiography with a small pleural effusion. He remains with dietary exclusion of long-chain triglycerides.

**Discussion:** This clinical case reports an idiopathic chylothorax. This is a rare type of pleural effusion that in most cases is caused by trauma or surgery. In this patient there was no history of any of them and there was no leakage found or malignant disease.

## Characteristics of patients with chronic obstructive pulmonary disease admitted to a tertiary referral hospital

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**Objectives:** Chronic obstructive pulmonary disease (COPD) is a common cause for admissions to hospital in Singapore. COPD exacerbations lead to utilization of health care services. The aim is to delineate the characteristics of patients who have been admitted to a tertiary referral hospital for COPD.

**Methods:** This is a retrospective cross-sectional study. Patients with COPD were recruited between February 2012 and November 2013. Data on age, gender, ethnicity, presence of co-morbidities, COPD Assessment Test (CAT) score, presence of long term oxygen therapy, inhaler compliance, FEV1 and FEV1/FVC were collected.

**Results:** 203 patients were recruited for the study. They had a mean age of 73.1±9.9. 91.6% were male; 57.6% were of Chinese ethnicity. 22.7% had frequent hospital admissions. 70% had

significant co-morbidities, 3.9% had long term oxygen therapy. Inhaler compliance data was available for 62 of the patients, and 16.1% were not compliant. CAT score data was available for 62 patients and 71% scored 10 or more. mMRC scale was available for 40 patients and 57.5% scored 3 or more. The severity of COPD was available for 165 patients with spirometric data: 24.2% mild, 44.2% moderate and 31.5% was severe or very severe.

**Conclusions:** Patients who are admitted for COPD in a tertiary referral hospital are older and more likely to be of Chinese ethnicity. They also have the presence of significant comorbidities. They have moderately severe COPD. These findings allow us to understand the characteristics of the inpatient COPD population and help us tailor services to address their needs, such as telemedicine.

## Evaluation of a chronic obstructive pulmonary disease telehealth program to reduce healthcare utilization in a Singapore tertiary healthcare institute

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**Objectives:** Chronic obstructive pulmonary disease (COPD) is a leading cause of recurrent hospitalizations. A telehealth program to support COPD patients post discharge from the acute hospital was established in 2011. This study aims to evaluate the effects of telehealth on health care utilization and time to first hospital readmission in the 6 months post discharge.

**Methods:** This is a non-randomized control study. COPD patients were recruited between November 2012-2013. Patients who enrolled into the program were the intervention group. Patients who rejected the program formed the control group. The intervention involved 4 telephone calls made within 6 months by a telecarer. Patients were educated on COPD, smoking cessation, nutrition and had a review of CAT score. Rates of hospital admissions, emergency department visits, specialist and polyclinic visits were extracted by the study staff from patient electronic medical records. Descriptive analysis and Mann-Whitney U tests were performed. Kaplan Meier survival analysis was used to determine time to first event.

**Results:** A total of 261 patients were eligible for the program (intervention – 138, control – 65, excluded – 58). Mean age was 73.1±9.9. There were more frequent admitters in the intervention group than control group (intervention – 24.6%, control – 18.5%, p=0.3). Patients in intervention group also had more comorbidities. The mean total healthcare resource utilization (COPD-related hospital admission, A&E, SOC and polyclinic visits) was 1.1±1.9 in the intervention group and 0.5±1.0 in the control group (p=0.7). Although there were reductions in all cause, COPD related hospital admissions and A & E visits over time within the intervention group, these were not significantly more than the control group. Telehealth did not extend mean time (days) to first event (intervention – 133.1 days (95% CI 122.4-143.8), control – 143 days (95% CI 128.5-157.6), p=0.3). The results could have been influenced by selection bias of the control

group that consisted of patients who rejected the program. **Conclusions:** The study is the first report of a telehealth COPD program in South East Asia. A single intervention of telephone education and support did not reduce short term health care utilization or extend time to first event. Longer observation period and inclusion of other interventions such as medication adjustments in the program may be considered to evaluate the effects of telehealth on COPD related healthcare utilization.

## Pleural tuberculosis: a case report

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**Introduction:** Pleural tuberculosis (PT) is the second most common form of extrapulmonary tuberculosis (TB) and, in adults, it is more often associated with reactivation rather than with primary disease. PT causes pleural effusions (PE) which result from a hypersensitivity reaction to Mycobacteria and its antigens in the pleural space.

**Case report:** 77 years old man with history of atrial fibrillation and alcoholic liver disease who presented with vomiting, diarrhea, asthenia, anorexia and 10 kg weight loss for previous month. He denied cough, sputum, hemoptysis or nocturnal sweats. On clinical examination he was hypotensive, tachycardic and apyretic. Laboratory showed leukocytosis (25580/L), elevated C-reactive protein 96,6 mg/L, acute renal failure and hyperlactacidemia. Chest x-ray revealed opacity along the left hemithorax and mediastinum enlargement. Urine analysis was normal. Taking into consideration the diagnosis of acute infectious gastroenteritis he initiated ciprofloxacin and intensive fluid therapy. Besides an initial clinical improvement, the patient started complaining of dyspnea and cough with sputum and the inflammatory parameters increased. As the left chest x-ray opacity remained even after diuretic optimization and no sign of heart failure was found on ultrasound we performed a chest computed tomography which showed a left located PE, lung atelectasis and mediastinal deviation to the right. Additionally, he kept vomiting and presenting melena. Upper gastrointestinal endoscopy revealed esophageal candidiasis, stomach erosions and a duodenum lesion which biopsy was negative for neoplasm. Hepatitis C antibody and HIV were negative. Laboratory of the pleural fluid (PF) revealed an exudate dominated by polyclonal lymphocytes and adenosine deaminase activity (ADA) of 56 U/L. Neither bacteria nor Mycobacteria were isolated and no malignant cells were found on PF. Pleural biopsy revealed epithelioid granuloma with multinucleated giant cells. The patient started antituberculostatic therapy with isoniazid, rifampin, pyrazinamide and ethambutol, with a favorable clinical and laboratory response.

**Conclusions:** Clinicians should be aware that PF cultures are positive in less than 30% of the cases. The probability of PT increases when PF ADA levels >45 U/L and pleural biopsy show granulomas. The diagnosis of PT remains a challenge and most often presumptive therapy is initiated based on clinical criteria since when it is not treated there is a high risk for developing pulmonary/extrapulmonary TB in the following 5 years.

## Antiphospholipid antibody syndrome in a patient with sarcoidosis: a case report

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**Introduction:** Various autoimmune diseases have been reported to occur in patients with sarcoidosis. However, coexistence of sarcoidosis and antiphospholipid syndrome (APS) is extremely rare. Sarcoidosis is an inflammatory disease characterized by the presence of non-caseating granulomas. The disease is often multisystemic and can affect virtually every organ of the body, although the lung is most commonly affected. Other organs commonly affected are the liver, skin, and eye. APS is a disorder characterized by thrombosis and/or pregnancy loss associated with antiphospholipid antibodies.

**Case report:** We describe a clinical case of a 51 years old male, followed in our Internal Medicine consult due to prior history of obesity, arterial hypertension, dyslipidemia and sarcoidosis with multi-organ involvement (like skin, liver, lung) asymptomatic. He had no specific therapy for the past 5 years. Who presented with edema in lower limb, with no other inflammatory signals, and no history of trauma. An ultrasound study confirmed deep vein thrombosis in the right leg, specifically on posterotibial, popliteal and femoral veins. In the meantime, the procoagulant risk factors were investigated. Laboratory studies showed that levels of antithrombin III, protein S and protein C were within normal range. Homocysteine, activated protein C, factor V Leiden and prothrombin G20210A mutations were absent. On the other hand, lupus anticoagulant (LAC), anticardiolipin antibodies (ACLA) (54 U/mL) and  $\beta_2$  glycoprotein (57 UA) were found to be positive. The patient was diagnosed as APS and he fulfilled the preliminary classification criteria of APS. He was anticoagulated initially with low molecular weight heparin, and then was maintained on oral warfarin.

**Discussion:** The association of these two clinical conditions is rare and that the presence of antiphospholipid syndrome may lead to greater morbidity and mortality. Although the presences of antiphospholipid antibodies (APLA) have been reported and may be detected in sarcoidosis generally without clinical consequences, the occurrence of APS seems extremely rare. In conclusion, APS should be recognized as one of the accompanying disorders of sarcoidosis. If the thrombotic event occurs in sarcoidosis patient the presence of a concomitant APS should be considered.

## Protocolized multidisciplinary evaluation of patients presenting with interstitial lung disease: searching for underlying systemic autoimmune diseases in 247 patients

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**Objectives:** Diagnosis of an underlying systemic autoimmune disease (SAD) in patients with interstitial lung disease (ILD) is a clinical challenge. The aim of the study was to assess the usefulness of a protocolized multidisciplinary diagnostic approach search for underlying SAD.

**Methods:** A multidisciplinary clinical committee integrated by pneumologists, internists, radiologists, pathologists and thoracic surgeons have evaluated a cohort of 247 patients with ILD who were consecutively evaluated between September 2012 and March 2015 at a tertiary referral center. In all patients, a specific search of SAD including an organ-specific clinical evaluation (oral and ocular symptoms, cutaneous involvement, articular features, Raynaud's phenomenon, neuromuscular symptoms) and determination of a specific immunological panel of autoantibodies (ANA -triple tissue and Hep2 techniques-, RF, anti-centromere/Scl70, anti-CCP, anti-dsDNA, anti-Ro/Ro52, anti-La, anti-RNP, anti-Sm, anti-tRNA synthetase, anti-PM-Scl/Jo1, anti-Mi2/Ku/PI7/PI12/SRP, ANCA) were performed. All patients were subsequently discussed by the multidisciplinary committee. Diagnosis of SAD was carried out according to the fulfillment of the currently accepted classification criteria for each SAD; patients who did not fulfill the minimum criteria were classified as having an undifferentiated SAD.

**Results:** Of the 247 patients evaluated (125 men and 122 women, mean age at evaluation 65.1 years, range 20-88 years), 27 had a previously known SAD and were excluded from the analysis. After evaluation by the committee, 68 (31%) out of 227 patients had autoimmune diseases (30 were classified as undifferentiated and 38 fulfilled criteria for SAD). Positive ANA (titer >1/40) were found in 78.7% of patients and ANA Hep2 in 96.9%. After discarding equivocal results, only two autoantibodies showed a frequency >5% (7.2% for anti-Ro/Ro52 and 6.8% for RF). The most frequent underlying SAD identified were Sjögren syndrome in 17 patients (4 in association with other SAD), sarcoidosis in 15 and other SAD in the remaining 6 cases (systemic sclerosis in 2, inflammatory myositis in 2, amyloidosis in one and microscopic polyangiitis in one). Variables that were associated with the diagnosis of a new ILD-related SAD were female gender (68% vs 43% in non-SAD,  $p=0.007$ ), lower mean age (56.5 vs 67.2,  $p<0.001$ ), positive RF (16% vs 4%,  $p=0.011$ ), positive Ro/Ro52 autoantibodies (30% vs 2%,  $p<0.001$ ), any positive specific autoantibody (47% vs 27%,  $p=0.019$ ) and positive ANA using Hep2 substrate classified as high or very high (50% vs 28%,  $p=0.017$ ). Multivariate analysis adjusted by age and gender identified a younger age ( $p<0.001$ ) and anti-Ro/Ro52 ( $p<0.001$ ) as independent variables associated with the diagnosis of an underlying undiagnosed SAD.

**Conclusions:** In patients with ILD, a protocolized multidisciplinary approach identified that nearly 20% of patients fulfilled classification criteria for a well-characterized SAD (overwhelmingly sarcoidosis and Sjögren syndrome), while an additional 14% were diagnosed with undifferentiated SAD. The diagnostic role of using a wide panel of autoantibodies in a large, unselected population of patients with ILD was poor, except for RF, Ro/Ro52 autoantibodies and Hep2-ANA at high/very high titers.

## Superior vena cava syndrome as a first presentation of non-small-cell lung cancer in a non-smoker: case report

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**Introduction:** Superior vena cava syndrome (SVCS) results from the obstruction of blood flow through the SVC into the right atrium and it can be caused by invasion or external compression of the SVC.

**Case report:** A 76 years old man presents with a 2-year history of loss of appetite and 30 kg of his body weight, edema of the lower limbs for 3 months, neck and bilateral upper limb swelling for 3 weeks and progressive dyspnea on exertion for the past week. The patient came to the emergency department presenting anasarca. Past medical history of arterial hypertension (AH), diabetes mellitus (DM) type 2, chronic kidney disease (CKD), panretinal photocoagulation for proliferative diabetic retinopathy and passive smoking for 30 years. Poor medication adherence. On physical examination, he was hypertensive, acyanotic but with general pallor, face, periorbital, neck, and marked left upper limb edema with visible collateral veins on his abdomen. Heart and lung examination revealed no abnormalities. Routine laboratory tests were not striking showing just a decline of patient's renal function. Chest computed tomography (CT) demonstrated a consolidation without air bronchogram in the apical segmental bronchus (ASB) of the right lower lobe, an adjacent parenchymatous nodule of 3 cm and moderated pleural effusion bilaterally. Head CT without irregularities. Echocardiography with normal global left ventricular systolic function, no pericardial effusion, normal pulmonary artery systolic pressure. Bronchoscopy showed occlusion of right superior ASB by a bleeding multilobulated endobronchial lesion with necrotic areas and collection of the bronchoalveolar lavage and transbronchial biopsy were performed. Immunolabelling presented intense and diffuse positivity for CK5/6 and P63, and local for CD56. CK7 and TTF1 were negative. Histomorphological and immunohistological examination indicated epidermoid carcinoma moderately differentiated. Cytologic examination suggestive of non-small-cell carcinoma, probably an epidermoid carcinoma.

**Discussion:** The most common malignant causes are non-small-cell lung cancer with approximately 50% of cases. The investigation should check for brain metastases, major compression of the tracheobronchial tree or of the heart. Management should include relief of the symptoms of obstruction.

## Microbiological characteristics of pneumonia in immunocompromised patients with hematologic malignancies

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**Objectives:** In the 21st century pneumonia still remains an important medical and social problem. Implementation of standardized protocols for diagnosis and treatment of

pneumonia from the standpoint of evidence-based medicine into medical practice allowed achieving some success. Patients with hematologic malignancies due to adverse drug effects, which lead to defects in humoral and cellular immunity, have a significantly greater chance of developing pneumonia. Almost 50% of patients with hematologic malignancies receiving high-dose polychemotherapy fall ill with pneumonia. However, the mortality rate is quite high, reaching up to 28%. That is why, nowadays, the research interest in issues of microbiological diagnostics and treatment of pneumonia in patients with impaired immunity and hematological diseases is scientifically grounded, due to the peculiarities of microbiological diagnostics as well as to a high percentage of deaths and a significant increase in the cost of treatment. The aim of this work was to determine the microbiological characteristics of pneumonia in patients with hematologic malignancies and impaired immunity.

**Methods:** A total of 324 (110 females and 214 males) immunocompromised patients with hematologic malignancies had been evaluated. The age of patients ranged from 32 to 67 years. The diagnosis of hematologic malignancies and pneumonia was proved according to generally accepted clinical and morphological criteria. Bronchoalveolar lavage fluid, obtained by flexible fiber-optic bronchoscopy, had been used for identification of microorganisms.

**Results:** According to the results of microbiological studies in immunocompromised patients with pneumonia and hematologic malignancies, the microbiological features of lower respiratory tract infections, depending on the time and place of occurrence had been defined. Approaches to the definition of pneumonia as "community-acquired" and "nosocomial", taking into account the results of microbiological tests, are relevant when choosing antibiotics for the initial treatment of pneumonia in patients with hematologic diseases. Main microbiological characteristics were – bacterial-bacterial and bacterial-fungal mixed infections. Association of bacterial pathogens had been identified in 31,3% and 43,4% of case studies. Association of bacteria with fungal flora had been established in 28,1% and 42,4% of patients.

**Conclusions:** Gram-negative non-fermentative bacteria had been playing an important role as an etiologic agent of pneumonia in immunocompromised patients with hematologic malignancies, regardless of the time and place of occurrence. It is important to consider the results of microbiological testing outlined above in choosing the best initial antibacterial scheme in the treatment of pneumonia in patients with hematologic malignancies. Optimization of antibiotic treatment of pneumonia in patients with hematologic malignancies and impaired immunity according to the results of the microbiological tests is an urgent problem and requires further research.

### **Pleural effusion: characteristics and etiology in a third level hospital**

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**Objective:** To describe the patients' characteristics and the pleural effusion (PE) etiology in a third level hospital.

**Methods:** Revision of the medical histories of adult patients, to whom a diagnostical thoracentesis for the analysis of pleural fluid (PF) was made during an 8-months period.

**Results:** 137 patients with PE were included in the study, with an average age  $63 \pm 17$  years (21-99), 59% men.

**Background:** neoplasm 24%, heart failure 20%, pneumonia 13%. The most frequent symptoms were: dyspnea 61%, chest pain 42%, non productive cough 25%, and productive cough 20%. 99% of PE fulfilled at least one of Light's criteria for exudate: proteins  $>3$  g/l – 79%, proteins pleural fluid/serum  $>0,5$  – 76%, LDH  $>2/3$  normal upper limit for serum – 75%, LDH PF/serum  $>0,6$  – 82%, albumin gradient  $<1,2$  – 48%, proteins gradient  $<3,1$  – 76%. Gram's stain was positive in 6%, culture in 9%, stain and culture for mycobacterias in 3%, cytological examination was positive for neoplasm in 21%. Other diagnostic tests were also used: thoracic CT 70%, abdominal CT 45%, ultrasound 24%, bronchoscopy 23%, Mantoux test 12%, and pleural biopsy 7%. Etiology of PE: neoplasm – 29% (40% – lung cancer), parapneumonic/empyema – 25%, heart failure – 11%, multifactorial – 5%, tuberculosis effusions – 4%, others diagnoses – 14%, undiagnosed – 12%.

**Conclusions:** The choice of diagnostic tests and the interpretation of their results are related with the pre-test probability of the different PE causing diseases, which is why it is of great interest to know the characteristics of patients as well as the frequency of the different PE etiologies in our environment. Neoplasms (mainly pulmonary) and bacterial infection (parapneumonic effusion/empyema) are the most common causes of PE that needs evaluation in the hospital environment. Most of the PEs studied biochemical have characteristics of exudative, indirectly indicating that the diagnosis of PE secondary to heart failure can be safely done based on clinical assumptions.

### **Pulmonary toxicity secondary to rituximab: a rare but relevant complication**

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**Introduction:** Rituximab has a well-established role in the treatment of diverse hematologic disorders, displaying an acceptable safety profile. Nevertheless, some complications, such as pulmonary toxicity in the form of interstitial lung disease (ILD), though rare, deserve attention due to their potential mortality/morbidity.

**Case report:** The authors describe a case of a 78 year-old female with a history of follicular lymphoma submitted in the previous 3 months to R-CHOP chemotherapy scheme. She was admitted to the emergency department with a 2-week long presentation of fever and progressively aggravated dyspnea and cough with mucous sputum. She had already completed a 7-day course of levofloxacin. On physical examination she was dyspneic, with accessory respiratory muscles usage. Arterial blood gas analysis with high-flow face mask revealed severe hypoxemic respiratory insufficiency with a PO<sub>2</sub>/FiO<sub>2</sub> ratio of 140. Chest X-ray exhibited bilateral pulmonary infiltrates. Laboratorial examination displayed an elevated C-reactive protein (102 mg/L). Negative

PCR for influenza virus. A diagnosis of healthcare associated pneumonia was assumed, and antibiotherapy with a carbapenem instituted. Despite maintained afebrile, there was no resolution of the respiratory insufficiency. A transthoracic echocardiogram exhibited severe pulmonary hypertension (absent in a previous exam from 4 months before), raising the hypothesis of pulmonary embolism. Thoracic angio-CT showed no signs of embolism but displayed multiple and diffuse parenchymal areas of mosaic pattern and ground glass attenuation (not present in studies previous to the chemotherapy). Facing these findings, the hypothesis of ILD secondary to rituximab was considered. To further exclude an infectious etiology a bronchofibroscopy with bronchoalveolar lavage (BAL) was performed. All microbiologic samples (blood, sputum, BAL) were negative, including for *Pneumocystis jirovecii*, leading to antibiotherapy suspension and institution of corticotherapy (methylprednisolone 62.5 mg tid). Rapid resolution of the respiratory insufficiency was verified (in 48 h), with no need for supplemental oxygen at discharge, under a corticoid-tapering regimen.

**Discussion:** The potential mortality increases the relevance of being acquainted with this complication. The clinical similarity with more frequent etiologies of respiratory distress stresses the importance of keeping a high index of suspicion.

## Measurement of dynamic of hyperinflation, pulmonary ventilation and dyspnea during 6-minute walk testing in patients with COPD

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**Objectives:** Limitation of tolerance to physical exercise is one of the important functional disorders in patients with COPD. Increased ventilation demand in patients with limitation of air flow during 6-min. walk testing (6MWT) leads to formation of air traps and dynamic hyperinflation. Development of dynamic hyperinflation leads to onset of dyspnea during physical loads. Functional parameters, reflecting lung hyperinflation are assessment of inspiration capacity (IC). The aim of this study was to assess dynamic hyperinflation and lung ventilation in patients with COPD during 6MWT, to reveal correlated connection with dyspnea and tolerance of patients to physical exercise.

**Material and methods:** Male patients with COPD (n= 38) II-IV degree of severity (FEV1 45,1±6,4% predicted) [mean±SEM] were enrolled in the study. Control group consists of male patients without COPD (n= 35). Equipment Spiropalm 6MWT (Cosmed, Italy), which allows to measure minute ventilation, IC in the process of standardized 6MWT was used. Methods of descriptive statistics are used for analysis of obtained data. Differences were considered to be true with p<0,01.

**Results:** Decrease of the level of peak ventilation and final ventilation in group of patients with COPD in comparison with control group is marked during the test, reliable differences (p<0,01) according to ventilation indices are marked in patients with COPD III-IV degree of severity in comparison with control group, peak ventilation (l/min) in these groups is 36,6±8,2; 32,6±9,7; 47,6±5,1 correspondingly, final ventilation (l/min) 33,7±7,4; 28,6±9,3; 44,5±4,6. It is marked that decrease of

dynamic hyperinflation is growing with decrease of level of bronchial obstruction. At the same time IC at rest and IC at the end of the load correlated well with the distance, which have been walked by the patients for 6 min (r=0,43 and r=0,54 correspondingly, p<0,001). Statistically important interrelation between changes of IC and changes of dyspnea according to Borg scale (r=-0,48, p<0,001) was also revealed.

**Conclusions:** Dynamic of hyperinflation and minute ventilation during 6MWT were carried out in this study. Obtained data indicate that dynamic hyperinflation is connected with significant decrease of IC during exercise. Significant negative correlation between decrease of IC and increase of dyspnea is also considered to be a reason for development of dynamic hyperinflation.

## Assessment of the immune status of patients with COPD, which used the phytocomplex "Rolesol" containing phytoecdysteroids

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**Objective:** To investigate changes in the immune status of COPD patients when added to standard therapy phytocomplex "Rolesol" consisting of Tussilágo fárfara leaves, *Plantago major* leaves, *Lédu*m palústre shoots, *Chamomilla* flowers, *Glycyrrhíza* root, *Bétula* leaves, *Rhapónticum carthamóides* rhizomes and roots or *Silene tatarica* herbs.

**Material and methods:** Randomly selected 30 COPD patients were treated (average age 66,7±1,76 years). Patients were divided into 3 groups: group 1 – COPD patients with standard therapy and "Rolesol"; group 2 – COPD patients treated with standard therapy and 20% alcohol solution phytoecdysteroids; group 3 – the control, COPD patients treated with only standard therapy. Immunograms was assessed before treatment and since 10 days of treatment. Statistical analyses were carried out using Statistica 6.0.

**Results:** In the group 1 the total number of lymphocytes increased from 31±3,2% to 32,2±3,1%, and the mature CD3+ amount increased from 57,6±0,9% to 59,5±0,3%. The CD4+ subpopulation increased from 3,18±0,49% to 33,9±0,7%, and the CD8+ subpopulation decreased from 25,5±0,4% to 24,6±0,2%. The percentage of phagocytosis increased significantly from 81,2±2,3% to 88,8±1,3%. The phagocytic number increased from 7,92±0,53 ED to 9,46±0,32 ED. In the group 2 the immunograms changes tended to immunosuppression. There was a decrease of CD4+ subpopulation from 37,6±1,8% to 37,3±0,7%. The CD8+ subpopulation decreased from 28,5±0,4% to 27,8±0,5%. As a result, the ratio CD4+/CD8+ did not change from baseline and was 1,3±0,06. The number of active phagocytes decreased more significantly from 5,35±0,5 to 3,77±0,2×10<sup>9</sup>/L. The percentage of phagocytosis increased by only 3% (72±0,6% 75±0,3%). In the control group there were no significant changes in immunograms within 10 days.

**Conclusions:** Phytocomplex "Rolesol" has complex immunomodulatory effect in COPD patients. Phytoecdysteroids *Silene tatarica* and *Rhapónticum carthamóides* immunosuppression, while *Chamomilla*, *Plantago major*, *Glycyrrhíza* trigger immunostimulation.



## Liraglutide treatment in obstructive sleep apnea in obese type 2 diabetes patients

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**Objectives:** Liraglutide, a long-acting GLP-1 analogue, is a class of type 2 diabetes mellitus (T2DM) treatment that exerts its glucose-lowering effect through different mechanisms that lead to clinically significant reductions in HbA1c and fasting glucose levels with weight loss. Concerns about the health impact of obstructive sleep apnea (OSA) among obese patients with T2DM have been increasing. We aimed to evaluate the impact of liraglutide in the OSA symptoms-somnolence in obese T2DM patients.

**Material and methods:** This was a observational, unicentric study conducted in obese (BMI  $\geq 30$  kg/m<sup>2</sup>) T2DM subjects receiving treatment with liraglutide (1,8 mg QD) for at least 3 months after study inclusion. Following routine clinical practice, data of the HbA1c, anthropometric measures (weight and waist circumference) and the Epworth Sleepiness Scale (EES) were collect at the study initiation (A1) and month 3 (A2).

**Results:** A total of 19 subjects were evaluated (mean age, 62,7 $\pm$ 10,6 years; male 63,4%). Significant differences between A1 and A2 were found in mean values of body weight (102,1 $\pm$ 13,9 kg vs 98,3 $\pm$ 12,8 kg;  $p < 0,001$ ), BMI 39,2 $\pm$ 5,9 kg/m<sup>2</sup> vs 37,8 $\pm$ 6,4 kg/m<sup>2</sup>;  $p < 0,001$ ), waist circumference (121,7 $\pm$ 13,5 cm vs 118,4 $\pm$ 12,3 cm;  $p < 0,001$ ), HbA1c (8,3 $\pm$ 1,9% vs 7,1 $\pm$ 1,6%;  $p < 0,001$ ) and EES (7,5 $\pm$ 4,4 vs 4,1 $\pm$ 3,6). A significant correlation was observed between baseline ESS score and body weight ( $r = 0,217$ ;  $p < 0,05$ ) and BMI ( $r = 0,219$ ;  $p < 0,05$ ).

**Conclusions:** Our study show that liraglutide (1,8 mg QD) significantly reduce the ESS score in obese T2DM patients. Besides this, an improvement in glycemic control and body weight was also achieved.

## Rosuvastatin effects on systemic inflammation and endothelial dysfunction in patients with chronic obstructive pulmonary disease

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**Objective:** To analyze influence of rosuvastatin on systemic inflammation, endothelial dysfunction and lung function in patients with chronic obstructive pulmonary disease (COPD).  
**Methods:** 80 patients men (age 63 $\pm$ 7 years) with stable COPD II-III stages (Global Initiative for Chronic Obstructive Lung Disease, 2011) without cardiovascular events were analyzed. Their cardiovascular risk SCORE was 10 [7,0; 18,0] (high and very high). The patients were divided into 2 groups. One group (60 patients) received 5-10 mg rosuvastatin during one year. The other group was control (20 patients), these patients refused to take cholesterol lowering drugs. The target values of low-density

lipoprotein-cholesterol (LDC-C) was  $\leq 1,8$  mmol/l (very high risk) and  $\leq 2,5$  mmol/l (high risk). The basic COPD therapy was not changed. The patients used ipratropium bromide, tiotropium bromide, fenoterol. High sensitive C-reactive protein (hs-CRP), interleukin-8 (IL-8), tumor necrosis factor (TNF)- $\alpha$ , vascular cell adhesion molecule type 1 (VCAM-1) – marker of endothelial dysfunction, were estimated before and after the treatment. We also analyzed spirometry, quantity of COPD exacerbations, exercise capacity (the 6 minute walking distance test (6MWT)), activity of COPD symptoms and the quality of life (the St. George's Respiratory Questionnaire) before and after the treatment period.  
**Results:** All patients reached the target values of LDC-C. After the rosuvastatin treatment hs-CRP decreased from 3,5 [2,8; 4,2] mg/l to 1,7 [1,3; 3,3] mg/l ( $p < 0,001$ ), VCAM-1 decreased from 1066 [870; 1180] ng/ml to 790 [670; 950] ng/ml ( $p < 0,001$ ), IL-8 decreased from 3,08 [2,74; 3,68] to 2,3 [1,93; 2,66] pg/ml ( $p = 0,001$ ), a-TNF decreased from 6,51 [5,57; 7,52] to 4,95 [4,25; 5,45] pg/ml ( $p = 0,001$ ). We observed a 20% decrease of COPD exacerbations ( $p < 0,001$ ). The activity of COPD symptoms decreased from 82,5 $\pm$ 24,3 to 66,4 $\pm$ 17,2 ( $p < 0,001$ ). Patients using rosuvastatin had a 13,2% increase of distance in 6MWT ( $p = 0,001$ ). The rosuvastatin treatment decreased decline in forced expiratory volume in 1st second. There was a 19% increase of a-TNF ( $p = 0,001$ ), a 5% decrease of distance in 6MWT ( $p = 0,001$ ) in the control group.

**Conclusions:** COPD patients need cardiovascular risk calculation and its correction. This study shows that rosuvastatin has anti-inflammatory and endothelial protective, immune-modulating effects, improves lung function, reduces COPD exacerbations, increases exercise capacity in patients with COPD.

## Let's talk about H1N1 co-infection...!

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**Introduction:** It is estimated that between 3-30% of patients with the diagnosis of influenza A/H1N1 presents concomitantly a bacterial infection due to synergism with this pathogen and other agent at the respiratory tract. The authors present three clinical cases of patients admitted in Intensive Care Unit with pneumonia from bacterial etiology and subsequent isolation of H1N1 in biologically sample-bronchial aspirate secretions.

Case reports: Common facts to the three patients: admission due to respiratory failure with PaO<sub>2</sub>/FiO<sub>2</sub>  $< 150$  mmHg and consequently need for invasive mechanical ventilation. Evolution to septic shock, with organ dysfunction being the respiratory and cardiovascular common at 3, and kidney failure for 2 of them. Different radiological findings but all of them extensive and bilateral, reflecting the severity of the infection. Due to their co-morbidities and by the epidemiological context, our suspicion was higher to co-infection, so we tested them to H1N1 virus by PCR from aspirated tracheas, which were positive. However the poor therapeutic response to the suitable antibiotics also contribute

to high suspicion of co-infection. The isolated microorganisms were: *S. aureus*, *P. aeruginosa* and *Sp. pneumoniae*. Two of them died and curiously the patient more ill at admission due to largest number of co-morbidities and higher index of gravity survived. We were submitted to Prone position with success, since all medical measures have failed to increase the oxygenation.

**Discussion:** The authors want to call attention to the clinical suspicion for this agent especially in seasonal periods and also when there is a bad clinical evolution besides adequate antibiotic therapeutic. Contrary to what was observed in other serious, where co-infection is not associated alone to mortality in our study 2 of 3 patients infected with H1N1 and other bacterial pathogen died.

### **Auscultation Master: lung sounds edition. Presentation of a clinical case with rich pulmonary semiology findings, using an innovative iPad app developed by the authors**

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Auscultation of lungs is still one of pillars of the initial approach to the patient in several clinical settings. Along with a chest X-ray, the cost-benefit of lung auscultation is tremendous. Physical examination skills, however, have been in frank decline. The authors have developed an innovative educational lung auscultation app, specifically built for the iPad, called Auscultation Master: Lung Sounds Edition, targeted at medical students and young residents. This app is based on real clinical cases and is visually immersive and interactive. High-fidelity patient's auscultation recordings, obtained with a digital stethoscope are used and mapped to highlighted areas on a torso that can be rotated with a finger swipe. By touching and holding his finger over each area, the student activates each individual recording, which can then be heard. Egophony, bronchophony and whispered pectoriloquy can also be evaluated through parallel recordings and chest percussion can be assessed by double tapping on the screen. Also, a chest X-ray of the patient can be dragged over from the side for comparison of auscultatory and radiological findings. This allows for an impressive and didactic visualization of the pathophysiological correlates involved in the production of abnormal respiratory sounds. We wish to perform a live presentation of a clinical case, using our app, of a patient that was admitted to our hospital. He presented with interesting semiologic findings on physical examination of the thorax. We mapped each these findings (auscultation and percussion recordings) to the interactive three dimensional torso on our app. After reproducing these findings back to the audience, we'll ask them for the probable diagnosis and generate an interesting discussion before finally presenting the chest X-ray of the patient. We believe that this app represents a fresh and sorely needed approach to lung auscultation education, a skill that still remains absolutely essential in today's clinical practice.

### **Outbreak of Legionnaires disease, 12 October to 4 December, 2014 in Portugal**

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**Background:** Legionnaire disease (LD) was first recognized at mid 1970 after an outbreak of pneumonia at an American Legion Convention in Philadelphia. Soon after the etiologic agent was identified as a fastidious Gram negative bacillus, and named *Legionella pneumophilla*. *L. pneumophilla* is the most frequent cause of human legionellosis and a relatively common cause of community-acquired pneumonia in adults. Legionellosis refers to 2 distinct clinical syndromes: Legionnaires disease – most often manifests as severe pneumonia accompanied by multisystemic disease, and Pontiac fever, which is acute, febrile, self-limited viral-like illness. In Portugal, according to General Direction of Health there were only 80-140 cases annually.

**Objective:** Ascertain the population admitted in the Urgency Service with antigen test in the urine positive to *L. pneumophilla*, during the outbreak period. Study type: cross-sectional, descriptive.

**Methods:** Review of records of patients admitted in urgency service 192 (51.7%), during the outbreak. The variables to study were: gender, age, area of residence, non-specific symptoms, neurological and gastrointestinal symptoms.

**Results:** Males were the most affected with over 62%. The most affected age range of 40-70 corresponds being greater than 80% cases. Most of the affected population lived in three locations: Vila Franca de Xira, Póvoa de Santa Iria and Vialonga (80%). Of the non-specific symptoms found the prevalence of the fever (41%), cough (25.6%) and dyspnea (13.6%), among others. Gastrointestinal symptoms predominated vomiting (48.1%) and diarrhea (35.1%). Among the neurological symptoms was the prevalence of headache (51.6%), confusion and prostration (30%).

**Conclusions:** In conclusion term of this outbreak demonstrated that the observed symptoms are similar to what is described in the literature, affecting younger age groups, with nonspecific symptoms, which usually occur in outbreaks. There being essential for effective prevention measures because they usually have a high mortality and morbidity rate.

### **Chronic hemothorax**

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**Introduction:** Bleeding into the chest cavity most commonly occurs after chest trauma, either blunt or penetrating. Depending on the nature of the injury, bleeding may vary from minor to massive.

**Case report:** We describes the case of a 73 years old patient, male gender, independent in activities of daily living, admitted by malaise, dyspnea on minimal exertion, orthopnea, asthenia,

anorexia and loss of 8 kg, with one month of evolution. He also reported frame with about two weeks of evolution with cough and sputum mucosa, chills and refusal to eat, with worsening on the day he went to the emergency room. No other symptoms were reported. As known pathological history are noted high blood pressure, dyslipidemia, ex-smoker, heavy drinking habits in the past, ulcer gastric surgery, diverticulosis of the sigmoid colon, benign prostatic hyperplasia, and a fall a year and a half earlier, resulting in fracture of the right clavicle. He was chronically treated with simvastatin, clopidogrel, irbesartan + hydrochlorothiazide and finasteride. Laboratory tests showed normocytic and hypochromic anemia with hemoglobin 10.7 g/dL; without leukocytosis or neutrophilia; renal function without change; C-reactive protein 3.8 mg/dL. Chest X-ray: atelectasis signs of the right hemithorax. CT scan of the chest: Fill the right pleural cavity by heterogeneous content, well defined, with pleural calcifications, conditioning compressive collapse of much of the ipsilateral lung and left mediastinal shift. CT scan of abdomen: aneurysms of the infrarenal abdominal aorta with a maximum diameter of about 6 cm and a diameter of the lumen near the permeable cm 3 circumferentially with mural thrombus. Measures craniocaudally extension of about 12 cm. Multifocal calcium atheromatosis of the entire abdominal aorta, iliac arteries and visceral origin of main branches of the aorta. Transthoracic biopsy: blood clot organization.

**Discussion:** This was therefore a case of large volume chronic hemothorax, probably secondary to fall a year and a half earlier. The patient was transferred to Cardiothoracic Surgery of the reference hospital where underwent decortication, eventually died 26 days after surgery for complications after surgery.

## Pulmonary embolism in young adults

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**Objective:** To study the pulmonary embolism (PE) in young patients (under 45 years), analyzing the risk factors, clinical presentation and complications.

**Methods:** A descriptive and retrospective study in our hospital between 1996 and 2014. Patients were collected from an electronic database. The diagnosis of PE was performed by ventilation perfusion scintigraphy, CT-scan or autopsy.

**Results:** We identified 94 patients with PE, 57 (61%) women and 37 (39%) men, with a mean age of 34±6.6 years old (range 17- 44) and a Charlson index of 0.85 (range 0-9). There were 4 patients (4%) with no risk factors (RF) at admission. 29 patients had 1 RF (31%), 46 patients had 2 RF (49%), 11 patients had 3 RF (12%) and 4 patients had 4 RF (4%). The most frequent was cigarette smoking (62%) followed by hormone therapy (32%), obesity (21%) and splint (11%). 6 patients (6%) had previous venous thrombosis and 19 (20%) had family thrombotic history. The most common clinical presentation was: chest pain 64 (68%), dyspnea 57 (61%), syncope/pre-syncope 16 (17%), haemoptysis 16 (17%), confusional syndrome 5 (5%) and cardiorespiratory arrest in 4 (4%). In 42 patients (45%) a deep vein thrombosis was confirmed and it was asymptomatic in 19%. In 60 cases

D-dimer was requested, with an average of 2678 µg/l. The chest radiography was normal in 51 cases (54%) and a pulmonary infiltrate was found in 27 (29%). The ECG was normal in 42 patients (45%), tachycardia in 31 (33%) and S1Q3T3 pattern in 14 (15%). Study was done with ventilation perfusion scintigraphy in 16 patients (before 1999) and CT-scan in 76 (since 1999). Autopsy diagnosis occurred in 2 patients. About 96% patients underwent anticoagulation with heparins and 12% received fibrinolysis. Oral anticoagulants were initiated during hospitalization in 73 (78%) patients, with a mean of 5.8 days after diagnosis. 21 patients (22%) required admission in ICU. Thrombophilia was studied in 61 patients and it was pathologic in 46% (prothrombin G20210A and increased F VIII levels were the most common alterations). In-hospital mortality was 5% (5 patients) and 2 patients died before the first year of follow-up.

**Conclusions:** The EP risk in young adults is the amount of different risk factors, mainly smoking, hormone therapy and obesity. The most common way of presentation is chest pain and dyspnea with normal ECG and chest radiography, so a high level of suspicion is really important because we found quite important in-hospital mortality.

## Calcium metabolism in Latvian patients with a newly diagnosed sarcoidosis

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**Objectives:** Sarcoidosis is a multisystem granulomatous disease with unknown etiology that in 90% of cases affects the lungs. Clinical manifestation and severity of the disease varies in different countries and ethnic groups. Calcium metabolism testing can be useful in diagnostics. Extensive research on sarcoidosis has not been made in Latvia. The aim of the study is to assess a correlation of the calcium metabolism with sarcoidosis radiological stage and demographic indicators.

**Material and methods:** Almost all patients with primary diagnosed sarcoidosis in Latvia have been investigated in the "Centre of Tuberculosis and Lung Diseases" of Riga Eastern Clinical University Hospital. In the study retrospectively were analyzed medical records of all patients (n=275) who had been hospitalized during time period from January 1st 2013 till December 31st 2014. Further analysis included only patients with histologically confirmed sarcoidosis (n=208). Medical data has been analyzed in relation to patients' age, gender, radiological stage of disease manifestation (acute or chronic).

**Results:** 208 patients (109 men, 99 women) have histologically proven sarcoidosis. Patients' average age at the time of diagnosis was 37±12 years. Acute manifestation was found in 69 patients (33.5%). Calcium in serum was tested in 165 patients and in 24h urine – 181 patients (96 men, 85 women). Elevated serum calcium was observed in only 12% cases, but no statistically significant correlation between serum calcium, age, gender, or disease manifestation has been found. Mean calcium in 24h urine was 137.2 mg/24h or 3.4 mmol/24h (within normal range), the levels were higher in men (141.8 mg/24h) than in women (123.4 mg/24h), and it was statistically significant correlation

( $p < 0.01$ ). No relation was found for hypercalciuria with age. No statistically significant correlation between acute or chronic first disease manifestation and calcium in serum or urine was found ( $p > 0.5$ ). PTH and vitamin D was tested in very little patients, not allowing making any significant conclusions.

**Conclusions:** We can conclude that in Latvia sarcoidosis affects mostly young and middle-aged people. 24h urinary calcium more than serum calcium is a very important parameter for sarcoidosis diagnostics. No significant correlation between serum calcium and other parameters was seen. Hypercalciuria could be found in 20.2% of patients, and it was significantly higher in men, regardless of age.

### Chronic obstructive pulmonary disease awareness campaigns: a 3-year analysis

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**Background:** Chronic obstructive pulmonary disease (COPD) is responsible for significant morbidity and mortality in Portugal, with an estimated prevalence of 10 to 14%. It constitutes a major public health problem and its early diagnosis is proprietary.

**Methods and objectives:** From 2012 to 2015, the Pulmonology Department at Hospital de Braga developed awareness campaigns regarding COPD and other respiratory diseases on World COPD Day, in which participants answered a questionnaire and performed a spirometry. The main objectives of this work were to explore participants' knowledge about COPD and spirometry, to determine the prevalence of COPD risk factors, known respiratory diseases and comorbidities and to analyze the spirometric results.

**Results:** The sample included 489 participants (51% males, mean age  $58 \pm 12$  years, mean BMI  $27 \pm 4$  kg/m<sup>2</sup>), mainly with a low education level. Around a fifth of them admitted to have ever heard about COPD or spirometry and to have ever performed a spirometry. Less than half of them (41%) had a smoking history, 21% smokers and 23% former smokers, with a mean  $20 \pm 18$  (1-92) pack-year. Around 38% referred smoking passive exposure and the majority admitted exposure to noxious particles, whether work-related (43%) or at home (48%). A quarter of the participants had a known respiratory disease and the commonest were COPD (29%), asthma (29%) and rhinosinusitis (27%); 15% stated a previous respiratory disease, mainly tuberculosis (52%) or pneumonia (38%). The most frequent comorbidities were cardiovascular risk factors (62%), allergies (29%), depression (21%), osteoporosis (19%) and gastric pathology (15%). In respect to spirometry results, an obstructive pattern was observed in 11%, with a mean FEV1, FVC and FEV1/FVC of 70%, 88% and 64%, respectively.

**Conclusions:** Underdiagnosis of COPD is a well-known problem. These campaigns raised awareness about respiratory diseases

and disclosed COPD as an important cause of morbidity and mortality.

### The ability to identify patients at risk of pneumonia late recovery

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**Background:** In 2014 the Ivanovo Regional TB Dispensary has received 129 immunocompetent patients diagnosed with community-acquired pneumonia protracted course, which after 10-14 days of antibiotic therapy, against recourse clinical manifestations, radiographic changes in the lungs decreased by less than 50% therefore of interest to the therapist signs of a protracted course of nonspecific inflammation in the lung tissue from a particular patient.

**Objective:** To identify predictors protracted course of community-acquired pneumonia.

**Material and methods:** 60 patients: 30 people with the classic over community-acquired pneumonia (group №1) and 30 people a protracted process (group №2). Conducted conventional clinical laboratory tests, diaskintest, spirometry, pulse oximetry, radiography test with a 6-minute walk test, echocardiography, sputum and secretions obtained by fiberoptic for acid-fast bacilli and non-specific flora. Monitoring was carried out in 1, 5, 10-day inpatient treatment. Patients were treated according to the protocol of patients with community-acquired pneumonia.

**Results:** Microbial Landscape of the mucous membranes of the respiratory tract and oropharynx in the group №1 in 1 day was characterized mainly (60% of patients) pathogenic hemolytic streptococci and 40% of opportunistic non-hemolytic streptococcus in a concentration (108 CFU/ml) associations of microorganisms have been identified. Under №2 – predominant opportunistic (34.5%) and pathogenic microorganisms as a monoculture streptococci (107-109 CFU/ml) or microbial associations, often with enterobacteria (9.9%, 107 CFU/ml). After 5 days of inpatient treatment in a group №1 determined by the same spectrum of microorganisms and reducing their concentration (by 1-3 orders of magnitude); group №2 hemolytic Streptococcus group B were determined in the same concentration, and the concentration was opportunistic above. 10th day in the resorption of infiltration in the lung concentration of microorganisms decreased to 104-106 CFU/ml, there was the elimination of pathogenic hemolytic streptococcus group B, microbial associations. Patients with save changes in the lungs was also observed elimination of pathogenic streptococci, and the concentration of conditional – pathogenic microorganisms colonizing became close to (104 CFU/ml).

**Conclusion:** The current protracted community-acquired pneumonia combined with respiratory dysbiosis and extended normalization microbiocenosis.

## Rare diseases

### Familial multiple lipomatosis

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**Introduction:** Familial multiple lipomatosis (FML) is an extremely rare benign hereditary syndrome, with an incidence of 0.002%. The encapsulated lipomas associated with FML are found on the trunk and extremities, with relative sparing of the head and shoulders. Men are affected twice as commonly as women. Inheritance occurs frequently by autosomal dominant transmission, though cases with recessive inheritance have also been reported.

**Case report:** A 76-year-old woman was admitted to the hospital due to a community-acquired pneumonia. On physical examination, she evidenced a curious finding: numerous (in number of approximately 40), rubbery, non-tender, mobile and non-fluctuant, large (maximum 18 cm of diameter) subcutaneous nodules in the upper and lower limbs. Personal inquiry revealed that these nodules started appearing when she was a teenager, getting larger and numerous with age. Familial history of this disease was also established in her mother, uncle, two brothers and her son. The patient's lipid profile was normal. Over the years, specialists had not advised her to perform surgical excision of the nodules, once she had never experienced functional limitations. This condition's only concern was an altered cosmetic appearance but as the patient denoted "she had already gotten used to it".

**Discussion:** Patients with FML, usually maintain their normal daily activities without any repercussion. However, in a few cases they may experience some difficulties as the lipomas multiply or enlarge. Notwithstanding, we should be aware that the differential diagnosis of this condition may include other pathologies not so innocuous such as: adiposis dolorosa (Dercum's disease), also a rare disorder characterized by multiple, painful lipomas often associated with obesity; Madelung's disease, characterized by painless symmetrical diffuse deposits of fat beneath the skin of the neck, upper trunk, arms and legs, frequently associated with chronic alcoholism; and the Bannayan-Zonana syndrome, a rare hermatomatous disorder with macrocephaly, multiple lipomas and hemangiomas.

### Fever of unknown origin – a rare cause

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**Introduction:** Fever of unknown origin (FUO), is defined as fever lasting for at least 3 weeks with no identifiable cause

after 3 days of hospital evaluation or at least 3 outpatient visits in its classic form (distinguished from health-care associated, immune-deficient or HIV related FUO). In spite of its many known etiologies and the array of investigative techniques available to the practitioner, depending on the series in 10-50% of cases no cause is found. Takayasu arteritis is a rare, systemic, inflammatory large-vessel vasculitis of unknown etiology that most commonly affects the aorta and its main branches, typically in young women.

**Case report:** A 19 years old Caucasian female with no significant medical history, presenting with a 3 week long history of fatigue, adynamia, fever (38.5-39°C) and weight loss (3-4 kg) with absence of any other accompanying symptoms (namely musculoskeletal, cutaneous, respiratory, cardiovascular, gastrointestinal or genitourinary), was admitted to our hospital for investigation. Preadmission she was observed in the ER department 3 times and twice as an outpatient in 2 different institutions, having been medicated with 3 different antibiotics with no improvement. Upon clinical examination, besides a fever and a faint holosystolic heart murmur best audible over the tricuspid area, no other changes were found on her physical examination. She underwent extensive investigation; with blood and urine cultures, complete blood count, renal and liver function tests, inflammatory markers, serology testing for several infectious agents and connective tissue disorders, echocardiography and CT scanning. All the exams were negative with the exception of a markedly elevated ESR and CRP (96 mm/h and 16.6 mg/dL), anemia of acute inflammation with a hemoglobin of 9 g/dL and a ferritin of 572 ng/mL and multiple serological markers for infectious agents suggestive of cross reactivity due to negative DNA testing, previous antibiotic coverage and absence of compatible medical history. Due to the lack of diagnosis thus far, we conducted a 18-FDG PET scan which revealed hypercaptation in the aortic arch suggestive of Takayasu arteritis. Starting the patient on oral prednisolone at 1 mg/kg/day we observed fever remission and symptomatic improvement within 48 hours, accompanied by marked reduction of the inflammatory markers. She was discharged to outpatient care, awaiting her first follow up consultation.

### Prevalence of Fabry disease as a factor end-stage renal disease on hemodialysis patients in Turkey

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**Objectives:** End-stage renal disease (ESRD) is a serious complication of Fabry disease (FD). According to the 2010 annual data report by the United States Renal Data System, Fabry

disease represents approximately 0.02% of the incident patients each year. The aims of the present study were to determine the prevalence of FD in Turkish hemodialysis population.

**Methods:** A total of 236 hemodialysis patients (52% female, 48% male) were enrolled. Plasma alpha-Gal A levels was measured in 114 consecutive males (age 60,3±13,3 years) and molecular analysis of the alpha-Gal A gene were performed in 122 female (age 63,6±12,3 years) on hemodialysis patients.

**Results:** Mean plasma alpha-Gal A levels of the male patients was 5.4±1.7 µmol/L/h. There was no found under 0,6 µmol/L/h on male. 2 women were diagnosed with FD by molecular analysis. In consequence of genetic analysis of mutations [hemizygot c.1117G>A (p.G373S) and c.937G>T (p.D313Y)] were identified. Family screening of cases identified five additional cases. A total of was achieved 7 cases. First screening was detected as 0.8%, and family screening was added as 2,9%.

**Conclusions:** The prevalence of FD was determined as 2.9 % on hemodialysis patients and family in Turkey. Prevalence seems to be high due to screening FD can perform on hemodialysis patients. In additional, family screening studies are important for detecting hidden cases.

### **The Brown-Sequard syndrome in a patient with Paget's disease – a neurological complication or two different entities?**

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**Introduction:** Paget's disease of bone is a chronic skeletal disease of unknown etiology, characterized by an accelerated focal bone turn over. It leads to structurally abnormal bone formation, and can affect any bone in the skeleton, but having affinity for the column, skull and lower legs. The spine is frequently affected, spinal stenosis being one of the complications which may lead to progressive loss of muscular control, walking difficulties, pain or paralysis of the back and legs. The patient prognosis can be good if diagnosis and treatment are established before the onset of major changes at bone level.

**Case report:** We present the case of 48 years old patient hospitalized in orthopedics, showing the left leg weakness, swelling, pain and functional impotence in the calf left. Investigations carried out establish the diagnosis of chronic osteitis occurred on an old left tibial fracture. The patient was transferred to the Internal Medicine department due to the alteration of the general condition, weight loss, persistent joint swelling and functional impotence in the large joints (knee, ankle). He was diagnosed with Paget's disease and Brown-Sequard syndrome. Under specific treatment, evolution of the disease was slowly favorable, but in terms of neurological symptoms, our patient was delaying the neurosurgical intervention.

**Discussion:** There are few cases in literature which report the Brown-Sequard syndrome (a rare and severe myelopathy, with difficult diagnosis and treatment) secondary to degenerative diseases of the spine. The particularity of the presented case consists exactly in this association, unreported yet in the literature to our knowledge.

### **Cervical neurofibroma and autoimmune thyroiditis – coincidence or association?**

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**Introduction:** Neurofibroma is a benign nerve sheath tumor of the peripheral nervous system. There are three major clinically and genetically distinct forms of neurofibromatosis: type 1, the most common, type 2, and schwannomatosis. The natural course of the disease is marked by a wide range of symptoms from physical disfiguration and pain to cognitive impairment.

**Case report:** We report the case of a 46 years old woman known with autoimmune thyroiditis who was admitted for bilateral cervical tumors. Clinical examination revealed mobile and tender tumors without other abnormalities. The neck, pulmonary and abdominal native computer tomography showed multiple cervical adenopathies, pleural bilateral nodules and a left kidney nodule. Lymph node biopsy was performed and the histopathology exam was suggestive for neurofibroma. The etiology of the pleural and kidney tumors needs further investigations.

**Discussion:** Cervical neurofibromas are rare, usually asymptomatic and with good prognosis. The association between neurofibromatosis and autoimmune thyroiditis has been reported but is excessively rare.

### **Hereditary angioedema with dominant abdominal symptoms mimicking surgical emergency: a case report**

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**Introduction:** Hereditary angioedema (HAE) is a rare and potentially fatal life-threatening disease associated with episodic attacks of edema formation. The prominent sites involved are upper airway and tongue; subcutaneous tissues; and abdominal organs. The abdominal pain is triggered by edema of the mucosa of any portion of the gastrointestinal tract. Management of HAE comprises short or long-term prophylaxis, including prophylactic therapy in situations where attacks may occur, and management of acute attacks. The purpose of this paper is to report a case of abdominal angioedema attack due to HAE and alert for the diagnosis and timely approach of this entity.

**Case report:** We report the case of a 46 years old male patient with the diagnosis of type I HAE on long-term prophylactic treatment with danazol 200 mg/day. He was admitted to the emergency room with vomiting and severe paroxysmal colicky pain. Abdominal examination revealed signs consistent with acute abdomen or abdominal obstruction. The remaining physical examination was uncharacteristic. Analytical evaluation showed increased white blood cell count. It was primarily considered abdominal angioedema secondary to HAE. The patient was medicated with a single subcutaneous injection of selective

bradykinin B2 receptor antagonist (icatibant 30 mg). The potential precipitant was not identified. During hospitalization, there was a marked and progressive clinical improvement and the patient was discharged after 48 hours of hospitalization.

**Discussion:** Clinical history includes questions about previously gastrointestinal attacks and if the current symptoms are similar to past episodes. Nausea, vomiting and acute abdominal pain are the dominant symptoms in 25% of patients with HAE and are rarely seen in patients with other forms of angioedema. Gastrointestinal attacks can be challenging to diagnose, as the clinician has to conclude if the abdominal symptoms are related to angioedema or to an unrelated disease, especially in the first episode. Abdominal radiographs may have features of ileus and abdominal ultrasonography or computed tomography may reveal edematous thickening of the intestinal wall, a fluid layer around the bowel and free peritoneal fluid. Abdominal angioedema can mimic a surgical emergency which can lead to unnecessary surgery and consequently delay in diagnosis. One-third of patients with undiagnosed HAE may undergo unwarranted abdominal surgery due to clinical similarities.

### **Xanthogranulomatous pyelonephritis: an unexpected diagnosis of a rare disease?**

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**Introduction:** Xanthogranulomatous pyelonephritis (XGP) is a rare, severe and chronic inflammatory variant of chronic pyelonephritis characterized by substantial destruction of the kidney due to granulomatous tissue containing lipid-laden macrophages. The kidney is commonly nonfunctional, since most cases are a diffuse process. The most common organisms involved in XGP are *Escherichia coli*, *Proteus mirabilis*, *Pseudomonas*, *Enterococcus faecalis* and *Klebsiella*. XGP occurs in approximately 1% of all renal infections. Owing to its rarity we report such a case encountered in our clinical practice and alert for the diagnosis and timely approach of this entity.

**Case report:** An 81 years old non-diabetic woman presented to our institution with one week of progressively worsening dyspnea. Given the symptoms, physical examination and diagnostic tests the patient was admitted to our service with acute chronic obstructive pulmonary disease and was medicated accordingly. During hospitalization, the patient complained of dysuria. She had no fever, hematuria, or weight loss. Abdominal examination was innocent. We obtained serum laboratories, which revealed leukocytosis with increase in neutrophil count, raised blood serum creatinine and urea level. A urine analysis demonstrated positive nitrites, 5–10 WBC/hpf, 2–5 RBC/hpf, and negative leukocyte esterase. Urine culture grew out *Klebsiella ozaenae*. Abdominal computed tomography showed a urethral calculus combined with radiological findings suggestive of XGP of the left kidney, even in the presence of negative history of diabetes, prior known episodes of urinary infections or hematuria. Additionally, moderate hydronephrosis of the right kidney was evident associated with ureteropelvic dilatation and abrupt reduction in the diameter in the right pyeloureteral

transition. Coverage with cefuroxime was performed and the patient underwent right urethral stent placement. The patient recovered well with uneventfully post-operative period and was discharged on 8th post-operative day proposed for left radical nephrectomy.

**Discussion:** XGP should be considered in the differentials of dysuria even in non-diabetic patients. Radiological diagnosis of XGP can be challenging as it can often be difficult to differentiate it from pyonephrosis, renal malignancy and other retroperitoneal mesenchymal tumors, carrying a preoperative diagnostic dilemma. When encountered it should be timely treated with optimal surgical removal.

### **Identification of patients with Gaucher disease: a needle in a haystack?**

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**Objective:** The aim of this study is to establish criteria to find patients with undiagnosed Gaucher disease.

**Methods:** Medical record of all patients admitted to our center between January 1, 2013 and December 31, 2014 were reviewed. Patients between 18 and 50 years old were selected if they met one of the following three criteria: 1) splenomegaly of unknown origin; 2) hip replacement of unknown cause; 3) avascular bone necrosis of unknown cause. All patients who, after reviewing medical history, had any justifiable cause to present any of the three diseases (infections, trauma, steroid use, etc) were excluded. After obtaining patients informed consent, test for the glucocerebrosidase enzyme activity was performed. If glucocerebrosidase activity was diminished, concentrations of the biomarker lyso-Gb1 were measured and the GBA (glucosidase, beta, acid) gene was sequenced in order to detect a possible mutation.

**Results:** 126 patients were included in the study. After reviewing medical history, 105 were excluded as they had some other reason to justify their disease. The remaining 19 patients were classified according to their clinical probability of suffering from Gaucher disease in high (0 patients), medium (2 patients) or low (17 patients). 2 patients could not be located; 7 patients were not analyzed because they rejected to participate in the study; 2 patients have yet to be tested. Thus, 8 patients were tested to date: 2 with medium and 6 with low probability. Glucocerebrosidase activity levels ranged between 4,5 and 10,2  $\mu\text{mol/l/h}$  (reference range  $>6,2 \mu\text{mol/l/h}$ ) in the 8 patients analyzed. 2 patients had low levels of glucocerebrosidase activity (4,6 and 4,5  $\mu\text{mol/l/h}$ ). In one of them, lyso-Gb1 levels were normal (4,3 ng/ml, reference  $<4,8$ ) and the sequencing of GBA gene showed no pathogenic mutation. In the second patient, lyso-Gb1 levels were elevated (6,8 ng/ml), but the sequencing of GBA gene showed no pathogenic mutation, making the presence of Gaucher disease unlikely.

**Conclusions:** After reviewing 2 year medical record to identify patients with Gaucher disease, we did not find any cases. Clinical record review may be a useful method to detect undiagnosed rare diseases, but larger studies are needed.

## A slowing arise disease. Clinical case

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**Case report:** A 58 years old man with progressive loss of weight (about 40% of his corporal body weight), malaise, lymphadenopathy, anemia and pigmentation. The patient had a long history of inhaled drugs, alcohol intake, and was a heavy smoker. He had been at hospital for atypical pneumonia when it was found several multiple intra abdominal adenopathy and hepatosplenomegaly, confirmed by CT. He was study for lymphoproliferative disease without positive results. At follow up, he maintained complains and increase of loss weight and arthralgia. Objectively his neurological exam was normal; he had no cardiac murmur alterations. His main laboratory features were anemia, VS 120 mm, albumin 2.7, with total protein 9.8. Serology studies, histology of peripheral adenopathy, bone marrow were negative. He was submitted for a laparoscopy for excision of a mesenteric adenopathy. Result was a PAS staining of microorganisms in histiocitaries cells, and granulomas without necrosis. The lumbar puncture performed, was normal, and PCR for *Tropheryma whipplei* was negative. His ocular examination was also normal. Echocardiography showed moderate aortic insufficiency. He started parenteral ceftriaxone 2 g daily for 2 weeks, since PCR in liquor was negative, with clinical improvement, and after continued oral administration of 160 mg of trimethoprim and 800 mg of sulfamethoxazole, twice, as long duration treatment.

**Discussion:** Whipple's disease is a rare multisystemic disease, with varied presentation, roughly a small amount of patient have the classical signs and symptoms. Diagnosis should be considerate in many different clinical circumstances, making differential diagnosis for a wide spectrum of diseases that include inflammatory rheumatic diseases, malabsorption, with small-intestine involvement (celiac disease, sarcoidosis and lymphoma).

## Gaucher disease – thirty years of experience

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**Objectives:** Gaucher disease (GD) type 1 is caused by the enzymatic activity deficit of glucocerebrosidase with glucerebrosideos accumulation in macrophages, leading to hepatosplenomegaly and bone disease with progressive cytopenia. GD can be diagnosing through the demonstration of glucocerebrosidase deficiency but it may be suspected in the presence of abnormal cellular deposits in tissue biopsy. The main treatment is enzyme replacement (ERT); substrate reduction therapy is less effective in regression of the disease changes. The aim of the work is a review the cases of DG, disease status at diagnosis, evolution and current state of both the bone and hematological involvement and autonomy in daily life activities such as clinical markers of treatment response.

**Methods:** Braga hospital has been for 30 years monitoring patients with DG, in total 5 female patients, all in ERT. Four of

the patients are being treated with imiglucerase and one with velaglucerase.

**Results:** Three of the patients were diagnosed after splenectomy and remaining two patients by the study of asthenia and hepatosplenomegaly. One of the patients have Parkinson syndrome. All patients showed significant improvement in bone pain, reduced hepatomegaly and resolution of anemia and thrombocytopenia, presenting actually clinically stable.

**Conclusion:** This review demonstrates the benefits of ERT, and the current different alternatives require individual consideration and analysis to better benefit to the patient.

## Eritema elevatum diutinum: a rare disease with gloom associations

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**Introduction:** Erythema elevatum diutinum (EED) is a chronic and rare dermatosis, considered a variant of leukocytoclastic vasculitis. It is characterized by red, brownish or violaceous persistent plaques and nodules which tend to distribute symmetrically on the extensor, articular surfaces of the extremities. Systemic involvement is rare. Nevertheless, an association with neoplastic, autoimmune and infectious diseases has been reported.

**Case report:** A 74 years old female, with a history of EED diagnosed several years before and under immune suppression with prednisolone 20 mg/day, azathioprine (AZA) 50 mg/day and colchicine 0.5 mg/day. She also had history of hypertension, dyslipidemia, hemorrhoids and osteoporosis. The patient was referred to internal medicine's assessment for fatigue, dyspnea and wheezing for several months, with recent worsening. She reported no chest pain, orthopnea or paroxysmal nocturnal dyspnoea. She also denied any weight loss, anorexia or night sweats. Her physical examination was unremarkable except for severe kyphoscoliosis. Blood work shown normocytic anemia, erythrocyte sedimentation rate of 70 mm/h, B2 microglobulin 3,82 mg/dL, normal calcium level and abnormal serum creatinine (2.04 mg/dL) and alkaline phosphatase levels (160 U/I). Proteinogram revealed monoclonal IgA kappa ( $\kappa$ ) gammopathy. Myelogram showed 26.5% of clonal plasma cells consistent with multiple myeloma (MM). Bone marrow biopsy had not significant bone marrow tissue. There were no lytic bone lesions or pathologic fractures. Due to previous history of hemorrhoids the patient also performed a colonoscopy that unveiled an ulcerous rectal lesion which was then proved to be a diffuse large B-cell lymphoma (DLBCL). Staging computerized tomography showed no enlarged lymph nodes or organ enlargement. The patient was diagnosed with IgAk MM (III-B stage of Durie Salmon classification) and rectal DLBCL (I-E stage of International Prognostic Index) and was referred to hematology assessment for treatment.

**Discussion:** Hematological malignancies are present in approximately 30% of the cases of EED. The most frequently reported is, as in the presented case, IgA monoclonal gammopathy which can evolve to MM. There have also been described rare cases of malignant lymphoma in patients with EED. In this case we cannot exclude the possible association of



DLBCL with prolonged immune suppression with AZA, as it is a well-known consequence of its use.

## A rare but lethal cause of hematuria

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**Introduction:** Amyloidosis is a rare systemic disease caused by the deposition of misfolded aggregated autologous proteins. Tissue biopsy is the gold standard for diagnosis. Though the incidence of AA amyloidosis is decreasing, it is still causing a wide range of clinical symptoms and organ dysfunction.

**Case report:** We report the case of a 70 years old woman presented with an obstructive acute renal failure due to AA bladder amyloidosis (BA) following untreated rheumatoid arthritis (RA). She was referred to our hospital for evaluation of acute heart and renal failure with hyperkalemia. Physical exam showed global heart failure signs, tender swelled joints at the wrists and knees. Labs showed anemia, high CRP (>100 mg/L), rheumatoid factors and anti CCP were strongly positive. Hands and wrists X-ray were typical of RA. Ultrasonography detected bilateral hydronephrosis and within the bladder a tumoral lesion of 5x4 cm near urethral insertion. Biopsies made through cystoscopy and revealed AA amyloidosis. Echocardiography showed global hypertrophic cardiopathy. Dramatic improvement occurred with steroids and methotrexate therapy, renal failure disappeared after urethral stenting, no specific treatment where made within the bladder. Unfortunately she died 6 months later from uncontrolled bladder bleeding.

**Discussion:** BA whether AA or AL share the same clinical presentation. Due to vessel's involvement both can lead to lethal bleeding. Moreover biopsies are mandatory because it is not possible to distinguish BA from bladder carcinoma through cystoscopy. When decided, treatment consists mostly in endoscopic resection. Though rare BA should be recognized due to potential fatal issue.

## Tumoral lesions mimicking cancer: think of Erdheim-Chester disease. One case and review

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**Introduction:** Erdheim-Chester disease (ECD) is an extraordinary rare condition. The main localization of this non-Langerhans cell histiocytosis is skeletal but can also be systemic; therefore it can be easily misdiagnosed as metastatic neoplasm.

**Case report:** We report the case of a 69 years old male with ECD first diagnosed as urothelial carcinoma with peritoneal carcinomatosis. He was first referred to the urology ward by his primary physician because of ascites. First CT scan showed bilateral kidney infiltration along with peritoneal carcinomatosis and huge ascites. After second interpretation by expert radiologists, the exam also showed circumferential thickening

of the aorta (coated aorta) with retroperitoneal fibrosis (hairy kidneys). The patient was then sent to Internal Medicine. Labs were normal except for inflammatory syndrome (CRP 80 mg/L). Analysis revealed sterile exudative ascitic fluid, without any tumoral cells. Bone scintigraphy did not show typical long bones osteosclerotic lesions but osteosclerosis of right maxillary sinus. PET scan revealed hypermetabolic foci in kidneys, aorta, ascites, peritoneal carcinomatosis along with right maxillary sinus previously detected with bone scintigraphy highly suspicious of ECD. Renal biopsy found several CD68+/CD1A- foamy histiocytes. Because the patient complained of polydipsia, pituitary MRI was done showing lost of posterior pituitary gland physiological hypersignal suggesting diabetes insipidus. The search for BRAF mutation was positive on kidney biopsy allowing us to start treatment with BRAF-inhibitor vemurafenib. Dramatic clinical improvement was observed and TEP scan done after 3 months therapy was cleared of all hypermetabolic foci.

**Discussion:** Cardiovascular and central nervous system involvement is associated with the worst prognosis and need to be identified and treated most rapidly. Interferon is still the first line treatment but nearly half of patients with ECD bare a mutation in BRAF that allow physicians to use BRAF inhibitors. Though used with success in small series, data on its long term efficacy and safety are still too scarce to promote vemurafenib as a first line therapy.

## Vogt-Koyanagi-Harada disease: description of 4 cases diagnosed of 2010-2014 in a local hospital

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**Objective:** To describe the clinical manifestations and treatment of 4 patients with the diagnosis of Vogt-Koyanagi-Harada disease.

**Material and Methods:** Retrospective study of a cohort of 4 patients with Vogt-Koyanagi-Harada disease diagnosed and treated in the internal medicine and ophthalmology department during the period from 2010 to 2014.

**Results:** 4 patients (all women, aged between 16 and 61). All of them were diagnosed in acute phase. Symptomatology associated with visual affectation was headache in three patients and tinnitus and dizziness in the other one. Eye examination shows panuveitis with exudative retinal detachment in all of them. Disease manifestations were initially unilateral in a patient which caused a delay in the diagnosis. Lumbar puncture was performed to all the patients and the cerebrospinal fluid showed pleocytosis and lymphocytosis. The 4 women were treated with 3 corticosteroids boluses (between 1500 and 3000 mg of methylprednisolone) and then added descending doses of prednisone. In all of them an immunosuppressive therapy was added (azathioprine in 3 cases and tacrolimus in the other one). One of the patients suffered several relapses due to treatment suspension. In all patients symptomatic control was achieved with the treatment.

**Conclusions:** Vogt-Koyanagi-Harada Disease is a rare cause of bilateral panuveitis associated with systemic manifestations

that include meningismus, headache, tinnitus, vitiligo, poliosis and alopecia. Diagnosis in the acute phase is usually based on ophthalmological disorders, which are very characteristic and are associated with meningeal involvement. Normally, steroids are the mainstay of treatment, although in most cases immunosuppressive therapy is required. Prognosis is usually good, especially if correct treatment is started in early stages.

## Acute stroke revealing Takayasu's arteritis in a patient with Crohn's disease

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**Introduction:** Both Takayasu's arteritis (TA) and Crohn's disease (CD) are chronic inflammatory diseases of uncertain etiology that increase the risk of ischemic stroke, and their coexistence provides a perfect milieu for cerebrovascular presentation. CD-TA coexistence is much higher than that expected by chance and suggests a pathophysiological link between these diseases. We report herein a case of a 36-year-old Caucasian male with known CD who presented with acute ischemic stroke revealing TA. We discuss the unexpected coexistence of these two diseases, and their common association with cerebrovascular accidents.

**Case report:** A 36-year-old male with CD presented with motor aphasia and right hand weakness. Neurological test revealed weakness in his right arm. Brain CT in the ER did not demonstrate any focal lesion. Carotid Doppler revealed left common carotid artery (CCA) occlusion with a collateral flow in the left internal CA and thickened right CCA wall with 60% narrowing of the lumen. CTA followed by MRI exam demonstrated an acute left middle cerebral artery territory infarction and acute left CCA thrombosis with a concentric narrowing and thickening of the left and right carotid arteries. Trans-thoracic echocardiography ruled out cardiac source of suspected emboli. A diagnosis of TA was made and steroid pulse therapy was initiated together with anticoagulation.

**Discussion:** TA is a rare granulomatous vasculitis of unknown etiology that primarily affects the aorta and its branches. Although 10–20% of patients will have cerebrovascular manifestation during the course of the disease, stroke as the first clinical manifestation of TA has been rarely reported. The increased risk of venous thromboembolic events in patients with inflammatory bowel diseases is well established, but the risk of atherothrombotic diseases such as stroke has been a topic of debate. Recent evidence showed that IBD is also associated with an increased risk of stroke (probably because of impaired coagulation state) and that cerebrovascular disorders are probably underestimated. The actual rate of TA-CD association is more than 10,000 times higher than the statistical expected value, suggesting that some common pathophysiological background may exist. In most of these cases, TA was diagnosed simultaneously or following a diagnosis of CD, supporting the possibility that it could be regarded as an extra-intestinal manifestation of CD. A clear etiological explanation of the pathogenesis is absent for both diseases, but they share some similarities in the autoimmunity and granulomatous inflammatory processes.

**Discussion:** Though rare in western countries and especially as an acute cerebrovascular presentation, TA should be considered

as a possibility in young patients presenting with acute stroke. Both CD and TA are independent risk factors for an ischemic stroke and their coexistence should be kept in mind.

## Rowell's syndrome: a rare association between lupus erythematosus and erythema multiform

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**Introduction:** Rowell's syndrome (RS) was described in 1963 as lupus erythematosus (LE) associated with erythema multiform-like lesions (EM) affecting the same patient simultaneously. It was also associated with changes in laboratory tests which included the following: positive for antinuclear antibodies (ANA's) with a speckled pattern; positive for rheumatoid factor (RF) and positive for antibodies against the slain extract of human tissue (anti-SJT or anti-La/SSB). The diagnosis criteria have been modified and include a wider range of clinical and analytical characteristics.

**Case report:** A 91 years old woman is referred to us from her health centre after a 2 month period in which she presented evolved symptoms of macular exanthema with scabbed areas, mainly on the upper part of her torso, both on her chest and on her back, upper and lower limbs, of circinate shape, evolved, super-infected and presenting several blisters. She had been treated with topical and oral corticoids and antihistamines, as an outpatient, and did not respond well to the treatment. No triggering factors were associated. Blood tests showed the following: hemoglobin 9,9 g/dL, VSG 100 mm the first hour, RF 83,1 UI/mL, ANA's: positive 1/2560 speckled pattern, negative Ac native Anti-DNA, positive anti SS-A (Ro52+Ro60) and anti SS-B (La). The skin biopsy which was performed on the lesions showed histopathological results: epidermis with vacuolar degeneration of basal layer, isolated necrotic keratinocytes and lymphocytic infiltration. Lymphoplasmacytic infiltration in papillary dermis. Compatible with erythema multiform-like lesions. In 2000, Zeitouni and others updated the diagnosis criteria for Rowell's syndrome. Major criteria: 1) LE (systemic, discoid or acute subcutaneous); 2) EM-like lesions with or without affecting the mucous membranes; 3) ANA's with a speckled pattern. Minor criteria: 1) Chilblains; 2) Anti-Ro or anti-La antibodies; 3) Positive RF. In order to be diagnosed with Rowell's syndrome, the patient must meet the three major criteria and at least one of the minor criteria. Our patient meets all the criteria except chilblains.

**Discussion:** SR is a rare condition which affects mainly Caucasian women, and which associates any form of lupus with EM-like lesions. Clinical and analytical criteria must be met to reach a diagnosis. The histopathological study of the lesions is not among said criteria, but it is essential to reach a diagnosis. Some authors question the existence of this pathology as an independent condition, since it is believed that it could be a subtype of subcutaneous LE, because of the occurrence of certain clinical, analytical and histopathological characteristics

in both conditions, which makes it difficult to clearly distinguish one from the other. Initial treatment usually consists of systemic corticosteroids and hydroxychloroquine. If there is any resistance to the shock treatment, dapsone, cyclosporine or azathioprine can be used.

## Blue finger: a rare clinical disorder

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**Introduction:** Achenbach's syndrome is a rare clinical disorder, also known as paroxysmal finger hematoma. It's characterized by recurring spontaneous bruising on the volar aspects of fingers or hand associated with burning pain and swelling of the digits, with complete resolution in a few days. Women are affected more often than men, and the age of onset is usually over 50. The etiology is not yet established but it is probably of vascular origin.

**Case report:** 55 years old woman referred to internal medicine outpatient clinic with a history of recurring sudden onset of pain followed by bruising on the proximal phalanx of her thumb. The patient mentioned at least three similar episodes in other fingers without trauma or a specific trigger, which resolved completely and spontaneously. She had no medical history or medication. On examination brachial, radial and ulnar pulses were normal, the thumb showed swelling and bruising of the proximal phalanx, was well-perfused, retained mobility and sensitivity was normal. Blood work, including complete blood count, prothrombin time, partial thromboplastin time, erythrocyte sedimentation rate and C-reactive protein, was normal. Immunological study was negative. Doppler ultrasonography revealed normal flow in the subclavian, brachial, radial, ulnar, and digital arteries of the affected hand. The nail-fold capillaroscopy showed a normal capillary array and no structural changes of the microvessels. No specific treatment was proposed and spontaneous resolution followed within one week.

**Discussion:** This case shows the importance of being aware of this syndrome. In patients with an acute blue finger we should investigate for connective tissue diseases and hypercoagulable states but no other investigations appear to be necessary. If no systemic disease is identified, then patients can be re-assured that the condition is benign and it should resolve spontaneously.

## Acute fatty liver in pregnancy: a rare and sometimes fatal disorder

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**Introduction:** The acute fatty liver in pregnancy (AFLP) is a rare and a potentially fatal clinical disorder that occurs once in every 7000-16000 pregnancies. It usually occurs in the third trimester, but in about 2/3 of the cases the diagnosis is only

achieved upon delivery or in early postpartum period. Early diagnosis of AFLP can be difficult because it shares features with other common conditions such as preeclampsia, HELLP syndrome and cholestasis of pregnancy.

**Case report:** The authors present the case of a pregnant 19 years old African woman, at 31 weeks gestation, referenced to the obstetric unit of a tertiary care center for evaluation due to fever, nausea, vomiting and abdominal pains with one week of evolution. Her pregnancy had no complications other than a ferropenic anemia. On admission, her vitals were stable, but she had abdominal pain in the right quadrants. The blood work was: hemoglobin (Hb) 12,1 g/dL, white blood count  $6,3 \times 10^9/L$ , platelets  $341 \times 10^9/L$ , aspartate aminotransferase (AST) 66 U/L, alanine aminotransferase (ALT) 51 U/L. General surgery evaluation excluded appendicitis and cholecystitis. A week after, she spontaneously entered in preterm labor (32w) and delivered a live male baby with good Apgar scores and weight of 1455 g. In early postpartum, she suffered worsening of abdominal pains and bloating, associated with vomiting and prostration. Laboratory findings revealed: Hb 13,4g/dL, hematocrit 42%, prothrombin time 17 sec, activated partial thromboplastin time 32 sec, glucose 73 mg/dL, AST 137 U/L; ALT 179 U/L, albumin <1 g/dL and lactate dehydrogenase 1549 U/L. Abdominal ultrasound revealed slight periportal hyperechogenicity with possible inflammatory changes. Within hours, she began hemodynamic instability and progressively worsening mental status. At this point, was transferred to the intensive care unit and referred to the transplant unit. During the following days, her status deteriorated despite intensive care measures and developed cardio-pulmonary arrest, refractory to resuscitation. Death occurred 5 days after admission. The necropsy report microvesicular steatosis of the liver compatible with acute fatty liver of pregnancy.

## Methicillin-resistant Staphylococcus aureus in the setting of leukemia – make or break

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**Introduction:** A few cases of spontaneous remission (SR) interrupting the invariably progressive course of untreated acute myeloblastic leukemia (AML) have been reported so far.

**Case report:** 80 years old woman with severe comorbidity. Worsening constitutional symptoms few days before hospital admission, when fever, shaking chills, and shortness of breath developed. The patient took acetaminophen, but the symptoms did not improve. Blood tests revealed pancytopenia (hemoglobin 8.1 g/dL, platelet count 30.000/uL, leukopenia 2020/uL – 12% blasts), elevated DHL 3400 U/L and elevated C-reactive protein. Workup defined an AML. Owing to a lobar pneumonia, with methicillin-resistant Staphylococcus aureus (MRSA) being the agent identified in blood cultures, antibiotic therapy was established. An echocardiogram had no evidence of endocarditis. Repeat blood cultures were sterile. During hospitalization, supportive care included red cells and platelet transfusions. Low-dose corticosteroid was also administered. Eventually, the patient felt better, did not have dyspnea and was afebrile, being

discharged home. Subsequently, one week after hospital discharge, the patient was evaluated. A hemogram showed mild anemia (hemoglobin 11.2 g/dL), normal platelet count (154.000/uL) and normal leukogram. Later, a complete remission, lasting about one year, was documented on bone marrow morphological and cytogenetical examination. Eventually, one year after, the disease rose again. The patient presented neutropenic and died of sepsis.

**Discussion:** More research is needed to understand possible mechanisms of the various SRs described during the course of AML.

## Not all that wheezes is bronchial asthma

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**Introduction:** Churg–Strauss syndrome (CSS), alternatively known as eosinophilic granulomatosis with polyangiitis (EGPA), is a small-vessel necrotizing vasculitis, characterized by asthma, allergic rhinitis, and eosinophilia, first described in the 1950s. The American College of Rheumatologists (ACR) state that a diagnosis of CSS is probable with 4 or more of the following: asthma, eosinophilia 10% on a differential count, neuropathy, pulmonary infiltrates (non-fixed), paranasal sinus abnormalities, and infiltration of eosinophils in extravascular areas.

**Case report:** 45 years old woman, Caucasian, married. Previous medical history: non allergic asthma since childhood; non allergic rhinitis since childhood; pansinusitis, nasal polyposis, frequent airway infections. No known allergies. Under inhaled bronchodilators. Admitted to our hospital because of violaceous pruritic lesions on the thighs that had started 3 days before. She looked well and had no fever. Auscultation revealed wheezing. Her blood tests were remarkable for eosinophilia of 38.6%. Markers for HIV, HBV and HCV were negative. VDRL and rheumatoid factor were negative. Antinuclear antibodies were negative. Positive P-ANCA – 51,7 RU/ml (0-19.9). Normal complement. Respiratory tests were normal. High resolution chest CT: no adenopathies; multiple heterogeneous opacities in both lungs. She started prednisolone 1 mg/kg/day. The skin lesions resolved and the eosinophilia diminished dramatically. She had a skin biopsy – marked eosinophilic infiltration with leukocytoclastic vasculitis. 7 years before, she had done nasal polyps' biopsy – similar histological results. She was discharged home and maintained in follow up, under corticoid.

**Discussion:** This patient didn't have overt CSS. However, the association of asthma, eosinophilia, skin lesions, goes beyond the mere diagnosis of asthma alone.

## Sarcoidosis – a diagnostic challenge

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**Introduction:** Sarcoidosis is a multisystem inflammatory disease, whose specific lesion is non-caseating granulomas.

It occurs predominantly in the lungs and intrathoracic lymph nodes.

**Case reports:** We present three clinical cases of sarcoidosis, with several diagnostics and evolution features. The first case is a female patient with incomplete Löfgren syndrome, iridocyclitis and bilateral hilar lymphadenopathy (sarcoidosis – stage I), with unfavorable outcome until the introduction of corticosteroid therapy. In the second case a male patient shows a history of malignant melanoma treated with type 1 interferon; the particularity of this case lies in the fact that sarcoidosis begins three years after discontinuation of type 1 interferon. The third case presented is that of a young man who was diagnosed with both, tuberculosis and necrotizing sarcoid granulomatosis.

**Discussion:** The initial idea consisted in demonstrating some clinical and biological particularities of sarcoidosis – a multifaceted systemic disease in which inflammation can involve various tissues in the body.

## A novel diagnostic algorithm for recurrent fever of unknown origin

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**Background:** Fever of unknown origin (FUO), as defined by Petersdorf and Beeson in 1961, is a rather rare clinical syndrome, well known as a major diagnostic challenge. Recently, patients having more than 3 febrile attacks with fever-free intervals of variable duration have been proposed to be subcategorized under recurrent FUO (18-42% of total FUO). A substantial number of patients with recurrent FUO have an autoinflammatory genetic fever; many patients remain undiagnosed (51% in a series of 45 patients with recurrent FUO vs. 18% of 154 cases with continuous fever). We hypothesize this undiagnosed subgroup may comprise a number of rare diseases (such as acute porphyria, Crisponi disease, Fabry disease, and Ross disease) or atypical presentations of more common diseases.

**Objectives:** To propose a diagnostic algorithm for this specific patient population; to identify the key features or potential diagnostic clues for each specific disease and to adopt a common approach to patients with recurrent FUO.

**Methods:** An advisory board involving specialists in recurrent fevers, such as internists, infectiologists, rheumatologists, gastroenterologists, nephrologists, and medical geneticists convened to review the existing algorithms and to suggest recommendations for reaching accurate diagnosis on the basis of available literature and clinical experience.

**Results:** A novel integrated algorithm combining several features (hypo/anhydrosis, acroparesthesias, proteinuria etc.) has been designed to help identify infectious, autoimmune or autoinflammatory diseases from other conditions such as lysosomal diseases.

**Conclusions:** The proposed algorithm may be a useful tool for the diagnosis of rare diseases in cases of recurrent FUO. A wide prospective series of patients will be needed to validate the algorithm in the clinical setting.

## DRESS to impress

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**Introduction:** Adverse drug reactions are a daily medical concern, with an outcome ranging from benign to fatal. Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare drug-induced hypersensitivity reaction. Allopurinol is one of its most reported causes.

**Case report:** In January 2015 a 66 years old male with a gout crisis started allopurinol. No relevant medical history, no chronic medication and no history of allergic reactions were reported. A month later a purpuric rash and malaise developed and he was hospitalized with allopurinol toxicity with liver, renal and skin damage. Corticotherapy was initiated and allopurinol suspended. He was discharged after 3 days with normal liver enzymes and creatinine of 1.4 mg/dL, medicated with prednisolone. He returned to the hospital 2 weeks later with a generalized rash, and showed an unremarkable complete blood count with no eosinophilia and normal liver enzymes. He sustained an acute kidney injury (creatinine of 8.5 mg/dL, urea 165 mg/dL), with abundant eosinophils and leukocyturia in urinalysis. Due to hyperkalemia refractory to medical therapy, he initiated dialysis along with high dose corticotherapy. Kidney biopsy revealed interstitial nephritis. Renal function improved and dialysis was stopped. During hospitalization the rash aggravated to cover >50% of body surface, became scaly and aggravated after ceftriaxone initiation. Skin biopsy showed toxidermatitis. He showed intermittent fever with no microbiological isolations and developed eosinophilia with elevated inflammatory parameters. A RegiSCAR score of 7 with exclusion of other etiologies confirmed the diagnosis of DRESS. The clinical course was characterized by cachexia, malnutrition, remission/relapsing disease with multi-organ damage and reactivation of Epstein Bar and cytomegalovirus infection. Pancytopenia, ferritin, lactate dehydrogenase and triglycerides rose markedly and bone marrow biopsy showed hemofagocytosis. Later, respiratory failure requiring mechanic ventilation support developed. TC scan showed bilateral infiltrates of acute respiratory distress syndrome. 5 days later the patient was declared dead due to circulatory failure refractory to vasopressor support.

**Discussion:** DRESS is a severe drug reaction with unique clinical features. Early recognition, withdrawal of possible causative drugs and supportive care are mainstays to improve prognosis. Virus reactivation and hemophagocytosis can be fatal complications.

## Atypical presentation of arrhythmogenic right ventricular dysplasia: a case report

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**Introduction:** Arrhythmogenic right ventricular dysplasia (ARVD) is a rare, frequently autosomal dominant cardiomyopathy, typically characterized by fibro-fatty replacement of myocardial

tissue causing structural changes from localized aneurysms to ventricular dilatation, with areas of ventricular wall hypokinesia or dyskinesia. Associated dysfunction and ventricular tachyarrhythmias may develop which can increase the morbidity and the risk of sudden cardiac arrest or death.

**Case report:** A 67 years old male, former aircraft pilot, was admitted at our hospital after an episode of syncope preceded by malaise and diffuse cervicothoracic discomfort. No family history of sudden death was reported. Laboratory workup was within normal limits, namely D-dimer test, serum troponin I and arterial blood gas determination. Electrocardiogram showed sinus rhythm with T-wave inversion in leads V1-V3. Further investigation for pulmonary embolism was performed with spiral CT angiography showing no abnormal findings. Transthoracic echocardiogram (TTE) displayed a massive enlargement of the right ventricle with intact interatrial septum and no pulmonary arterial hypertension. Cardiac MRI confirmed right ventricular dilatation and revealed a marked hypokinesia of its lateral wall. Exercise stress test was negative for ischemia. In light of the 2010 Task Force criteria for ARVD this patient presented 2 major criteria (I. Global and/or regional dysfunction and structural alterations – by MRI: regional RV akinesia or dyskinesia or dyssynchronous RV contraction and RV ejection fraction  $\leq 40\%$ ; III. Repolarization abnormalities – inverted T waves in right precordial leads (V1-V3)), hence the diagnosis of ARVD was made. At the time of this abstract, electrophysiology study (EPS) is pending, and with it, the decision concerning implantation of cardioverter-defibrillator (ICD).

**Discussion:** The late clinical presentation of arrhythmogenic right ventricular dysplasia (ARVD), in a former aircraft pilot, enhances the importance of TTE screening, eventually complemented by MRI. The associated sudden death risk is being tackled by EPS with the decision concerning ICD pending. Genetic studies should be offered to ARVD patient's offspring.

## “Mediastinal-cane” – a simple radiograph case

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**Introduction:** Congenital anomalies of aorta are rare disorders associated with other cardiovascular diseases, which result from an abnormal development of the embryonic pharyngeal arch system. Aortic arch abnormalities represent less than 1% of the congenital cardiac defects, and their clinical representation, usual in the first years of life, depend on esophageal or tracheobronchial compression or abnormal blood patterns.

**Case report:** Female, 51 years old, Caucasian. Clinical background included inguinal hernia, appendectomy and hysterectomy. No use of regular medication. The patient displayed cough, generalized myalgia and some degree of dyspnea several days after taking the vaccine against the Influenza virus. Due to persistence of the symptoms a simple anterior-posterior radiograph was made, displaying a mediastinal "cane-like" deformity of the aorta's arch. A thoracic computerized

tomography scan ensued, exhibiting an anomalous route of the thoracic aorta, with a severe sinuosity of the distal segment of the descending aorta and a relevant kinking phenomenon of the common brachiocephalic branch. The patient's further exams, including, digital coronarography, echocardiogram, and electrocardiography were all normal. Congenital connective tissue diseases were also excluded.

**Discussion:** This clinical case serves the purpose to illustrate a rare and most probably congenital variation of the aortic route in an otherwise healthy middle-aged woman.

## Yellow nail syndrome: a rare condition

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**Introduction:** Yellow nail syndrome (YNS) is a rare disorder of unclear origin characterized by dystrophic yellow nails, lymphedema and respiratory manifestations (recurrent tract respiratory infections, pleural effusions, bronchiectasis and sinusitis). Sometimes it is also associated with pericardial effusion.

**Case report:** A 58 years old woman, heavy smoker, was admitted to the emergency room complaining of dyspnea and swelling of the lower limbs for 5 days. The patient had a clinical history of total thyroidectomy subsequent to Grave's disease, lymphedema, chronic sinusitis and multiple episodes of respiratory infections, as well as chronic cough and her nails have become thick and yellow. Physical examination revealed an obese patient, with dystrophic yellowish, increased respiratory rate, low cardiac sounds without extra sounds, vesicular murmur diminished on the right hemithorax and severe lymphedema of both legs. Chest radiography demonstrated small right pleural effusion and cardiomegaly. High-resolution computed tomography of the chest revealed a small right pleural effusion and a moderate pericardial effusion; transthoracic echocardiogram confirmed a bulky pericardial effusion without hemodynamic instability and a mild hypertensive cardiomyopathy. Routine laboratory blood tests were unchanged except PaO<sub>2</sub> of 53 mmHg. At admission the patient underwent a diagnostic thoracocentesis which revealed and exudative pleural fluid with lymphocytic predominance, negative for malignant cells. Cultural exams of blood and pleural liquid were negatives. Pleural biopsy was in favour of chronic fibrosis. Extensive laboratorial investigation was carried out but till the present no other etiology was found. It was prescribed hyposaline diet, diuretic therapeutic and her clinical condition improved gradually, including the pericardial effusion. However, since then the patient has been hospitalized multiple times for recrudescence of pleural effusion and lymphedema and remains in our follow-up consultation.

**Discussion:** In view of the clinical facts presented above and all performed etiological investigation it was assumed Yellow nail syndrome as the clinical condition on the basis of this clinical case. As the cause and pathogenesis of YNS maintains unclear no specific treatment exists and it is based mainly on relief of symptoms. The authors pretend to draw attention to this little-known clinical entity and probably underdiagnosed.

## Familial Mediterranean fever in Canary Islands. Different clinical and genetic patterns

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**Introduction:** Familial Mediterranean fever (FMF) is an autoinflammatory disorder characterized by recurrent self limited bouts of fever and sterile inflammation mostly confined to serosal membranes, joints, and/or skin. The defective gene in FMF is MEFV that is located on the chromosome 16p13.3, displays 10 exons, and encodes a 781-amino acid protein known as pyrin or also "marenostin". This syndrome occurs most commonly among people originating from the Mediterranean basin but has been recognized in every country of the world.

**Case report:** We report a 28 years old Caucasian woman who presented with a 1-year history of recurrent fever of short duration (1 day) associated with diffuse abdominal pain, arthromyalgias, transient maculopapular eruptions and leukocytosis. She had no family history of fevers. Her medical history is remarkable for a hypercoagulable state related with heterozygous factor V Leiden and low levels of plasma protein S. Moreover, she has been diagnosed 2 years ago of a myeloradiculoneuritis without etiological diagnosis and a bilateral carpal tunnel syndrome. Complete blood count, C-reactive protein, serum electrolytes, blood urea nitrogen, serum creatinine, liver function test, serum ferritin and urinalysis were normal. Autoantibody serology was also negative. Due to the lack of evidence supporting an infectious, malignant or autoimmune cause for his febrile illness the diagnosis of a periodic fever syndrome was considered. As the Livneh criteria for familial Mediterranean fever were satisfied, the patient was started on oral colchicine for the purpose of diagnostic treatment. Mutation analysis showed a heterozygous mutation of exon 2 of MEFV [p.(Pro180 Arg) o p.P180R]. Familiar analysis shows the same mutation in her asymptomatic mother. The patient was successfully treated with colchicine.

**Discussion:** The most relevant data of this report are: 1) This is, at our knowledge, the first communicated patient with this FMF in Canary Islands. 2) The undescribed neurological findings in a FMF patient (myeloradiculoneuritis and carpal tunnel syndrome). 3) An autosomic transmission pattern of MEFV in this family. 4) The different clinical pattern in this family with asymptomatic and symptomatic patient. Maybe, the coagulation disorders (factor V Leyden and S protein deficiency) can be related with symptomatic manifestations.

## Liver iron overload in a C282Y heterozygous hereditary hemochromatosis patient: case report

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**Introduction:** Hereditary hemochromatosis (HH) is an autosomal recessive disorder of the iron metabolism that courses with increased intestinal iron absorption, and can lead to iron overload and end-organ damage. The most common form is caused by C282Y mutation in the HFE gene. Whilst it is well established that C282Y homozygosity and C282Y/H63D compound heterozygosity increases the risk of iron overload-related disease, patients who are heterozygous for HH rarely present clinical manifestations of iron overload.

**Case report:** 60 years old former smoker, obese, dislipidemic and hypertensive man with history of an acute myocardial infarction when he was 39. He reported social alcohol consumption. He had type 2 diabetes recently diagnosed (previous year). The patient had no organ-specific complaints other than erectile dysfunction and his risk factors were controlled. Skin hyperpigmentation was absent. He presented persistent polycythemia (Hb >17-18 g/dL, Ht >50%), with normal white cell and platelet counts. He had normal liver enzymes, lactate dehydrogenase 172 U/L, albumin 45.8 g/L and prothrombin time was 11.8 sec. The serum erythropoietin was normal (7.9 mUI/mL) and the iron kinetics showed iron overload (serum iron 176 g/dL, serum ferritin 574.4 ng/mL, transferrin saturation 50%). The genetic testing showed C282Y heterozygous mutation of the HFE gene, no other gene mutations were present. Abdominal ultrasound: hepatomegaly, steatosis but no apparent cirrhosis and no splenomegaly. Echocardiogram showed normal chamber size, normal ventricular function and no hypertrophy. Free testosterone 3.91 pg/mL (5.6-19), LH 4.75 mU/mL (1.7-8.6), TSH 1.64 µU/mL, free T4 0.91 ng/dL. Liver magnetic resonance documented iron overload: liver iron concentration of 75 µmol/g (normal <36). Hepatitis B and C virus were negative. The patient was started on weekly phlebotomies during half a year, after which he had Hb 10.5 g/dL, Ht 34.1%, transferrin iron saturation of 5% and ferritin 12 ng/mL. Phlebotomies were stopped and one year after suspension he had Hb 16.5 g/dL, Ht 44.1% and ferritin 64.6%. Phlebotomies were re-initiated on a monthly basis and he has no evidence of additional organ damage related to iron overload.

**Discussion:** Clinical manifestations of iron overload in HH often occur in the setting of homozygosity or compound heterozygosity. Despite rarely, single heterozygosity can also course with end-organ damage and should not be overlooked since phlebotomies are a proven effective treatment.

## Prolonged fever and pancytopenia in a 40-year-old woman: the diagnosis of the diagnostic process

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**Introduction:** The aim of this work is to communicate a case of visceral Leishmaniasis presenting as hemophagocytic lymphohistiocytosis (HLH) and to describe the complex process of clinical reasoning that lead to successful diagnosis in a challenging and life-threatening case.

**Case report:** A 40 years old Brazilian woman was admitted in a regional teaching hospital due to fever up to 40°C of 7 days

duration. She had no relevant past medical history. Her heart rate was 113/minute and physical examination was otherwise unremarkable. Blood tests revealed pancytopenia (hemoglobin 90 g/l, leucocytes 2.3x10<sup>9</sup>/l, and platelets 113x10<sup>9</sup>/l), slight elevation of liver enzymes and LDH, and increased C reactive protein (162 mg/l). Chest radiography and urine tests showed no alterations. Blood cultures were sterile and fever persisted under empirical antibiotic therapy. As pancytopenia worsened, a conscious workup was warranted in order to rapidly achieve the correct diagnosis avoiding time consuming examinations. Persistence of high fever and worsening pancytopenia as well as sterile cultures suggested a different origin. Serology for HIV, CMV, EBV, Parvovirus B19, and viral hepatitis were negative. Thoracic and abdominal CT-scanner showed a slight hepatosplenomegaly. HLH was evocated. Ferritin blood levels were extremely increased. Bone marrow aspiration and biopsy confirmed this diagnosis. Thorough reviews of HLH causes, as well as a meticulous review of the history with special attention the patient's country of origin, lead to the suspicion of visceral leishmaniasis. This was confirmed by positive serology for *L. infantum* as well as *Leishmania's* PCR in bone marrow specimen. The patient was treated with liposomal amphotericin. Fever disappeared and blood cell counts increased achieving normal values within 3 weeks.

**Discussion:** Clinicians unconsciously use multiple strategies to solve clinical problems, suggesting a high degree of mental plasticity in the diagnostic process. Both intuitive pattern recognition and comprehensive analytical approaches were necessary to get to right diagnosis and to provide specific therapy. We believe that there is no substitute to clinical experience and that intuitive and analytical approaches occur simultaneously at all levels of clinical expertise.

## Glatiramer acetate induced refractory immune thrombocytopenic purpura

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**Introduction:** Glatiramer acetate (copaxone) is an immunomodulatory agent, approved for the treatment of relapsing-remitting multiple sclerosis. Adverse effects of glatiramer acetate include mostly local site injection reaction along with transient systemic reactions. Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by immunologic destruction of otherwise normal platelets, leading to platelet counts of less than 100x10<sup>9</sup>/L. ITP may occur in isolation (primary) or in association with other disorders (secondary). We present a case of glatiramer acetate induced refractory immune thrombocytopenic purpura in a multiple sclerosis patient.

**Case report:** A 40 years old woman was admitted to the hospital with a chief complaint of new onset rash. Past medical history included multiple sclerosis diagnosed at age 27, treated with interferon beta. Two months before admission the interferon beta was switched to glatiramer acetate. The physical examination was unremarkable except for petechial rash on her legs and shoulders. The hemoglobin level was 12.1

g/dL, the leukocyte count 4,870/mm<sup>3</sup> and the platelet count 1,000/mm<sup>3</sup>. Two month prior to admission the platelet count was 263,000/mm<sup>3</sup>. LDH was 515 U/L. ANA, RF, anticardiolipin, HCV, HIV, CMV IgM and EBV IgM were all negative. Bone marrow aspiration demonstrated normo-cellular marrow except for multilobulated forms of megakaryocytes, without evidence of tumor. On admission glatiramer acetate was stopped. The patient received prednisone 1 mg/kg from the time of her admission, with a four day trial of dexamethasone 40 mg daily in between. The patient was treated with Rh0 (D) immune globulin 75 µg/kg on the fourth day of hospitalization, followed by a trial of intravenous gamma globulins (IgG) 2 gr/g. Failure of all these treatments prompted the decision to perform a splenectomy. The patient was treated for three weeks with romiplostim as a bridging therapy before the procedure, however there was no increase in platelet count. The patient underwent splenectomy without complications. Platelet counts started to increase immediately after the procedure. On discharge platelet count was 328,000/mm<sup>3</sup>.

**Discussion:** To the best of our knowledge this is the first report of glatiramer acetate induced ITP. Physicians should be aware of this side effect, and consider performing routine blood counts during glatiramer acetate treatment.

## Sensibility and specificity of new criteria of Behçet's disease in Tunisian population

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**Objectives:** Study the performance of revised criteria of Behçet's disease (ICBD) in Tunisian population and compare to that of ISG criteria.

**Methods:** We conducted a case-control retrospective, evaluative and comparative study. Two groups of patients were included: the first (G1) including 430 patients followed for Behçet's disease (BD) between 1989 and 2010 and diagnosed according to ISG criteria. The second group (G2) including 571 patients with other miscellaneous diseases having common manifestations with BD. Epidemiological and clinical characteristics were compared between 2 groups. Subsequently, we applied the ICBD score in patients of 2 groups.

**Results:** Sex-ratio was 2.2 in G1 and 0.23 in G2. The average age of onset of the disease was 34 years in G1 and 41 years in G2. Significant difference was noted between 2 groups. All patients of G1 had oral aphthosis versus 20 patients in G2. Genital aphthosis, skin, ocular and vascular involvements were significantly more frequent in G1 (respectively 79.3, 85.1, 46.5 and 34.9%) in G1 than in G2 (0.4, 8.9, 16.3 and 10.9%). We calculated the score of ICBD revised criteria in 2 groups and we classified patients in sick (score <4) or healthy (score ≥4). We concluded that: 3 patients of G1 did not meet the ICBD criteria (false negative) and 7 patients of G2 (with diagnosis of benign recurrent aphthous stomatitis) met the ICBD criteria (false positive). To study performance of these criteria in our population, we calculated different evaluative parameters: sensibility was 99.3% and specificity was 98.6% with optimization of 0.7%. The accuracy was 91.5%. The positive and

negative predictive values were respectively 98.4 and 99.4%. The Youden index was 0.98.

**Conclusion:** Diagnostic efficacy of ICBD criteria was better than that of ISG criteria with better sensibility and specificity.

## Prevalence and influence of pulmonary arterial hypertension during systemic sclerosis

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**Objectives:** Pulmonary arterial hypertension (PAH) is a severe complication of SSc and the leading cause of morbidity. It can be isolated revealing a vascular disease or secondary to interstitial lung disease. This paper aimed to investigate the prevalence of PAH, characterize the demographic, clinical, paraclinical and evolutionary features of patients with SSc-PAH and to conduct a comparative study of patients with and without PAH.

**Methods:** Retrospective study, descriptive and comparative including 141 patients with SSc hospitalized in Internal Medicine Department of the Hospital Rabta from 1981 to 2013. The SSc was diagnosed according to American College of Rheumatology. The diagnosis of PAH was carried by a systolic pulmonary artery pressure >25 mmHg to cardiac Doppler echography and a mean pulmonary artery pressure measured during right heart catheterization >25 mmHg at rest or 30 mmHg during exercise with a pre-capillary pulmonary pressure <15 mmHg. Patients were divided into 2 groups: G1 = SSc with PAH and D2= SSc without PAH. For the study of links between two variables, the significance level was set at 0.05.

**Results:** 141 patients with SSc (F/M = 127/14) were included in the study. The mean age at onset of the disease was 42.3±14.3 years. The average age at diagnosis was 48.1±14.2 years. PAH was found at the cardiac Doppler echography in 25 patients (17.7%). It was confirmed by RHC in 3 cases. The majority of patients with SSc complicated by PAH were women (92%) and had limited sclerosis (76%). The average age at diagnosis was 48.8±12 years and the average time of follow-up was 52.3±53.7 months. CREST syndrome was present in 2 cases and one patient had Sine Scleroderma. The average value of the PAPs to cardiac Doppler echography was 45.4±14.6 mmHg. PAH was isolated in 19 cases and secondary to interstitial lung disease (PH-ILD) in 6 cases. Predictors of the onset of PAH in our study were: dyspnea (p=0.01), ECG abnormalities particularly heart rhythm disorders (p=0.006), pericarditis (p=0.01), esophagitis (p=0.01), a scleroderma renal crisis (p=0.03), mediastinal lymphadenopathy (p=0.03), the positivity of AC anti-SSB (p=0.02) and latex (p=0.03) and the association with Sjögren's syndrome (p=0.03). The calcium channel blockers were prescribed in 84% of patients (p=0.01) and Bosentan in 16% (p=0.004). Two patients had died.

**Conclusion:** The severity of PAH in SSc justifies the annual practice of cardiac Doppler ultrasound which should be repeated particularly in patients with clinical and laboratory characteristics drawn up by our study, especially as survival was improved by the advent of new therapies.



## Mesenteric panniculitis: an over-diagnosed entity? A dilemma between mesenteric computed tomography and biopsy. A series of 58 cases in a single hospital

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**Objectives:** The mesenteric panniculitis (MP) is a rare and chronic inflammatory process of mesenteric fat which has been associated with cancer although MP may be idiopathic. Despite of the histological diagnosis is the gold standard only in a minority of cases published the mesenteric biopsy is done being relegated for cases refractory to standard treatment which combined with the non-specific findings by CT scan may contribute to an overestimation of the number of cases. In this sense, we propose to describe the characteristics of patients diagnosed of MP in our Hospital and discuss about possible factors involved in the overestimation of cases.

**Methods:** Medical records of 58 patients (31 men and 27 women) diagnosed of MP between January 2009 and March 2015 at the University Hospital Clinic San Carlos from Madrid was reviewed retrospectively. We collected epidemiological data, symptoms, treatment and outcome. Data were analyzed with SPSS Statistics 20.0.

**Results:** The median of age of these patients was 76 years (range 38-93). Of the 58 patients, 14 had a history of cancer being the prevalence of cancer in our series of 24% and the average time from cancer diagnosis and the MP diagnosis were 5 years. The most frequent cancer was the colon adenocarcinoma (44%) followed by lung carcinoma (21%), melanoma (14%), urothelioma (14%) and cervical carcinoma (7%). At presentation, 82.5% of patients had abdominal pain, 8.5% fever, 7% dyspnea and 2% diarrhea. Of the all of patients with abdominal pain, 19% of them had simultaneously other pathologies causing abdominal pain (9% cholecystitis, 4% pancreatitis, 2% appendicitis, 2% abdominal hernia complicated and 2% bowel pseudo obstruction). The diagnosis of PM was performed by computed tomography (CT) in all cases and only in 3 cases histological studies were made. All were treated because they had symptomatology and the treatment consisting of discontinuation of oral intake, antibiotics, antiinflammatory drugs or steroid treatment. In our series, a patient died.

**Conclusions:** 1) The MP could be even less frequent than described; 2) the prevalence of cancer in this series was 24% being the colon adenocarcinoma the most frequent; 3) more than 80% of patients had abdominal pain but almost 20% of them concomitantly had other causes abdominal pain; 4) the over-diagnosis could increase morbidity of these patients due to the use of unnecessary treatments; 5) we think the mesenteric biopsy is needed to confirm the MP diagnosis.

### Peliosis lienalis

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**Introduction:** Peliosis lienalis is a non-neoplastic lesion of the spleen, characterized with cystic blood-filled cavities. Its etiology

includes chronic diseases, HIV, anabolic steroids, AZT use after renal transplantation and chronic starvation. It is usually seen in the liver but rarely in the spleen and under 5 cm in diameter. Bigger lesions have the possibility of rupture and sudden death. It is usually asymptomatic and detected incidentally. Here, we present a case with recurrent fever, bicytopenia, elevated sedimentation rate and CRP level episodes, first diagnosed and treated with polymyalgia rheumatica, then incidentally diagnosed with peliosis lienalis and recovered after a splenectomy.

**Case report:** 57 years old female patient presented with fever and fatigue. In her history, there was enhanced sweating at night-time, limited effort capacity, headache and shoulder ache and hypertension. Her physical examination revealed normal. Her laboratory results showed: WBC 2700, Hct 28%, Plt 151000, ESR 60 mm/h, CRP 10, Fe 11, FeBC 355, rheumatologic and infectious markers (-), beta-2 microglobulin 8.1 mg/L (N: 1.1-2.4 mg/L). Protein electrophoresis showed a slight polyclonal hypergammaglobulinemia. Chest X-ray and CT, thyroid ultrasonography (USG) were normal. Abdominal USG showed a 5 cm mass (hemangioma? hamartoma?). Bone marrow biopsy was normal. Abdominal CT and MRI were performed. CT showed iso-hypodens, 5 cm, nodular, smooth contoured mass which enhanced splenic volume and had homogenous contrast. In MRI, it was hyperintense in T2A examination and hypointense in T1A. Those findings were consistent with ordinary spleen masses and was considered as hemangioma or hamartoma. Thus, the patient was diagnosed with polymyalgia rheumatica and steroid therapy was started. Her symptoms partly relieved but bicytopenia and elevated sedimentation and CRP levels persisted. After 1 year, in control abdominal MRI, the splenic mass was found to grow to 91 mm and a splenectomy was performed. Patient's symptoms relieved completely and blood test turned to normal. The pathological result of the mass was peliosis.

**Discussion:** Like in our case, peliosis lienalis can present with only constitutional symptoms and systemic inflammatory signs, mimicking several diseases. Most common benign masses in the spleen are hemangiomas and hamartomas and peliosis is rarely seen in healthy individuals, but it should be kept in mind in differential diagnosis of splenic masses.

### Transfusion, the last nail in the coffin

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**Introduction:** Transfusion-related acute lung injury (TRALI) is a rare but potentially fatal complication of blood product transfusion (BPT). TRALI is associated with a significant mortality rate (5-10%). Symptoms of TRALI develop during or within 6 hours of a transfusion. Treatment of TRALI is supportive, with no role for diuretics or corticosteroids, but mild forms of TRALI may respond to supplemental oxygen therapy. However, severe forms may require mechanical ventilation and ICU support. It is imperative that the physicians identify suspected cases of TRALI and report them to the blood services. This way, an investigation of donors involved in these cases can be done, deferring them from further donations. We present a case of a terminal stage patient that died following a transfusion.

**Case report:** A 77 years old woman, with previous diagnosis of vulva carcinoma (TNM Stage IV), diabetes mellitus type 2, arterial hypertension, dyslipidemia, heart failure II-III NYHA class, stage 3 CKD, multinodular goiter, hypothyroidism, recently discharged from the hospital for cellulitis of the hand, bedridden, came to the emergency department with vomits (dark color) and prostration. At the physical examination, the patient was hemodynamically stable, without alterations on the respiratory, cardiovascular, abdomen or rectal exam. Nasogastric tube: exit of normal gastric content. Chest X ray: condensation in the median lobe of the right lung, ECG normal. Blood test results: white blood cells (WBC) 31.8x10<sup>3</sup>/uL, neutrophils 90.4%, hemoglobin 7.5 g/dL, urea 60 mg/dL, creatinine 1.9 mg/dL, CRP 133 mg/l. The patient was admitted to the infirmary with the diagnosis of nosocomial pneumonia and initiated a BPT and during the procedure, the patient initiated dyspnea and decrease in the periphery oxygen levels, respiratory exam with rales. It was started high flow oxygen, bronchodilator, corticosteroids and diuretic, but within an hour the patient died.

**Discussion:** A BPT is not innocent, since in this case it was the cause of death. This way, blood components should be used only for indications that are justified based on medical evidence. This way, it is important for hospitals to have protocols regarding the blood utilization and it's mandatory that doctors and the blood service staff to communicate to prevent and manage better these situations.

## Esophageal necrosis

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**Introduction:** Acute esophageal necrosis (AEN) is rare (prevalence of up to 0.2%) in autopsy series. In endoscopy series, the prevalence of acute esophageal necrosis has ranged from 0.001 to 0.2% of cases. The incidence of AEN is >4 x higher in men as compared with women, and patients have a mean age of 68 years at diagnosis. This condition is often diagnosed incidentally in patients undergoing upper endoscopy for evaluation of upper gastrointestinal bleeding, but has mortality rates between 13-35%, largely due to the underlying disease. The most of the patients get better with supportive care, but the most common long-term complication is esophageal stricture formation, which often requires esophageal dilation. We present the case of a patient that was accidentally diagnosed with this rare syndrome, usually fatal, but not in this case.

**Case report:** A 76 years old Caucasian woman, with diagnosis of diabetes type 2, dyslipidemia, status post stroke (25 years before), bedridden, came to the emergency department with hematemesis, epigastric pain, back pain and fever (39°C) with 12 hours of evolution. At the physical examination the patient was hemodynamically stable, without alterations on the respiratory, cardiovascular, abdomen or rectal exam. Nasogastric tube: coffee grounds mixed with normal gastric content. Chest X ray normal, ECG normal. Blood test results: white blood cells (WBC) 20.2x10<sup>3</sup>/uL, neutrophils 90.9%, hemoglobin 15.2 g/dL, CRP 48.6 mg/l. Urinalysis: WBC 20, red blood cells 50. Urine culture

negative. Upper endoscopy detected esophageal necrosis with signs of re-epitelization in the lower third of the oesophagus (confirmed by the histological examination). No signs of active bleeding. Gastric paresis. The patient was admitted to the infirmary with the diagnosis of pyelonephritis and esophageal necrosis due to gastric paresis and infection. After 8 days of cefuroxime, pantoprazole and sucralfate, the patient was discharged, clinically stable.

**Discussion:** AEN is a rare condition, but has a high rate of mortality, largely due to the underlying disease that has to be treated promptly. This case is interesting because it happened in a woman (when this syndrome is more prevalent in men) and it was a case of success relating to the management and prognosis, because the patient remains asymptomatic almost a year after the diagnosis.

## A rare case of Gaucher disease presented in late age

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**Introduction:** Gaucher disease (GD) is a rare metabolic disease associated with lack of glucocerebrosidase enzyme. In the disease, abnormal accumulation of sphingolipids occurs in tissues, causing organ dysfunctions. The early recognition of the disease is crucial in terms of treatment and prognosis. Here we present a case of GD, who was diagnosed rather late period of age with widespread organ involvement.

**Case report:** A 54 years old female patient was admitted to the clinic with 3-4 years history of progressive weakness, fatigue and easy bruising in her body. She indicated that her complaints were increasing with physical effort. She had DM, hypertension and morbid obesity on medical history. On physical examination, height was 155 cm, weight was 130 kg, and she was marked hepatosplenomegaly. Her laboratory exam showed a marked anemia and thrombocytopenia (Hb 8.5 g/dL, PLT 90000/ml). Ultrasonographic exam showed diffusely enlarged liver and spleen. There was no finding of portal vein thrombosis. Peripheral blood smear was consistent with normocytic-normochromic anemia and thrombocytopenia. Bone marrow aspiration was normocellular, with x10 magnification revealing 2-4 megakaryocytes, 1:1 myeloid/erythroid ratio, 1% plasma cells, 0.5% blast cells, and 2 Gaucher cells. Peripheral blood samples were sent to two different laboratories with pre-diagnosis of GD.  $\beta$ -glucocerebrosidase enzyme activities were detected low in both of them (measuring 2.3 mol/l/h; reference >3.2). According to these findings, patient was diagnosed with type1 GD and started imugluseraz 60 IU/kg enzyme replacement therapy once fortnightly.

**Discussion:** Of the known 3 types of GD, type1 is usually diagnosed in adulthood. In fact, GD is known as a childhood disease, it is less considered by physicians during the differential diagnosis particularly for adult patients. This raises significant disadvantage in terms of treatment and prognosis of the disease. Our case also was diagnosed at a fairly advanced age in spite of being investigated for a long time for thrombocytopenia and hepatosplenomegaly. As a result, GD should be kept in mind,

even in older patients during differential diagnosis of cases with coexistence of hepatosplenomegaly and thrombocytopenia.

## Septicemia by *Chromobacterium violaceum*: a rare case

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**Introduction:** *Chromobacterium violaceum* is a large motile gram-negative bacillus facultative anaerobic found commonly in soil and water in tropical and subtropical climates. The bacteria enter the body through the skin with minor trauma or by drinking contaminated water. The organism rarely causes infection in humans, but when it occurs, rapidly progresses to septicemia, with necrotizing lesions and multiple abscesses in the skin, lung, liver, spleen, lymph nodes, and brain, resulting in fatal multiorgan failure. Since the first human case described in Malaysia, only 100 cases have been reported worldwide. Diagnosis is based on cultures. The quick evolution and antibiotic treatment failure result in a mortality rate of over 60%. This study describes a fatal case of *C. violaceum* infection in a young man. This is probably the fourth documented case reported of *C. violaceum* infection in Brazil.

**Case report:** A previously healthy 28 years old man reported to have been exposed to soil and water from a lake in a rural area with both feet injured. 10 days after, he was taken to a local hospital with headache, diffuse abdominal pain, fever and diarrhea, from where he was discharged with oral amoxicillin 500 mg tid. Over the next 5 days he developed purple micronodules on the thigh and abdomen, and rapidly evolved to septicemia, with respiratory failure, acute renal insufficiency disseminated vascular coagulation and hemodynamic instability that required inotropic drugs. He was immediately admitted to the ICU, but evolved to death. Two samples of hemoculture isolated *C. violaceum*.

**Discussion:** Human infection caused by *C. violaceum* results in systemic severe disease with a high mortality rate. In tropical and subtropical regions it should be considered in the differential diagnosis of sepsis, especially when associated with skin or multiple organ abscesses or with a history of exposure to stagnant water. The organism is sensitive to gentamicin, ciprofloxacin, tetracycline, ceftazidime, imipenem, and amikacin, but is extremely resistant to penicillin and cephalexin. *C. violaceum* is an uncommon cause of infection and the diagnosis requires a high degree of suspicion. Early diagnosis, proper and timely treatment are extremely important aspects for survival.

## Kikuchi-Fujimoto disease: rare or underdiagnosed?

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**Objectives:** Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is a rare, benign entity, presenting as lymphadenopathy, mostly cervical, frequently associated with a series of systemic manifestations such as fever and malaise. The pathophysiology of this disease remains controversial and may be associated with autoimmune diseases, especially systemic lupus erythematosus (SLE) and certain infectious agents. The aim of this study was to evaluate the clinical, laboratory and epidemiological features of KFD in a regional hospital setting in Spain.

**Methods:** Review of KFD cases followed-up at the Granollers General Hospital, Barcelona, Spain, which has an area of influence of 300.000 inhabitants.

**Results:** 6 cases of KFD were diagnosed between 1990 and 2015. The mean age of the patients was 27.5 years (with an age range from 13 to 42), with 5 out of 6 cases being female. 1 patient was originally from Pakistan and the rest from Spain. 5 patients presented with cervical lymph nodes, and 1 with axillar and inguinal, while all of them presented systemic manifestations. Histological examination of a lymph node biopsy was realized in all patients, confirming the diagnosis. 4 patients had previous diagnosis or concomitant autoimmune disease: 1 had been already diagnosed of a Systemic Lupus Erythematosus (SLE), 1 had a previous history of autoimmune thyroiditis, 1 had Raynaud phenomenon and Jaccoud arthropathy and 1 an autoimmune thrombocytopenic purpura. At the moment of diagnosis, only 2 patients presented positive anti-nuclear antibodies, one of them being previously diagnosed with SLE. The rest had a negative autoimmunity screening. During follow-up, 2 more patients were diagnosed with SLE, based on suggestive clinical features and positive immunological work-up, 2 and 4 years after KFD diagnosis respectively. 3 out of 6 patients presented a relapse of the KFD sometime during follow-up.

**Conclusions:** KFD is a rare, but probably underestimated disease. It can be associated with other autoimmune entities. Systemic lupus erythematosus can precede or accompany of follow the diagnosis of KFD.

## Interrelation between myocardial structure and efficacy of treatment

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**Objectives:** Interrelation between myocardial structure and efficacy of treatment in patients with rheumatoid arthritis (RA) in our time is studied insufficiently. The aim of the current study is to investigate the relationship between the echocardiographic parameters of myocardium and efficacy of the anti-rheumatic therapy in patients with RA in prospective observation.

**Methods:** 74 patients of rheumatology department of Saratov regional clinical hospital with RA have been observed (initially and after 1 year). The treatment efficacy was assessed using the index activity RA DAS 28. Myocardium masse (MM), myocardium masse index (MMI), final systolic (FSV) and diastolic (FDV) volume and size (FSS and FDS), posterior wall thickness (PWT) of left ventricle (LV), ejection fraction (EF), right (RAS) and left atrium (LAS) size, right ventricle size (RVS), systolic blood pressure in pulmonary artery (SPPA) were measured by «Apogee CX».

**Results:** 71,6% patients RA have arterial hypertension (AH) and ischemic heart disease. MMLV, MMI, FSS, PWT in those patients were significantly higher than in RA patients without cardiovascular disorders ( $p < 0,05$ ). After 1 year 8,1% patients achieved remission or low activity, 43,2% – moderate activity of RA and 44,6% patients stayed on high activity. The patients with high and moderate activity RA have MMLV, MMI, FDS, RVS higher than persons with low activity ( $p < 0,05$ ). The duration of the RA positive correlates ( $p < 0,05$ ) with MMLV ( $r = 0,5$ ), MMI ( $r = 0,76$ ), PWT ( $r = 0,55$ ), SPPA ( $r = 0,45$ ) only in patients with low activity. C-reactive protein (CRP) level positive correlates with EF ( $r = 0,33$ ), RAS ( $r = 0,36$ ), LAS ( $r = 0,31$ ). In patients with moderate activity the duration of the RA positive correlates with LAS ( $r = 0,31$ ); EF correlates with DAS28 ( $r = 0,31$ ). There was no any relationship between CRP level and echocardiographic parameters. In patients with high activity echocardiographic parameters did not correlate with RA duration, DAS 28 and CRP level.

**Conclusions:** In this study was showed that left ventricle myocardium masse and mass index, right ventricle size, left and right atrium sizes in patients with high and moderate RA activity are higher than in persons with low activity or RA remission. The duration of the RA, CRP levels and DAS 28 activity index correlates with sizes of atriums and left ventricle in patients with low activity.

## Polymyalgia rheumatica — a diagnosis to consider

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**Introduction:** Polymyalgia rheumatica (PMR) is a relatively common inflammatory rheumatic disease. It is almost exclusively a disease of adults over the age of 50, with a peak incidence between ages 70 and 80. Its prevalence increases progressively with advancing age and affects 2 to 3 times more women than men. The aim of this work is to describe a case of an incidental diagnosis of PMR and subsequent therapeutic orientation.

**Case report:** Patient, male, 85 years old, previously autonomous, admitted to the medical ward by acute diarrhea and acute on chronic kidney disease. He referred intense asthenia with months of evolution and progressive degradation of autonomy. Physical examination without important changes. Clinical analysis with normocytic/normochromic anemia, discreet leukocytosis, impaired renal function, C-reactive protein (CRP) 16.5 mg/dL and sedimentation rate (ESR) 120 mm/h. Negative stool culture. Endoscopic study without significant changes. During hospitalization, the patient reported symmetrical pain and stiffness in the neck, shoulders and torso with morning predominance and brief duration. Physical examination revealed inability to actively abduct shoulders past 90 degrees, causing severe functional limitation. Without muscle tenderness. Treatment with prednisolone 15 mg/day was initiated with improvement of symptoms. Study of autoimmunity in particular rheumatoid factor was negative. At the time of medical release, patient had complete resolution of infectious enteritis, renal function at baseline, CRP 7.34 mg/dL and ESR 104 mm/h. The authors concluded for PMR.

**Discussion:** The authors emphasize the importance of early diagnosis of PMR because of the strong influence on functional capacity and quality of life of older people. However, it acknowledges the difficulty in its recognition due to the numerous possible differential diagnoses. Despite the favorable prognosis, patients should maintain follow-up to symptomatic control, screening of recurrence and other diseases and monitoring of adverse effects of corticosteroid therapy.

## Cardiovascular risk in rheumatoid arthritis: does obstructive sleep apnea play a role?

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**Objectives:** We assessed the rate of obstructive sleep apnea (OSA) in patients with rheumatoid arthritis (RA) and identified its significance in pre-clinical CVD.

**Material and methods:** It was a cross-sectional, retrospective study. A total of 39 female patients (median of age 51 years, range from 20 to 63 years) with RA were included. 67% of RA patients were RF-positive and 87% had moderate-to-high disease activity according to DAS values. All patients were on non-steroidal anti-inflammatory drugs treatment, 54% patients were being treated with disease-modifying antirheumatic drugs

and 31% were taking prednisolone. All study subjects underwent careful clinical examination, OSA screening using Epworth sleep scale, echocardiography, high-resolution carotid ultrasound. OSA detected by portable monitor that measures airflow through a nasal pressure transducer and performs pulse oximetry. AHI and oxygen desaturation index (ODI) were used for OSA detection.

**Results:** OSA (AHI  $\geq 5/h$ ) was detected in 56% RA patients. There were no differences in cardiovascular risk factors between patients with OSA and without OSA ( $p < 0.05$ ). Left ventricular mass index was slightly higher in patients with OSA ( $p = 0.08$ ). Carotid intima-media thickness was significantly higher in patients with OSA ( $p = 0.011$ ). Interestingly, there was no difference in atherosclerotic plaque numbers between the groups (38% vs 31%,  $p = 0.545$ ). The positive correlations of AHI with carotid intima-media thickness ( $r = 0.43$ ;  $p = 0.017$ ) and ODI with left ventricular mass index ( $r = 0.48$ ;  $p = 0.003$ ) were found. ODI also correlated with tender and swollen joints scores and DAS28 ( $r = 0.45$ ;  $0.35$ ;  $0.41$  respectively,  $p < 0.05$ ).

**Conclusions:** The rate of OSA in our sample of RA patients is 56%. OSA presence is associated with pre-clinical CVD (subclinical carotid atherosclerosis and left ventricular hypertrophy). Oxygen desaturation index (intermittent hypoxia marker) is correlated with RA activity. Our findings confirm that OSA can be a potential risk factor for cardiovascular diseases in RA patients.

## Polyarthralgia and bilateral pulmonary infiltrates

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**Introduction:** The approach of polyarthralgia is always challenging. A careful history, together with a thorough physical examination and the search for extra articular symptoms are critical for the diagnosis.

**Case Report:** Male, 54 years old, smoker, admitted with productive cough and dyspnea, without fever, evolving in the last two days. He also referred, in the last 3 months, inflammatory additive polyarthralgia, affecting the shoulders, hands, proximal metacarpophalangeal and knees, accompanied by weakness of pelvic and shoulder girdles, and umbilical abdominal pain radiating to the back. The initial analytical study showed only increased C-reactive protein. Chest X-ray showed diffuse bilateral opacities in a butterfly wing pattern. Additional study included autoimmune panel (negative/normal), erythrocyte sedimentation rate (100 mm/h), abdominal imaging (normal) and bronchoscopy (normal, with negative cytology for neoplastic cells). Microbiological study, including atypical agents and Mycobacteria, was positive for Influenza A. Knowing this, we assumed polymyalgia rheumatica complicated with viral respiratory infection. The patient started corticosteroid therapy, with resolution of the joint complaints.

**Discussion:** Clinical presentation and initial investigation led to consideration of multiple diagnostic possibilities, from connective tissue disease with pulmonary involvement or respiratory infection, to the possibility of neoplasm (lung or pancreatic cancer), integrating the osteo-articular manifestations as paraneoplastic. The identification of the responsible agent

for respiratory infection, associated with the negativity of the remaining study with the exception of glomerular sedimentation rate, put us on track of polymyalgia rheumatic, confirmed by the therapeutic response.

## How big a clue is the Doppler in the diagnosis of giant cell arteritis?

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**Introduction:** Horton's disease, or giant cell arteritis, is a vasculitis of unknown cause that affects the elderly (average age of onset is 72), mainly women (2 times more than men). It affects the medium and large-sized arteries, specially the extracranial branches of the carotid, with transmural inflammation, lymphocytary infiltration and giant cells, sometimes causing distal ischemia. Its complications are systemic, neurologic and ophthalmologic (irreversible blindness being the most feared), being hard to diagnose for its multiple possible symptoms. The most common symptoms are headache, pain in the neck, shoulders and hips, jaw claudication, fever and blurred vision. Giant cell arteritis accounts for 16% of fever of unknown origin in the elderly.

**Case report:** 74 years old woman with fever of unknown origin, long time headache, anorexia (5% weight loss) and neck pain. No significant findings in the physical examination. Analytically, iron deficiency anemia and increased inflammatory parameters (ESR 120 mm/h and CRP 17 mg/dL) with normal leukocyte count and negative procalcitonin. Doppler showed inflammatory halo in the temporal arteries and biopsy confirmed the diagnosis. Was discharged under corticosteroid therapy (1 mg/kg, currently weaning) with clinical and analytic improvement.

**Discussion:** Giant cell arteritis should be considered in the differential diagnosis of patients over 50 years old with these kinds of symptoms and high erythrocyte sedimentation rate. Timely start of treatment can prevent blindness or other potentially irreversible ischemic sequelae. Temporal artery Doppler is gaining weight as a noninvasive alternative to biopsy, so we present this case to discuss that issue.

## Cardiovascular risk in patients with psoriatic arthritis

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**Objective:** Assess the risk of cardiovascular (CV) disease in patients with psoriatic arthritis (PsA).

**Methods:** 61 patients (29 males) with PsA aged 30-55 years old who had no previous history of CV disease. Duration of PsA ranged 6 months – 33 years. The control group included 45 people without inflammatory rheumatic diseases, comparable with the main group by sex and age. Classic CV risk factors, high-sensitivity C-reactive protein (hs-CRP) were analyzed, carried out ultrasound

scanning of carotid artery (CA) and determined carotid intima-media thickness (cIMT) as well as carotid total plaque area (TRA).

**Results:** Increase in total cholesterol (TX) level was observed in 68.2% patients with PsA and 48.8% in the control group and averaged in both groups  $5.9 \pm 1.0$  and  $4.9 \pm 0.7$  mmol/l respectively ( $p=0.01$ ). Considerable increase of low density lipoproteins cholesterol level was found in 67.2% patients with PsA and 57.7% in control group, their mean values were  $3.7 \pm 0.8$  and  $3.3 \pm 0.7$  mmol/l respectively ( $p=0.05$ ). Dyslipidemia correlated with advanced stages and inflammatory activity of PsA. Hyperuricemia was more frequently detected in the study group (19.6%) than in the control group (11.1%). 8.2% of patients with PsA had diabetes while it was not observed in the control group. Overweight was found in 32.8% of patients with PsA and 11.1% in the comparison group, obesity in 19.4% and 13.3%, respectively. CRP level was associated with the degree of inflammatory activity in the main group and reached 93.1 mg/l. Average values of this index were  $20.4 \pm 23.3$  mg/l in the main group and  $1.13 \pm 1.37$  mg/l in the control group ( $p<0.05$ ). Atherosclerotic plaques in CA were detected in 21.9% of patients with PsA and 4.4% in the control group, subclinical manifestations of atherosclerosis occurred in 70.4% and 15.3% respectively. The average cIMT value in patients with PsA was  $0.88 \pm 0.1$  mm, the maximum value –  $1.19 \pm 0.12$  mm, in the control group –  $0.7 \pm 0.1$  mm and  $0.82 \pm 0.2$  mm respectively; it was found that there's a direct correlation between hs-CRP and cIMT ( $r=0.21$ ,  $p<0,05$ ).

**Conclusion:** The accelerated development of atherosclerosis in PsA is caused both by traditional CV risk factors that are more prevalent in patients with PsA, as well as by additional ones associated with chronic immune inflammation that underlies this disease.

### **Lack of association between low bone mineral density and subclinical atherosclerosis measured by pulse wave velocity in women with systemic lupus erythematosus**

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**Objectives:** Patients with systemic lupus erythematosus (SLE) are in increased risk for cardiovascular disease (CVD) because they had a higher atherosclerotic burden. Low bone mineral density (BMD) has been associated to CVD in general population. In this study we investigated whether in SLE women there is an independent correlation between BMD and pulse wave velocity (PWV), which is a surrogate marker of subclinical atherosclerosis.

**Methods:** 72 SLE women were included in the study. We measured BMD in lumbar spine and hip by DXA method for the diagnosis of osteoporosis (T score  $<-2.5$ ), osteopenia (T score  $-1.5$  to  $-2.5$ ) and low BMD (osteoporosis or osteopenia). A Mann-Whitney's test and Fisher's exact test was used to compare patients with and without low BMD, as appropriate. A linear regression analysis was used to determine the correlation between PWV and lumbar spine and hip BMD after adjustment by potential confounders.

**Results:** PWV was similar in patients with low and normal BMD ( $7.58 \pm 1.01$  m/s vs  $7.62 \pm 1.15$  m/s, respectively). Also, no other relevant differences were observed between both groups. PWV positively correlated with lumbar spine BMD ( $r=0.256$ ,  $p=0.038$ ) but not with hip ( $r=0.108$ ,  $p=0.389$ ) after adjustment by age, daily prednisone dose and the presence of obesity, menopause and chronic kidney disease.

**Conclusion:** Subclinical atherosclerosis measured by PWV was not found to be independently associated with low BMD in women with SLE.

### **Systemic sclerosis sine scleroderma: a case report of anterior uveitis**

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**Introduction:** Systemic sclerosis sine scleroderma (ssSSc) is characterized by the absence of skin involvement when other manifestations of systemic sclerosis are present. It is not known if ssSSc represents a forme fruste of limited cutaneous SSc or a distinct entity, but the 2013 American College of Rheumatology/European League Against Rheumatism criteria for the classification of systemic sclerosis (SSc) have considered SSc without skin involvement to be a distinct subset.

**Case report:** We present a case of 70 years old female that was referred to our consultation for Raynaud's phenomenon. She was being followed in ophthalmology consultations due to a chronic anterior uveitis (CAU), in gastroenterology consultations due to dysphagia, in pulmonology consultations due to a diffuse pulmonary emphysema and fibrosis in the upper lobes which was documented by biopsy, in cardiology consultations due to an idiopathic dilated non-ischemic cardiomyopathy with severe left ventricle systolic dysfunction and left bundle branch block. Antinuclear autoantibodies and anticentromere autoantibodies were positive, while manometry revealed distal esophageal hypomotility. After establishing the diagnosis of ssSSc and starting immunosuppression, ocular disease improved and pulmonary and cardiac diseases remained stable.

**Discussion:** This case underlines not only the importance of a high degree of suspicion for diagnosing systemic sclerosis when CAU is present and/or skin thickening is absent, but also the importance of Internal Medicine in integrating different manifestations of the same disease. To our knowledge, this is the first report of CAU in a patient with ssSSc.

### **Clinical characteristics of patients with erythema nodosum in Southern Israel**

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**Objectives:** Erythema nodosum (EN) is a type of panniculitis that affects subcutaneous fat in the skin. Streptococcal infections are the most common identifiable etiology, especially in children. Drug and hormonal reactions, inflammatory bowel disease,

and sarcoidosis are other common causes among adults. The purpose of our study was to determine etiological causes of EN in Southern Israel.

**Methods:** We performed a retrospective study of all patients older than 18 with EN admitted to the Soroka University Medical Center, a 1100 bed tertiary care teaching hospital that serves as the only tertiary referral hospital for Southern Israel (estimated population 1.000000) between 2004 and 2014. Clinical and demographic characteristics were obtained for these patients.

**Results:** In our study 50 patients with diagnosis of EN were hospitalized at Soroka University Medical Center. The majority of patients were woman (86%), recurrent episodes of disease was found in 14% of the patients. The prominent causes of disease were infectious diseases (28%). Other frequent causes of EN were autoimmune diseases, pregnancy, drugs (most frequently oral contraceptives) and idiopathic. The prevalent symptoms of patients hospitalized with EN were fever (50% of patients) and arthritis or arthralgia (28% of patients). Comparison of patients with diagnosis of EN according to decades (before and after 2010) we found that after 2010 compared to before 2010 increased lymphocytosis ( $2.1 \pm 0.7$  vs  $1.7 \pm 0.7$ ,  $p=0.54$ ), eosinophilia ( $0.13$  vs  $0.06$ ,  $p=0.052$ ) and elevation of RF ( $10 [47.6]$  vs  $2 [6.9]$ ,  $p=0.003$ ). No differences of etiologic causes of EN were found between these decades.

**Conclusions:** Immunologic differences that appeared in the last decade in patients with EN in Southern Israel might be related to environmental changes. Further research is needed to understand these differences.

### Clinical perspectives using computer programs in the diagnostic of the cardiovascular system vegetative regulation in patients with rheumatoid arthritis

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**Objective:** To study the activity of the autonomic regulation of the cardiovascular system in patients with rheumatoid arthritis (RA) by a computer program.

**Material and methods:** The study included patients with RA ( $n=89$ , mean age  $52 \pm 3,2$  years) and a control group ( $n=104$ ). Patients of the control group did not differ significantly from RA patients. Autonomic regulation of the cardiovascular system was evaluated by laser Doppler flowmetry. To calculate the coefficient of the autonomic regulation of blood circulation using a special program by authors (certificate of state registration computer program RU 2015614498). The program was developed on the basis of a patent for the invention RU 2526257 of 26 July 2014.

**Results:** In the group of patients with RA there were statistically significant differences in autonomic regulation of the cardiovascular system compared to the control group. Sympathicotonia was observed in 7% of RA patients and 4% of the control group ( $p=0.0052$ ). Easy manifested sympathicotonia – in 21% of RA patients and 12% in control group ( $p=0.0022$ ). Easy vagotonia – 18% of RA patients and 30% of patients control group ( $p=0.0045$ ). Severe vagotonia – 18% of RA patients and 30% in control group ( $p=0.041$ ).

**Conclusions:** Our findings indicate the predominance of sympathetic group in RA patients. This fact complements the picture of cardiovascular risk in patients with RA.

### Interaction of microcirculatory disorders and activity of rheumatoid arthritis on a scale of DAS-28-CRP

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**Objective:** To estimate the interaction of microcirculation in patients with rheumatoid arthritis (RA) with disease activity on a scale of DAS-28-CRP.

**Methods:** Research included patients with RA ( $n=114$ ). Mean age made  $55,8 \pm 1,1$  years. All patients had positive rheumatoid factor, duration of RA more than one year, an activity index on DAS-28-CRP  $4,25 \pm 0,54$ . At the time of inclusion patients had no clinical and laboratory data of the acute inflammatory process connected with an infection. Activity of RA was determined by DAS-28-CRP scale. C-reactive protein was determined by a quantitative method for biochemical automatic analyzer LW C200i (Shenzhen Landwind Industry Co., Ltd., China) latex immunoturbidimetric method using a reagent CRP FS (DiaSys Diagnostic Systems GmbH, Germany). Microcirculation explored by laser Doppler flowmetry "LAKK-2" ("Lazma", Russia) on index of microcirculation, flax and myogenic tone. Microcirculation was examined for distal phalang IV finger of the left hand.

**Results:** We received a positive correlation of medium strength ( $r=0,65$ ) between the value of the index of microcirculation and RA activity by DAS-28-CRP. Flax has a negative correlation of medium strength ( $r=0,48$ ) with the level of activity of the RA DAS-28-CRP. Myogenic tone had positive correlation of medium strength ( $r=0,42$ ) with the level of inflammatory activity on a scale of DAS-28-CRP.

**Conclusions:** These data again emphasizes the role of inflammation in the development of systemic microcirculation disorders, and at the same time, the pathogenesis – amplification of the inflammatory activity in areas of ischemic and hypoxic changes. These subtle interweaving require further in-depth study.

### Perspectives of hemorheological disorders correction in patients with rheumatoid arthritis and its impact on clinical parameters of disease

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**Objective:** To study the correlation of blood viscosity (BV) in rheumatoid arthritis (RA) patients and disease activity (evaluated by DAS-28-CRP) before and after administration of pentoxifylline. **Methods:** The study included women with documented diagnosis of RA ( $n=75$ ). Mean age was  $55,8 \pm 1,1$  years. All the patients were seropositive for rheumatoid factor, RA duration longer than one

year. RA activity was determined by the scale of DAS-28-CRP. C-reactive protein was determined by a quantitative method for biochemical automatic analyzer LW C200i (Shenzhen Landwind Industry Co., Ltd., China) latex immunoturbidimetric method using a reagent CRP FS (DiaSys Diagnostic Systems GmbH, Germany). Blood for determination of viscosity were taken from the cubital vein with 0,5% sodium citrate solution. Research was carried out on a capillary viscometer VKO-1 (Russia). All patients received standard treatment with methotrexate at a mean dose of 15 mg per week for at least 6 months prior to enrollment. During the study, the dosage of methotrexate did not change; do not enter other synthetic or genetically engineered disease-modifying antirheumatic drugs or glucocorticoids.

**Results:** BV in the study group was  $2,79 \pm 0,54$  mPa·s. DAS-28-CRP was equal to  $3,03 \pm 0,05$ . Between this parameters obtained positive correlation of medium strength ( $r=0,67$ ). After application of pentoxifylline average daily dose of 800 mg over 28 days BV totaled  $2,17 \pm 0,22$  mPa·s, which was significantly lower compared with the initial parameters ( $p=0,006$ ). Activity RA DAS-28-CRP was equal to  $2,47 \pm 0,62$ , which also was a statistically significant difference compared to baseline ( $p=0,004$ ). In addition, the completion of studies and there is a positive correlation of medium strength ( $r=0,51$ ) between BV and the activity of the RA for DAS-28-CRP. **Conclusions:** The resulting correlation coefficient values indicate the relationship of RA activity and BV. In addition, a statistically significant change in the activity of the RA correction BV in RA patients, making a promising treatment for the changes of hemorheology in these patients.

## Bisphosphonates-related osteonecrosis of the jaw. An entity recently discovered and poorly studied

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**Introduction:** Alert physicians about rise of incidence of this entity in our region, mainly in patients that have risk factors and clinical patterns, approaching them correctly since the start of therapy with bisphosphonates, knowing the disease and its treatment.

**Case reports:** Two patients, under treatment with bisphosphonates for long term due to prostate adenocarcinoma and monoclonal gammopathy respectively. Both had unspecific pain complaints in the jaw and local tumefaction that impaired progressively, requiring to be hospitalized to get intravenous treatment. The first patient had partial improvement while the other has a jaw fracture as a complication that was treated afterwards, having a stable evolution and improvement. They were discharged stopping bisphosphonates indefinitely. At the moment patients are under analgesics and flashes of antibiotics.

**Discussion:** This is a recently known entity with limited information, with therapeutic options depending on medical area of approaching. In the face of its presence, it is indicated to discontinue bisphosphonates, but due to biophosphonates'

long half-life into the organism, to stop them might not have immediate effects. Antibiotics are orientated by microbiological cultures, regarding empirical treatment with quinolones, metronidazole, clindamycin, or erythromycin. Long treatment is indicated only in refractory cases. Surgical intervention is limited to some stages of the disease. This is pathology with a rising incidence and a very significant morbidity. It is important to know this condition to be able to prevent and to treat it correctly in a short term.

## Disturbed angiogenesis in systemic sclerosis and very early systemic sclerosis

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**Objectives:** In systemic sclerosis (SSc), vascular involvement occurs early in disease progression and may precede other manifestations for years. A deregulation in angiogenesis is one of the contributing pathological factors, even if the main proangiogenic stimulus (vascular endothelial growth factor 165 – VEGF) and its receptor VEGFR2 are overexpressed in these patients, versus (vs) healthy controls (HC). Neuropilin-1 (NRP-1) was initially described as a receptor for semaphorin (Sema)-3A, which is involved in axonal pathways, but also functions as a co-receptor for VEGF, being necessary for its optimal signaling.

**Methods:** To study the role of NRP-1 in SSc, serum levels of pan-VEGF, soluble NRP-1 and Sema3A were analyzed by ELISA in 51 patients with SSc (45 women, median age 60), 37 patients with very early SSc (VEDOSS) (33 women, median age 50) and 50 HC. The expressions of NRP-1 and Sema3A in skin biopsies of SSc patients and in microvascular endothelial cells (MVECs) stimulated with SSc, VEDOSS and HC sera were evaluated by immunohistochemistry and Western blot. Clinical correlations were established. Capillarogenesis was evaluated after stimulation of MVECs with sera from the 3 groups (Matrigel). SPSS 20.0 was used for statistical analysis.

**Results:** Serum levels of pan-VEGF are increased in VEDOSS ( $p=0,01$ ) and SSc ( $p=0,002$ ) patients vs HC and higher levels correlate to the absence of digital ulcers ( $p=0,006$ , VEDOSS). Serum levels of NRP-1 are decreased in VEDOSS ( $p=0,006$ ) and SSc ( $p=0,02$ ) patients vs HC and lower levels correlate with an "active" capillaroscopic pattern. The expression of NRP-1 is decreased on the skin of SSc vs HC and in MVECs stimulated with SSc and VEDOSS sera vs HC. There were no significant differences for Sema3A. Capillarogenesis is decreased in MVECs stimulated with VEDOSS ( $p=0,01$ ) and SSc ( $p=0,001$ ) sera vs those stimulated with HC sera.

**Conclusion:** Decreased levels of NRP-1 may disturb VEGF signaling and contribute to deregulated local and systemic angiogenesis in SSc, from the very early onset of the disease.



## An unexpected lung nodule

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**Introduction:** Lung nodules are detected in 0.2% of chest radiographs; they're defined as 1-30 mm lesions surrounded by normal lung parenchyma, without concomitant adenopathies or atelectasis. The authors present a case of a lung nodule with an uncommon origin and atypical presentation.

**Case report:** 47 years old male, smoker (10 pack/year history); history of peptic ulcer and chronic arthralgias with regular non-steroid anti-inflammatory drug (NSAID) intake. Admitted to the emergency department with fatigue, dyspnea for moderate exertion, pleuritic chest pain on the left hemithorax base and non-quantified weight loss over the previous month. He also referred rest pain in several joints – right wrist, 3rd right metacarpophalangeal, 3rd to 5th right proximal interphalangeal and temporomandibular joint – along with inflammatory signs in both hands for over 4 years, controlled with NSAIDs. On examination: pulmonary auscultation suggestive of left pleural effusion; inflammation of the aforementioned joints. Blood testing: C-reactive protein 11,9 mg/dL without leukocytosis; thrombocytosis (platelet count 588000), sedimentation rate 30 mm/h; anti-citrullinated peptide antibody 16 U/mL, supporting the diagnosis of rheumatoid arthritis (RA), with Disease Activity Score (DAS28) of 6.39. Chest radiograph: well-defined lung nodule with approximate diameter of 20 mm on the right apex; moderate pleural effusion on the left hemithorax. Findings were confirmed in computerized tomography. Pleural fluid testing: exudate with mononuclear predominance (76%, 1110x10<sup>6</sup>), glucose 3 mg/dL, lactate dehydrogenase 2826 UI/L, adenosine deaminase 131.6 UI/L; neoplastic cell search, cultural exam and mycobacterium tuberculosis DNA testing negative – findings thoroughly consistent with necrotizing inflammation. Pleural biopsy: chronic active fibrinoid pleuritis. Nodule biopsy with Ziehl Neelsen staining and neoplastic cell search negative, also consistent with inflammatory process. Therapy was started with methotrexate, sulfasalazine and prednisolone, with significant respiratory and joint pain recovery; as such, after having ruled out tuberculosis, all symptoms were attributed to the rheumatologic illness.

**Discussion:** Pleural manifestations are the most common intrathoracic presentation of RA, with thickening in 38-70% of cases and effusion in 5%. It is more frequent in men older than 35 and after several years of disease progression. 30% of patients with pleural involvement also develop interstitial disease or lung nodules.

## Reynolds risk score for assessing the cardiovascular risk in systemic lupus erythematosus

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**Objectives:** The inflammatory syndrome in active systemic lupus erythematosus (SLE) is characterized by an impaired response for

the C-reactive protein (CRP). The aim of this study was to evaluate the Reynolds risk score (RRS), a score that incorporates also the high-sensitive CRP (hsCRP), in assessing the cardiovascular risk (CVR) when compared with other CVR scores.

**Methods:** Patients diagnosed with SLE according to SLICC 2012 diagnosis criteria were prospectively included. In all patients RRS, as well as the American College of Cardiology/American Heart Association (ACC/AHA) risk score and Framingham risk score (FRS) were assessed.

**Results:** Our lot consisted in 84 patients with mean age of 44.7±12.1 years, majority of female sex. In univariate analysis, the 10-year CVR assessed by the RRS was found to be significantly correlated with that obtained by both FRS and ACC/AHA risk score ( $p<0.001$ ;  $r=0.714$ , respectively  $p<0.001$ ;  $r=0.780$ ). Also, the RRS results were inversely correlated with the differences between the real and the vascular age assessed by the ACC/AHA risk score, respectively between the actual risk and that of the risk at same age by FRS ( $p<0.001$ ;  $r=-0.647$ , respectively  $p<0.001$ ;  $r=-0.502$ ). Even so, the estimated CVR at 10 years was significantly lower when estimated by RRS compared to the FRS or ACC/AHA risk score [1.0(0.2-7.9) vs 5.3(0.5-28.5) vs 3.15(0.0-21.9),  $p<0.05$ ].

**Conclusion:** The 10-years CVR estimated by the RRS in SLE patients was significantly lower than that assessed by the FRS or ACC/AHA risk score, even if the results of the 3 scores were well correlated.

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## Comparing diagnosis and treatment of gout in Serbia and in the Netherlands

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**Objective:** Our aim was to examine relationship and comparing diagnosis and treatment of gout in Serbia and in the Netherlands. **Methods:** We compared 104 patients with gout from polyclinic ambulance of Department of Rheumatology Radboud University Nijmegen Medical Centre in 2011 and 100 patients with gout from Department of Internal Medicine University of Kragujevac. 100% of Serbian patients and 40,3% of gout patients (42) from the Netherlands-diagnoses was established without crystal identification. This procedure is very unusual in Serbia. We do not use this procedure in Kragujevac, we use diagnostic rule without joint fluid analysis. Most important is elevated serum urate levels. Gout is diagnosed on mix of the clinical features of an acute arthritis, abrupt onset of a severe, usually mono-articular arthritis often at night, with extreme pain crescendo up to maximal intensity over 8-12hours the patients' characteristics and history (obesity, drinking alcohol, the use of diuretics, former attacks of gout, renal stones). For the treatment of acute gout arthritis three drugs are recommended non-steroidal anti-

inflammatory drugs (NSAIDs), colchicine and corticosteroids. In Serbia we use NSLE, allopurinol and corticosteroids. We do not use colchicine.

**Results:** 100% of Serbian patients and 40,3% of gout patients from the Netherlands-diagnoses was established without crystal identification. 100% of Serbian patients was without treatment of colchicine and 77% of gout patients (80) from the Netherlands used colchicine. As EULAR bursar I noticed two differences in clinical practice of diagnosis and treatment of gout in the Netherlands and Serbia: 1) microscopic crystals identification is the golden standard in the diagnosis of patients with gout in the Netherlands but in our Internal Clinic in Kragujevac we do not use this method; 2) treatment with colchicine is first option in the Netherlands but in Serbia, it is not registered and we do not use it.

**Conclusion:** Two big differences in clinical practice of diagnosis and treatment of gout in the Netherlands and Serbia have repercussion in prognosis of these patients.

### **Influence of denosumab on bone mineral density, structural damage in patients with osteoporosis and rheumatoid arthritis, depending to anti-inflammatory therapy**

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**Objectives:** RANKL (receptor activator of nuclear factor kappa B ligand) is essential for osteoclast development, activation, and survival. The aim of this study was to evaluate the effects of denosumab (monoclonal antibody that binds RANKL) on bone mineral density (BMD), structural damage in patients with rheumatoid arthritis (RA) and osteoporosis (OP).

**Methods:** 69 postmenopausal women with RA and OP received s/c denosumab 60 mg injections every 6 months for 12 months. The primary end point was the change from baseline in the Sharp/van der Heijde (SVH) score and BMD (by dual energy x-ray absorptiometry at lumbar spine (L1-L4), hip neck (HN) and distal forearm (DF) at 12 months. The Statistica 6.0 was used in the statistical analysis. The mean age was 59,6±7,4 years, the mean duration of RA 17,7±10,4 years. During the study 34 patients (49,3%) continued glucocorticoids (GC). According to X-ray 2 (2,9%) patients had the 1st, 21(30,4%) – 2nd, 22(31,9%) – 3rd and 24(34,8%) – 4th stage of RA.

**Results:** Mean BMD L1-L4 and HN was increased after the treatment: 0,82±0,1 g/cm<sup>2</sup> vs 0,86±0,1 g/cm<sup>2</sup> (p<0.0001), and 0,63±0,09 g/cm<sup>2</sup> vs 0,64±0,09 g/cm<sup>2</sup> (p=0,0003), respectively. At DF it was noted the tendency to increase: 0,5±0,09 g/cm<sup>2</sup> vs 0,5±0,09 g/cm<sup>2</sup> (p=0.0529). The mean change of BMD after 12 months was: at L1-L4 +4,6%, at HN +2,8%, at DF +0,7%. The significant increase of BMD at L1-L4, HN and stabilization at DF was noted both in groups, receiving GC or not. The erosion score, the joint space narrowing score (JSN) and total SVH score were increased after treatment: 26.5 [8.0; 70.0] vs 26.5 [8.0; 77.0] (p=0.0117); 101.0 [68.0; 128.0] vs 101.0 [70.0; 128.0] (p=0.027); 119.5 [76.0; 200.0] vs 119.5 [76.0; 200.0] (p=0.010),

respectively. It was established that patients with significant increase of erosions (n=8) had a bigger cumulative dose of GC, were more often positive on ACCP and had lower BMD L1-L4. Interesting to note that after separation on groups based on GC intake, the increase of erosion score and total SVH score was only seen in patients taking GC.

**Conclusions:** After 12 months of therapy with denosumab it was shown the significant increase of BMD at L1-L4 and HN, the stabilization in forearm – regardless of GC intake. Negative dynamics of radiological changes of joints is noted mainly at the patients receiving GC. The increase in number of erosion was associated with a bigger cumulative dose of GC, positivity on ACCP and lower BMD L1-L4.

### **Biphosphonate-related osteonecrosis of the jaw. A precise diagnosis is the first step for its prevention**

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**Background:** Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a condition found in patients who have received intravenous and oral forms of bisphosphonate therapy for various bone-related conditions. Bisphosphonate-related osteonecrosis of the jaw (BRONJ) manifests as exposed, non-vital bone involving the maxillofacial structures. The first reported cases of BRONJ were related with high doses of bisphosphonates, but it has a multifactorial etiology in most patients.

**Objectives:** To examine a group of 14 patients diagnosed of osteonecrosis of the jaw who were treated with oral bisphosphonates and evaluate if the diagnosis of osteoporosis and the use of bisphosphonates were correct in all of these patients.

**Methods:** We checked the criteria used for the diagnosis of osteoporosis and then we apply the FRAX index in every case. If the risk were 10% or above for major fractures or above 3% for hip fracture, then the use of bisphosphonates as the treatment of choice met the criteria.

**Results:** A total of 14 patients (13 female and 1 male) with a median age of 74.6 years (71-90), were diagnosed of osteonecrosis of the jaw. 11 patients had been treated with bisphosphonates for 3 years and three patients for 2 years. Two of them had a diagnosis of rheumatoid arthritis and both had received corticosteroids. One patient has ankylosing spondylitis and received anti-TNF as treatment. When we applied the FRAX index in all the patients, only 6 of them met the criteria for using bisphosphonates as the right treatment.

**Conclusions:** A correct use of bisphosphonates as the treatment of choice for osteoporosis using the FRAX index and applying the risk factors in each patient, would have prevented BRONJ in 8 of the 14 patients (57.1%). FRAX index appears to be the most valuable and most accepted tool in order to evaluate the risk of fractures. A precise diagnosis and treatment is the first step for decrease the incidence of BRONJ.

## Who dares to stop antibiotics?

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**Introduction:** Acute febrile monoarthritis is often due to septic arthritis, whereas sometimes other, rare, conditions may be underlying. Pseudoseptic arthritis (PA) is a relatively seldom described entity, and its diagnosis may frequently be missed.

**Case report:** A 74 years old woman with a history of rheumatoid arthritis diagnosed 6 months prior to admission, presented due to fever (39°C/102.2°F) and unilateral swelling, erythema and tenderness of the right knee. Her standard medical treatment included 7.5 mg of prednisolone daily and 10 mg of methotrexate once weekly. Knee arthrocentesis of 40 cc of purulent synovial fluid revealed pleocytosis (190.000 cells/mm<sup>3</sup>) with low glucose and elevated protein. While methotrexate was discontinued, treatment with piperacillin-tazobactam and vancomycin was immediately initiated, with no clinical improvement. The fluid stains and cultures proved negative, so a second arthrocentesis of 50 cc of purulent synovial fluid was performed, with similar laboratory findings and a negative culture. The diagnosis of pseudoseptic arthritis was then considered possible, so prednisone dosage was increased to 25 mg daily, while antibiotics were continued. Both fever and local symptoms subsided, and the patient was discharged with instructions to receive antibiotics per os for three weeks, while prednisone dose was modified to 20 mg, aiming to a gradual tapering.

**Discussion:** PA is an acute febrile monoarthritis with laboratory findings similar to these of septic arthritis, except from the cultures, which always prove negative. It has been described in the setting of rheumatoid, crystalloid or reactive arthritis, after trauma or repeated intra-articular injections. Treatment involves arthrocentesis, intraarticular steroids, and systematic non-steroid anti-inflammatory drugs (NSAIDs) or steroids. Recurrence is common. Differential diagnosis from septic arthritis, which is associated with a mortality of 5 to 20%, can be intriguing, considering the fact that the sensitivity of synovial fluid culture in non-gonococcal septic arthritis varies from 75 to 95%. Discontinuation of antibiotics should be considered only in the absence of concomitant infection, an obvious entry site of an infectious agent, and severe immunodeficiency, and in the setting of a previous episode of PA. Otherwise, this is reasonable to continue the antimicrobial treatment, while NSAIDs or steroid treatment is intensified.

## Palliative care in spondyloarthritis including ankylosing spondylitis (Bechterev's disease) and psoriatic arthritis

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**Objectives:** Currently palliative care (PC) includes medical care in patients with the end stages of chronic diseases when

treatment and rehabilitation could not improve the patient's status. The aim of the study was to determine the number of patients with spondyloarthritis (SpA) that have a permanent disability and need in PC.

**Material and methods:** Histories of 180 patients with SpA (ASAS criteria for axial or peripheral SpA, 2011), hospitalized in Saratov State regional hospital in 2010-2014 were analyzed. 102 patients had psoriatic arthritis, 76 patients – ankylosing spondylitis, two – undifferentiated arthritis. At baseline mean age was 43.2±12.1 years (17-73 years), 75 women (41.7%), 105 men (58.3%), and duration of the disease – 14.2±12 years. We determined the number of individuals with permanent disability and its reasons.

**Results:** At baseline persistent disability was observed in 37 (20.6%) patients: 3 patients (1.7%) maximal disability – 1st degree (incorrigible inability to self-service), 14 (7.8%) – disabled 2d degree (complete loss of ability to work with self-preservation), 20 (11.1%) – the disabled the 3d degree (inability to work according to specialty). The average age of patients with disabilities was 44±10.1 years, the disabled 1st degree – 47±11.2 years. In 2014, the number of patients with maximal degree increased to five (2.7%), with 2d – up to 52 (28.6%), with 3 d – 32 (17.6%). The total number of disabled persons increased to 89 (48.9%) patients, p<0.001 as compared to baseline. The causes of permanent disability of patients were the defeat of joints and spine, as well as vision loss due to uveitis. Disability of maximal degrees were established in patients with aseptic necrosis of heads of the shoulder and hip, with the formation of contractures of the extremities and total spine ankylosis, with loss of vision due to uveitis. These patients and their relatives, from our point of view, the need to provide competent palliative care with the integration of physicians – general practitioners, psychologists, surgeons, podiatrists, dietitians, rehabilitation specialists and others.

**Conclusion:** Our study shows that some patients with SpA (1.7%) are in need of palliative care due to permanent disability, chronic pain, loss of motor function, vision loss, and others reasons.

## Osteoporosis mimicking bony metastases

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**Introduction:** We present two cases with symptoms and appearance of bony metastases, in which further investigations showed osteoporotic fractures with no evidence of malignancy.

**Case reports:** Case 1: A 68 years old female presented with a 4 week history of back pain and urinary and fecal incontinence. There was no history of trauma or primary malignancy. She has SLE treated with prednisolone. On examination there was spinal tenderness and upper motor neurone signs in her lower limbs, with loss of anal tone. Cauda equina syndrome was suspected. Investigations showed hypercalcemia (calcium 2.59 mmol/L) and raised alkaline phosphatase (ALP 178 U/L). Myeloma screen was negative and vitamin D levels were normal. MRI spine showed multiple level vertebral body abnormalities, reported as extensive metastatic disease. Subsequent investigations

did not identify any malignancy. FDG-PET imaging showed multiple thoraco-lumbar wedge fractures with no significant focal uptake. A diagnosis of osteoporotic fractures was made. She was treated with alendronic acid and analgesia, and her back pain and incontinence settled. Case 2: A 62 years old female presented with a 4 month history of right hip pain. She has rheumatoid arthritis treated with methotrexate and prednisolone. There was no history of trauma or malignancy. On examination there was tenderness in the right groin, with painful and restricted movement of her right hip. Pelvic X-ray showed a lytic lesion in the right symphysis pubis. ALP was raised to 381 U/L. Myeloma screen was negative and vitamin D levels were normal. A diagnosis of bony metastases was suspected. MRI pelvis showed bone edema in the superior pubic rami bilaterally with underlying fractures. CT pelvis confirmed these fractures, but did not show any evidence of malignancy. Isotope bone scan showed abnormal uptake in the pubic symphysis. A diagnosis of osteoporotic fractures of the pelvis was made. This lady was previously taking raloxifene which was changed to alendronic acid.

**Discussion:** Insufficiency fractures may mimic bony metastatic disease on initial imaging. Interpreting the radiological findings in context with the patient's history and biochemical results is imperative to guide selection of further investigations to differentiate the cause of such lesions. In both cases the diagnosis of osteoporotic fractures was made by further imaging using CT/MR/PET scanning.

## Immunosuppressive therapy: friend or foe?

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**Case report:** We report the case of a 26 year old female patient diagnosed 2.5 years ago as having dermatomyositis (biologic inflammatory syndrome, typical electromyography pattern, positive muscular biopsy) who responded well to corticotherapy but subsequently developed severe cortisone myopathy and then responded excellent to azathioprine but developed severe leucopenia to it and then to methotrexate, with no major abnormality on bone marrow biopsy. As the disease was not controlled, to the point that the patient was no more able to take care of herself, we re-initiated low-dose corticotherapy associated to 50 mg of azathioprine, under which the evolution of the disease was, at first, favorable (lowering of muscular enzymes, re-initiation of self feeding, no inflammatory syndrome, initiation of a rehabilitation program by the patient). Suddenly, the patient developed, for a day, fever (39°C) and, 6 days later, loss of consciousness, was rushed to the ER of the local hospital, where, despite the intensive care provided to her, she deceased a week later, having a normal brain MRI and a "white" right lung on the pulmonary CT scan.

**Discussion:** The patient's death was probably determined by an infection; but one cannot certainly rule out a pulmonary flair of the disease, that could not be controlled with the high dose immunosuppressive therapy associated with wide-spectrum antibiotherapy.

## Comorbidity of knee osteoarthritis in postmenopausal women

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**Objective:** The aim of the study was to assess association of knee osteoarthritis (KOA) with arterial hypertension (AH), myocardial infarction (MI), angina pectoris (AP), chronic heart failure (CHF) and stroke in postmenopausal women.

**Methods:** A case-control study included 628 menopausal outpatients. Study group consisted of 314 with KOA diagnosed according to ARA clinical and radiographic criteria, control group consisted of 314 women without OA adjusted by age (median 54; range: 50-57 and 52,5 (48-57,3),  $p=0.531$ ) and body mass index (BMI, median 27.7 kg/m<sup>2</sup> (24.6-33.1) and 27.3 (24.5-30.4),  $p=0.373$ ). Standard interview, anthropometry and general physician examination were performed; Modified Menopausal Index (MMI) was used to assess menopausal symptoms. AH, MI, AP, CHF were verified according to National Guidelines. KOA symptoms were assessed by Lesquene Index.

**Results:** The groups were not different in smoking frequency: 12.1% of OA patients and 8.6% of controls ( $p=0.19$ ,  $\chi^2=1,716$ ), type 2 diabetes mellitus: 5.4% and 2.6% accordingly ( $p=0.103$ ,  $\chi^2=2.666$ ). All serum total cholesterol levels did not differ: main group median was 5.3; range: 4.5-6.2 mmol/l and 5.7 (5.2-6.4) mmol/l,  $p=0,976$ ) in the control group. Meanwhile AH was registered in 69.4% of KOA patients and in 58.5% of controls ( $p=0.006$ ,  $\chi^2=7.528$ ). AP was diagnosed in 16.2% KOA patients and in 12.7% controls ( $p=0.257$ ,  $\chi^2=1.285$ ), CHF was registered in 43.6% KOA subjects and in 27.1% controls ( $p=0.000$ ,  $\chi^2=18.123$ ). While previous MI had been registered in 1% KOA patients and in 1.9% controls ( $p=0.451$ ,  $\chi^2=0.502$ ), stroke was significantly more frequent KOA subjects (4.8%) than in controls (2.6%;  $p=0.202$ ,  $\chi^2=1.625$ ). So, OA was associated with heart failure in postmenopausal women.

**Conclusions:** Thus, in symptomatic early postmenopausal women, KOA was independently associated with hypertension, stroke and chronic heart failure. Smoking rate, type 2 diabetes mellitus and cholesterol levels did not differ between the groups. The data support the hypothesis of KOA as an independent risk factor for cardiovascular disease.

## Analysis of efficacy and tolerability of abatacept in patients with different duration of rheumatoid arthritis: preliminary data

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**Objective:** To compare effect of abatacept (ABA) in patients (pts) with different duration of rheumatoid arthritis (RA).

**Material and methods:** Patients with active RA and an inadequate response to synthetic DMARDs or biologics were enrolled in

the study. After that, they were divided in two groups, the first one, less than 3 years duration (ERA – 51%) and the second one, more than 3 years duration (LS RA – 49). There were 79% of women and 21% of men, aged 49±13 years, with a high disease activity (DAS28=5,28±1,1), RF-positive (75,7%) and ACPA-positive (75%). Abatacept (10 mg/kg) was administered intravenously 3 times every 2 weeks, after that every month. Disease activity was assessed by DAS28. Results were assessed every 12 weeks according to EULAR criteria.

**Results:** Before treatment patients with ERA and LS RA had high disease activity, DAS28 5,26±0,89 and DAS28 5,3±1,3, respectively. Abatacept significantly decreased activity of RA after 3 months ( $p<0.05$ ) in two groups. Good and moderate response by EULAR criteria was achieved in 82,2% in the group of ERA and in 67,5% of patients with LS RA after 3 months of therapy. We didn't find significant difference in achieving good EULAR response between two groups after 3 months (26,5% – ERA; 25,7% – LS RA) and 6 months of therapy (31,9% – ERA; 35,2% – LS RA). Nevertheless, the number of non-responders to the therapy in pts with LS RA was significantly higher both after 3 months and 6 months (32,4% and 25,3%) as compared to pts with ERA (17,6% and 17% respectively). 25 adverse events (AE) in 19 (23%) pts were registered. The most frequent AE were upper respiratory tract infections – 8 pts. One pt has herpes zoster and one, abscess of the right thumb.

**Conclusions:** Abatacept has shown significant improvement in reduction of disease activity in pts with an inadequate response to previous therapy. There was no significant difference in achieving good EULAR response between two groups. However, there were more patients with an inadequate response to ABA in the LS RA group. Abatacept has good safety profile, adverse events were registered only in 23% of patients.

### Activated protein C resistance in antiphospholipid syndrome: a common association?

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**Introduction:** Mechanisms of antiphospholipid syndrome (APS) associated to activated protein C resistance (APCr) are not totally elucidated yet. It has recently been described that anti-β2GP-I interfere with the protein C pathway and induce an acquired resistance to activated protein C (APC phenotype), that is, anti-β2GP-I inhibit the inactivation of activated factor V (FVa) by APC on a phospholipid surface. Although this finding seems to be independent of the presence of the FV Leiden mutation (APC genotype), the prevalence of the factor V Leiden mutation (APC resistance genotype) has not been widely studied in patients with anti-β2GP-I antibodies.

**Case report:** 22 years old woman without any relevant family history who was admitted to emergency department because of a generalized tonic-clonic seizure. She had cesarean delivery 6

months complicated with deep vein thrombosis of the 2 femoral and iliac veins and inferior vena cava prior to the present episode. Laboratory findings showed hypokalemia and marked proteinuria. The CT scan and the electroencephalogram were normal but the cerebral MRI angiography showed findings consistent with vasculitis. An abdominal MRI angiography was also performed and it showed right renal arterial stenosis associated to the venous one. The thrombophilic screening revealed positive APCr and antiphospholipid antibodies at high rates. The genetic study confirmed the factor V mutation in the heterozygous state.

**Discussion:** The APS is characterized by thrombosis and/or obstetric complications with positive antiphospholipid antibodies. It can be primary or secondary. This polymorphic entity must be known because of its vital risk due to thrombosis which may be increased in combination with other abnormalities of hemostasis. Phenotypic APCr may be associated with APS in the absence of genetic mutation in the factor V Leiden. The mechanism of this acquired resistance is not fully understood yet, but even in the absence of genetic mutation, this resistance is an independent risk factor for thrombosis. Thrombotic APS patients showed greater APCr to both rhAPC and activation of endogenous protein C. Nevertheless, it remains unclear whether anti-protein C or anti-β2 -glycoprotein I antibodies are responsible for APCr.

### Primary and secondary Sjogren's syndrome: which features?

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**Background:** Both primary (pSS) and secondary (sSS) Sjogren's syndrome are defined by consensual diagnostic criteria allowing good care for patients consulting for sicca syndrome. Predictive factors for both forms, seldom studied till now, could in turn contribute to a better management of this disease.

**Objectives:** This work was aiming at trying to define predictive criteria of the primitive character of Sjogren's syndrome (SS).

**Methods:** A retrospective comparative study including 90 patients fulfilling the American European Consensus Group criteria in 2002 was carried out. Patients were assigned in two groups considering it was a primary or secondary SS. These groups were finally represented by 47 patients and 42 patients respectively.

**Results:** The mean age of the study population was 46 years with a sex ratio F/M=7.6. The average age was 52.1 years in pSS group and 43.2 years in the sSS group ( $p=0.008$ ). Comparing clinical features between the two groups, only neurological manifestations were more frequent in the pSS group (85,6% vs. 17.1%,  $p=0.049$ ). On immunological study, anti Sm and anti DNA antibodies were significantly more frequent in the sSS group ( $p=0.023$  and  $0.011$  respectively).

**Conclusion:** Sicca syndrome remains a sign of major appeal of SS. Its present in association with neurological findings in middle age patients could predict its primitive character.

## Experience of no-associated NSAIDs in rheumatological practice

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**Objective:** According to several authors annually from 100,000 patients develop complications associated with NSAID in the form of bleeding, perforation of the wall of the stomach or intestines. Higher safety has selective cyclooxygenase second type, but their use increases the risk of thrombotic complications. Since 2013, the market appeared drug amtolmetin guatsil which, having all the properties of non-selective NSAIDs, is able to prevent the development of lesions of the gastrointestinal tract by stimulating the production of nitric oxide in the mucosa at physiological concentrations.

**Methods:** We observed 78 patients (20 men and 58 women) aged 18-45 years with joint syndrome: 45 people with osteoarthritis and 33 people with rheumatoid arthritis. The duration of the disease in most patients (56) had more than 10 years, others – up to 10 years. All patients had a secondary phenomenon synovitis, elevated levels of C-reactive protein. Patients with rheumatoid arthritis have the rheumatoid factor seropositive for antibodies and cytruline peptide high degree of activity (DAS 28  $\geq 4,2$ ). Severity of pain at baseline was a VAS at movement  $76 \pm 12$  mm and at rest –  $48 \pm 8$  mm; soreness was  $67 \pm 11$  mm. It notes the limited movement and swelling in the joints. After the cancellation of NSAIDs and the period of "wash", which lasted 2 weeks, all patients were given the drug amtolmetin guatsil (nayzilat) at a dose of 600 mg bid every day for 4 weeks of combination therapy.

**Results:** The treatment of nayzilat for 2 weeks in all patients noted a decrease in the severity of pain according to VAS: pain to  $38 \pm 8$  mm; pain at rest –  $24 \pm 5$  mm; pain load –  $45 \pm 9$  mm. By the end of the fourth week of treatment, there was a further reduction in pain of  $18 \pm 5$  mm VAS; pain to  $15 \pm 4$  mm and  $28 \pm 7$  mm respectively. All the observed increased range of motion in the joints and reduce stiffness in them. In parallel, the positive dynamics of indicators of inflammation, showed the anti-inflammatory activity of nayzilat. Allergic reactions have been reported. According to the trend towards endoscopy appearance of erosions were observed.

**Conclusions:** The drug amtolmetin guatsil has good anti-inflammatory and analgesic effects, high safety profile, it may be long-term use. The medication is more economical, because it does not require receiving gastroprotectors.

## Myofascial syndrome treatment options in rheumatological practice

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**Objective:** In clinical practice, pain in inflammatory and degenerative joint diseases – one of the most common reasons for treatment of patients with medical care. Expressed analgesic effect in the treatment of musculoskeletal pain is observed in

the appointment of non-steroidal anti-inflammatory drugs. To reduce the side effects of NSAIDs justified search of rational drug combinations in which may reduce the term of appointment of analgesic and anti-inflammatory therapy. In this regard, of particular interest is the study of the efficacy and safety of combination therapy with a muscle relaxant baclofen and systemic and local NSAIDs in rheumatic patients with secondary myofascial syndrome.

**Methods:** We observed 64 patients with osteoarthritis of the shoulder and hip joints (46 women and 18 men) aged between 40 and 70 years, with disease duration of more than 5 years, had a secondary chronic musculoskeletal pain cervical and lumbosacral localization stage exacerbation. Randomized patients were divided into 2 groups of 32 people. Patients in both groups were assigned bystrumkaps 200 mg/day (2 weeks), alflutop 1.0 ml/m (3 weeks), stretching exercises muscles, relaxing massage. In addition to standard medications, the patients of the 1st group received within 4 weeks baklosan in initial dose of 20 mg, with a gradual increase of the dose to 5 mg/day from the 4th to 7th day with 8 to 15 day. The observation was carried out for 4 weeks.

**Results:** Once we have started therapy even during the 2nd visit in 60% of patients the first group there was a reduction in pain intensity joints in rest and in motion, and myofascial pain syndrome doubled VAS and NRS scale, respectively ( $p < 0,03$ ). In the analysis of the pain questionnaire McGill was found a significant decrease in pain on the index of the intensity of pain. In the second group, the observed intensity of pain decreased by 40% in just the 3rd visit (4 weeks) treatment ( $p < 0,01$ ). Reports of adverse reactions from the gastrointestinal tract were absent. Elevation of aminotransferases and other indicators of blood chemistry were not registered in any group.

**Conclusion:** Our results showed a high analgesic activity of drugs bystrumkaps, bystrumgel, baklosan and the treatment of secondary myofascial syndrome in patients with osteoarthritis. Thus, the use of a combination of anesthetic drugs, with complementary mechanisms of action, provides a more pronounced analgesic effect and reduces the treatment duration.

## Features factors of cardiovascular risk in patients with psoriatic arthritis

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**Objective:** To assess the features of CVD risk factors in patients with psoriatic arthritis (PsA).

**Material and methods:** The study was conducted on the basis of rheumatic department. The study included 56 patients with definite diagnosis of PsA. Diagnosis of PsA based on availability of diagnostic criteria CASPAR (2006), the comparison group (CG) amounted 20 healthy individuals comparable by gender, age and body mass index (BMI) ( $p > 0.05$ ). The average age of patients was  $44.6 \pm 10.1$  years. For the evaluation of coronary risk the European scale SCORE was used. Age of initiate of psoriasis was  $24.3 \pm 5.9$  years. Age of initiate PsA –  $34.8 \pm 9.7$ . Most of patients (62.5%) had polyarthritic variant of PsA. Activity

evaluation by DAS4 was 3.5 (2.2; 3.9). The average score on the criteria CASPAS – 5.5 (3.8; 7.2).

**Results:** The average Smoking index at patients with PsA = 182.6±20.9. Anamnesis of smoking 21.3±12.1 packs/years. Arterial hypertension was diagnosed at 36 (64.3%) patients with PSA, in the CG – 7 (35%;  $p < 0.05$ ). Patients with PsA statistically significantly more often diagnosed BMI  $\geq 34.9$  kg/m<sup>2</sup> (12 p-ts), which corresponds to obesity of the II and III stage. At 28 of 56 surveyed PSA observed the changes in blood lipid spectrum, in the CG changes was at 3 of 20 p-ts. Total cholesterol at PSA patients was 5.25 mmol/l (4.39; 6.19), at healthy people – 4.92 mmol/l (4.28; 5.11;  $p = 0.06$ ). Family anamnesis of CVD had 34 (60.7%) PsA patients and 3 (15%) p-ts of CG ( $p < 0.05$ ). Low total cardiovascular risk was diagnosed at 12 (21.4%) p-ts, average – at 16 (28.6%), high – at 18 (32.1%), very high risk by SCORE – at 10 (17.9%) PsA patients. In the comparison group at 14 (70.0%) p-ts was registered the lowest and at 6 (30.0%) – average risk by SCORE.

**Conclusions:** A half of PsA patients noted the high and very high risk of developing CVD. Traditional cardiovascular risk factors correlate with the activity of chronic immune inflammation, which is the basis of PsA. It is necessary to consider the severity of systemic inflammation and endothelial dysfunction, contributing to the development of early atherosclerosis and its complications in determining cardiovascular risk, in spite of traditional factors.

### Correlation between erythrocyte sedimentation rate and C-reactive protein level in patients with rheumatic diseases

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**Objectives:** Erythrocyte sedimentation rate (ESR) is the oldest acute phase index, and was probably the most commonly used laboratory test in the 20th century. Currently, clinical usefulness of ESR is questioned and C-reactive protein level (CRP) is widely applied. Despite the diminished role of ESR in modern diagnostics, the test is still used in rheumatology. Moreover, some disease activity indices are based alternatively either on ESR or CRP. The present study was designed to determine correlation of ESR and CRP in patients admitted to the rheumatologic ward due to various rheumatic disorders. **Methods:** 200 of patients (25.5% male, 74.5% female) consecutive admitted to rheumatologic ward with definite rheumatologic diagnosis, aged 48.0±14.1 yrs with a mean duration of overt disease 6.1±5.3 yrs were investigated. Correlation between ESR (1h) and CRP was calculated.

**Results:** Despite different factors affecting ESR and CRP a satisfying correlation between the tests was found in all investigated patients and especially in those with ankylosing spondylitis and systemic lupus erythematosus. Analysis of all cases revealed enhanced ESR (25.3±21.4 mm/h) and CRP (18.7±28.9 mg/l) as well as a significant correlation between ESR and CRP ( $r = 0.6944$ ). There was no difference in ESR and

CRP between female and male patients. Patients older than 40 had higher ESR (27.1±22.3 versus 21.5±18.9 mm/h) and CRP (20.9±30.0 versus 14.3±20.7 mg/l). When the individual diseases were analyzed the highest ESR (31.2±33.2 mm/h), and CRP (19.3±38.8 mg/l) were found in patients with systemic lupus erythematosus. Correlation of both indices was significant ( $r = 0.8634$ ). The results for other diseases also indicated for correlation between ESR and CRP: rheumatoid arthritis ( $r = 0.6318$ ), ankylosing spondylitis ( $r = 0.9229$ ), systemic sclerosis ( $r = 0.7358$ ).

**Conclusion:** Usefulness of both ESR and CRP in clinical practice of rheumatologist was confirmed, but understanding of different underlying mechanisms leading to enhanced tested result should be always taken into consideration.

### Pathologic finding of increased expression of interleukin-17 in the synovial tissue of rheumatoid arthritis patients

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**Objectives:** Rheumatoid arthritis (RA) is a common autoimmune disease of chronic systemic inflammatory disorder that will affect multiple tissues and organs such as skin, heart or lungs; but it principally attacks the joints, producing a non-suppurative inflammatory and proliferative synovitis that often progresses to major damaging of articular cartilage and joint ankylosis. Although the definite etiology is still unknown, recent studies suggest that T-helper cells (Th17) may play a pivotal role in the pathogenesis of RA. And interleukin-17 (IL-17), which is a cytokine of Th17 cells, may be a key factor in the occurrence of RA. The binding of IL-17 to specific receptor results in the expression of fibroblasts, endothelial and epithelial cells and also synthesis of several major factors such as tumor necrosis factor alpha (TNF- $\alpha$ ), IL-1 $\beta$  that result in the structural damage of RA joints. Though some previous studies have shown that IL-17 exists in the synovium of RA, few have definite proof quantitatively by pathology about its existence in synovial membrane.

**Methods:** This study comprised of 30 RA patients and 10 healthy controls. Over 300 RA patients were treated at the department of rheumatology of the East hospital. Synovial tissues of 30 RA patients (9 males and 21 females; mean age 50.2±16.8 years; disease duration 73.8±49.6 months; DAS28 score 4.89±0.88 (3.89~7.41)) were obtained for pathologic studies when these patients received joint surgery. Control synovial tissue specimens were obtained during surgery for knee tear ligaments from 10 healthy patients. All the procedures were followed in accordance with the ethical standards of the Helsinki declaration of 1975, as revised in 2008.

**Results:** Pathologic study of the synovial membrane showed increased expression of IL-17 in the synovial tissue of RA patients, the intensity is compatible with clinical severity of disease as validated by DAS28 score and disease duration. Northern blot study also confirmed the increased expression of IL-17 in the synovial tissues.

**Conclusions:** This study has a major limitation is that the number of RA patients receiving tissue study is relatively small, but our results are consistent; which can shed more light in the field of IL-17 as a causative role in the pathogenesis of RA. In conclusion, thru histopathological investigation, this study again finds that the increased expression of IL-17 in the synovium of RA patients, which suggest that IL-17 may be one of the key factors in the etiology of RA.

## Retroperitoneal fibrosis related to HIV infection?

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**Introduction:** Retroperitoneal fibrosis is a benign neoplasm consisting in the proliferation of fibroblasts and collagenous fibers. The etiology is unknown in 2/3 of the cases, while the remaining are associated with drugs, retroperitoneal hemorrhage or surgery. There are some reports describing retroperitoneal fibrosis associated with HIV infection.

**Clinical case:** A 33 years old male presented to the emergency room with 10 days complains of hypogastric pain with lumbar irradiation. He had been medicated with ciprofloxacin for the past two days, without improvement. He denied fever, dysuria, urinary frequency, or vomiting. Intermittent claudication for over a week and edema of both lower limbs were reported, and also two episodes of deep vein thrombosis (2003), and appendectomy (2013). The patient takes rivaroxaban 20mg id. Family history, his mother suffered pulmonary embolism, the maternal grandfather had deep venous thrombosis, and a sister has systemic lupus erythematosus. On physical examination, there were anterior cervical adenopathy, elastic, mobile and not painful; abdominal tenderness; edema of both legs with palpable pulses. Blood tests: blood urea nitrogen 14 mg/dL, creatinine 0.83 mg/dL, Na 134 mmol/L, K 4.8 mmol/L, Cl 102 mmol/L, osmolality 270 mOsm/kg, CRP 12.9 mg/L. Leukocytes  $10.1 \times 10^9/L$ , hemoglobin 10.8 g/dL, MCV 69.5 fL, platelets  $156 \times 10^9/L$ , PT +6.8"; prothrombinemia 49%, INR 1.65, aPTT +11.5". Abdominal ultrasound showed thrombotic occlusion of the inferior vena cava (IVC) below the confluence of the renal veins, extending to the right common iliac vein; increased fat reflectiveness around the large abdominal vessels; several adenopathies in the topography of the iliac vessels. Further study revealed syphilis and anti-HIV1 positive. Hemostasis and thrombosis study revealed no alterations.

**Discussion:** Although the previous episodes of thrombosis and family history would lead to suspect hereditary component, relevant genetic alterations were not found. Although there's no urethral involvement, the fat densification adjacent to the IVC is suggestive of retroperitoneal fibrosis, which would justify the extensive thrombosis of these vessels. There is a case described in the literature of HIV related retroperitoneal fibrosis. HIV infection is also related to thrombosis phenomena with decreased levels of protein C and S. The patient is still awaiting

confirmatory biopsy of fat and the adjacent lymphadenopathy to exclude associated malignancy.

## Pericardial involvement in biopsy-proven giant-cell arteritis patients detected by CT angiography: prevalence at diagnosis and outcome with glucocorticoid treatment

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**Objective:** In giant-cell arteritis (GCA), cranial artery involvement is particularly frequent and underlies the classical manifestations and complications of the disease. Symptomatic pericarditis has been occasionally described as part of the presenting symptoms. However, the frequency of imaging-detected pericardial involvement has not been systematically evaluated. The aim of our study was to assess the prevalence of pericardial involvement detected by CT angiography (CTA) in patients with newly diagnosed GCA, as well as the potential relationship with pericardial symptoms, GCA manifestations, laboratory data, or the presence of large-vessel vasculitis (LVV). The outcome of pericardial involvement with glucocorticoid (GC) treatment was also analyzed.

**Methods:** From July 2007 to January 2015, 63 patients diagnosed with biopsy-proven GCA at our institution were subjected to CTA according to a defined protocol as part of a prospective study assessing LVV. These patients were treatment-naïve or had received GC for  $\leq 3$  days. A follow-up CTA was scheduled to evaluate the outcome of imaging-detected lesions with GC treatment. Post-hoc assessment of CTA images was performed in order to detect pericardial abnormalities including pericardial thickening (thickness of the pericardial membrane of at least 4 mm) and/or pericardial effusion (presence of liquid between the pericardial membrane and the heart). Specific GCA symptoms and laboratory features, as well as classical pericardial manifestation were recorded.

**Results:** Among the 63 patients included, 45 were women and 18 men, aged 78 years (range 56-92). At the time of GCA diagnosis, pericardial involvement was present in 18 patients (29%), consisting of thickening (4-7 mm) in 8 patients (13%) and effusion (4-18 mm) in 10 (16%). 46 patients completed the follow-up CTA assessment after a median follow-up of 16 months (range 12-135). At the second imaging, 8 of them (17%) still had pericardial involvement: thickening in 5 (11%) and effusion in 3 (6%). All patients were asymptomatic regarding classical pericarditis symptoms. No relationship was observed between the presence of pericardial involvement and GCA manifestations, laboratory data or the detection of LVV.

**Conclusion:** In our series, about one third of patients with newly diagnosed GCA have pericardial involvement, consisting of a subclinical mild to moderate pericardial thickening or effusion that improves during the follow-up with GC treatment. Acknowledgement: Supported by SAF14/57708-R.



## Giant cell arteritis refractory to corticosteroid therapy: therapeutic efficacy of methotrexate

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**Introduction:** Giant cell arteritis (GCA) is a large vessel vasculitis more common in men over 50 years, with a higher incidence in the countries of northern Europe (17/100000) compared to southern countries (10/100000). The 1st line therapy in these cases is systemic corticosteroids.

**Case report:** We describe the case of a 68 years old man, with poorly controlled diabetes, admitted with bilateral frontotemporal headache, sudden appearance of scotomas of the right eye (RE), blurred vision and jaw claudication associated with anorexia and weight loss of 10% with the last month. In the laboratory findings the sedimentation rate (ESR) stands out with 91 mm/h. Eye observation of RE showed pale optic disc contour on the nasal region. The echo-Doppler of the temporal arteries showed extensive bilateral ultrasound halo and increased flow velocity. The temporal artery biopsy confirmed the diagnosis of GCA. Given evidence of ischemic optic neuropathy associated with GCA, high dose (1 g) methylprednisolone pulses were initiated, followed prednisolone (1 mg/kg/day) and progressively tapered to 20 mg/day over 5 months. By maintaining clinical and imagiological evidence of disease activity after prednisolone tapering, methotrexate was associated, achieving clinical remission with ESR of 15 mm/h and resolution of imagiological findings.

**Discussion:** GCA refractory to corticosteroid therapy corresponds to 40-48% of cases. However there are no consensual criteria for choosing between the second line drugs for steroid-refractory cases (methotrexate, cyclophosphamide, azathioprine or infliximab). This case illustrates the effectiveness of methotrexate allowing to minimize steroids adverse effects, leading to disease remission and avoiding irreversible organ damage.

## Massive bone destruction: deceiving appearance, a clinical case

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**Case report:** We present a clinical case of a 80 years old woman with known history of degenerative osteoarthropathy admitted to the emergency department for intense right shoulder pain with a two weeks evolution, leading to severe functional impairment and associated spontaneous local hematoma. There was no history of trauma and no relief with oral and topic painkillers. Initial Orthopedic evaluation included a CT scan, which showed a massive tissue lesion (11x5x8 cm) centered on glenohumeral joint, conditioning the filling of the joint space and extra-articular expansion, lytic reuptake of the glene, humeral head and distal third of clavicle, and reshaping

of the adjacent bony elements, including distal clavicle, acromion, lateral edge of scapula and medial edge of humeral metadiaphysis, suggesting destructive osteoarthropathy of undetermined nature, needing to correlate to MRI/histology. She was then admitted to an Internal medicine ward, for further clarification of etiology and to obtain total pain control. During inpatient stay, multiple diagnostic techniques and procedures were carried out: 1) Thoraco-abdominal-pelvic CT scan revealed the presence of degenerative lesions on the left shoulder with no evidence of other lytic lesions or any primary focus of metastasis; 2) An right shoulder MRI showed massive synovial injury with features suggesting probable sarcomatous type, having less likely benign etiology, associated with rough metabolic arthropathy with inflammatory process; 3) Whole body bone scintigraphy demonstrated the known osteolytic lesion of the right shoulder and alterations of left shoulder, probably related to an inflammatory/degenerative etiology with no evidence of neoplastic bone lesions; 4) Blood cultures, including Mycobacteria, were negative; 5) Open biopsy of the right shoulder lesion revealed a mass appearing an organized hematoma with necrotic tissue and bone splinters, whose assessment demonstrated no evidence of acid and alcohol fast bacilli or another microorganisms, with negative bacteriological culture and negative TB nucleic acid amplification, and whose histopathological evaluation suggested destructive and reactive lesions with organized bleeding with no evidence of neoplastic lesions nor granulomas.

**Discussion:** Thus, we conclude these lesions were due to bilateral aseptic necrosis of proximal epiphysis of the shoulders, being excluded neoplastic and infectious causes. It had no indication for surgery, whereby only conservative medical treatment was instituted.

## Essential mixed cryoglobulinemia not associated with hepatitis C

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**Case report:** Women, 40 years old, complains of fatigue, muscle pain, joint pain, numbness on the left side of the body and Raynaud's phenomenon, also referred temperatures up to 38°C assignment with paracetamol, and a weight loss of 6.4 kg in the last year. Presents myalgia, arthritis polyarthralgia without the involvement of the proximal interphalangeal metacarpophalangeal, knees and joints warm-tarsicas joint morning stiffness and 10 minutes had worsened. Paresthesia affected the left side of the body and hemifacial. Related deterioration in contact with cold temperatures. Physical examination, cardiopulmonary auscultation showed no abnormalities. No latero-cervical lymphadenopathy. Lower limbs eruptions bilaterally with some residual lesions and hyperpigmentation face first finger of his right foot against a palpable purpuric lesion. It has positioned itself as hypothesis participation diagnosed febrile vasculitis box joints, skin, neuropathic and peripheral circulation. CBC, coagulation, liver function, kidney within normal. VS, serologic studies for cytomegalovirus, Epstein-Barr, pavovirus B19, Brucella,

hepatitis B and C virus and Mantoux were negative. Tumor markers, immunology with antinuclear antibodies, anti-DNA, ANCA, rheumatoid factor (RF) have been negative. The cranial CT scan, abdominal ultrasound and magnetic resonance imaging of the skull were normal. Electromyogram where signals compatible with light sensorimotor polyneuropathy were observed. The worsening with exposure to cold, and the first negative, put the hypothesis of a pathology mediated by cryoglobulins and the new determination in a laboratory test positive reference with a negative rheumatoid factor-poly pattern confirmation monoclonal without supplement consumption with cryoglobulinemia essential mixed. Corticosteroids started improving and stable disease.

**Discussion:** Cryoglobulinemia is a rare cause of vasculitis affecting vessels of small and medium caliber produced by the deposition of immune supplements are classified: type I – monoclonal cryoglobulinemia IgM or IgG, type II – mixed cryoglobulinemia IgM monoclonal component and polyclonal IgG and type III – polyclonal cryoglobulinemia. Type I is associated with lymphoproliferative disease and multiple myeloma, and types II and III are normally associated with connective tissue diseases and infections. The association between HCV and CMV can reach 90% of cases, but there are cases that are not related to any disease and are called essential cryoglobulinemia.

## Eye involvement of protest to repeat as autoimmune disease

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**Case report:** Female patient, 64 years old, with family history without interest, query sent by various self limited loss of vision in his right eye in the past year without a diagnosis by ophthalmology and treated with dorzolamide/timolol drops episodes. In the 6 months prior two new episodes of "red eye", the latest one week before the consultation. Has joint pain in hands and cervical spine classified as osteoarthritis. Painful oral sores refers repetition and painless vaginal sores outbreaks evolve and does not care because so takes "life". Denied photosensitivity, malar erythema, nodules, skin lesions or other symptoms. On examination conducted there IFP type of inflammatory arthritis, MCF, shoulders and cervical spine, thrush oral cavity residual, regular rest. Diagnostic testing positive ANA+ 1/160 (homogeneous pattern) and positive HLA B51. Gynecology assessment by confirming the existence of vaginal sores not herpetic. Valoración for ophthalmology, highlights vitritis fibrin in the anterior chamber. Given the data from the clinical history and tests carried etiology rule out infectious, neoplastic or inflammatory, pointing to an autoimmune etiology.

**Discussion:** In autoimmune diseases manifested in outbreaks of oral and vaginal sores and ocular involvement we would think such uveitis in Behcet's disease (BD). Reviewing current classification criteria "International Study Group of 1990 Behcet disease" and applying them to the manifestations we could assume the diagnosis of Behcet's disease, genetic association

and consistently confirmed in different populations between a gene and EB it is described with HLA B51. The HLA B51 in our patient was positive. We started treatment with doses of oral corticosteroids (0.5 mg/kg/day) with decreasing pattern with good initial control of symptoms. Upon reaching the dose of 2.5 mg per day presents new outbreak of sores accompanied uveitis and vaginal ulcers so we advertise new cycle of associating corticosteroids and colchicine 0.5 mg 2 per day the patient currently being tolerated without activity. To conclude reinforce once again the importance of the internist, able to encompass the signs and symptoms presented by patients in a systemic disease as in our case and trying not isolated events.

## Successive acute hepatitis in a woman with multiple sclerosis — drug toxicity, autoimmunity or both?

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**Introduction:** Multiple sclerosis is a demyelinating disease of autoimmune origin. It's management includes immunomodulating and anti-inflammatory agents. The potential role of certain drugs to induce or exacerbate autoimmune liver disease is controversial.

**Case report:** The authors describe a case of a 41 years old woman, with a history of multiple sclerosis for 12 years. She was initially medicated with interferon B1a. Five years ago, she suffered an exacerbation of the disease and she was given pulses of methylprednisolone followed by natalizumab and amantadine. After four months of treatment, she developed an acute hepatitis that was attributed to those drugs, after which natalizumab and amantadine were stopped and she started again interferon B1a. At that period she was positive for anti antimitochondrial antibody. No liver biopsy was performed. Five years later, in January 2015, she suffered another attack of multiple sclerosis, treated with 5 days of methylprednisolone 1g/day. Interferon B1a was maintained, with complete remission of neurological symptoms. About two months later, she developed another acute hepatitis, symptomatic, probably due to interferon/corticosteroids. Her liver enzymes were 30 times normal and bilirubin 2 times. Autoimmunity was negative, including auto antimitochondrial antibody. Infection with HBV and HCV was excluded. Liver biopsy was performed, displaying extended confluent centrolobular necrosis with areas of bridging necrosis. In portal tracts there is a mild inflammatory infiltrate with lymphocytes and plasma cells. The hypothesis of autoimmune mediated acute hepatitis was raised. During hospitalization, no steroids were used and interferon was stopped. Recovery was completed after 8 weeks.

**Discussion:** Liver abnormalities during interferon therapy are usually asymptomatic and seldom serious, more than 50% occurring during the first three months of exposure. Although autoimmune liver disease has been described, there is not any correlation between the positivity of autoantibodies and the occurrence of any liver abnormality yet.

## Clinical heterogeneity of early psoriatic arthritis

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**Objective:** To investigate the clinical heterogeneity of early psoriatic arthritis (PsA) and the possibility of timely diagnosis.

**Methods:** 57 patients with early PsA (disease duration was less than 2 years). In all patients counting the number of swollen and tender joints, dactylitis score, index Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) and Psoriasis Area Severity Index (PASI) are performed. X-rays of hands, pelvis, spine, the distal part of the foot were performed. MRI of hand and the distal part of the foot, heel ultrasonography (US) and the Glasgow Ultrasound Enthesitis Scoring System (GUESS) score.

**Results:** The majority (78%) of patients with early PsA had involvement of peripheral joint while only 7% had exclusive involvement of the spine. At the onset of the disease observed oligoarthritis in 40% and polyarthritis in 38%, arthritis in the distal interphalangeal joints in 19% of patients. In the first 3 months of the disease arthritis most often localized in the joints of the feet (metatarsophalangeal and proximal interphalangeal), by the end of the 2nd year of the disease arthritis of hands and feet joints occurs with equal frequency. Dactylitis in the first 3 months of the disease were detected in 37% and during the 2nd year in 61% of patients with early PsA. Enthesitis in the study group were observed in 69% and were frequently present at Achilles tendon, greater femoral trochanter and plantar fascia. Enthesitis and dactylitis are associated with inflammatory activity and nail lesion of psoriasis. GUESS index value ranged from 1 to 6 (mean 2,4±0,2). Radiographic hand erosions were observed in 12% and in foot (distal interphalangeal joints) in 7%, juxtaarticular new bone formation in 17% and sacroiliitis in 8% of study group. Simultaneous onset (skin and joints) were detected in 31 (54%) patients with early PsA.

**Conclusion:** The clinical manifestation of early PsA is characterized by heterogeneity and corresponds to national and international classification criteria of this disease.

## A case report of HLA B27+ arthritis caused by bone augmentation and dental implant

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**Case report:** A 58 years old man presented with a 3-week history of inflammatory left shoulder and bilateral knee arthralgia, daily fever, and fatigue. These symptoms began 5 days ago after a deproteinized bovine bone dental bone augmentation procedure followed by a dental implant, and incapacitated the patient for a week, followed by a period of a modest improvement with use of non-steroidal anti-inflammatory drugs (NSAIDs). 10 months prior to the current episode, the patient had a similar event following multiple

dental extractions, with severe inflammation of his right tibiotarsian joint, which completely resolved with NSAIDs in about 3 months. The patient also had a recent diagnosis of type 2 diabetes mellitus (therapy with metformin started one week prior to admission) and a distant episode said to be rheumatic fever. The physical examination revealed inflammation of the knees and right shoulder, with reduced mobility and intense pain in these joints, cervical and lumbar paravertebral muscle stiffness and lumbar spine rectitude. Blood tests revealed an impressive biologic inflammatory syndrome with increased ESR, CRP, WBC, neutrophilia; negative serology screening tests for rheumatoid arthritis, lupus, syphilis; negative tumor markers (AFP, CA 19-9, CEA, PSA); normal gastroscopy, dolichocolon and diverticulosis on colonoscopy; normal chest and upper abdomen CT, all of these ruling out a neoplasm; negative bacterial cultures of blood and urine; and no signs of endocarditis on echocardiography. X-rays showed bilateral gonarthrosis and calcification of the right supraspinatus tendon. The dental examination was normal. The patient was, however, positive for HLA B27. Anti-inflammatory treatment was scaled up from NSAIDs to corticosteroids, with steady improvement of symptomatology. Treatment was continued at home for 2 months, with complete recovery.

**Discussion:** This case is illustrative of reactive arthritis caused by dental procedures (extractions, bone augmentation, dental implant), in a patient with increased susceptibility (presence of HLA B27) and is exceptionally rare in medical literature.

## An unusual case of Takayasu arteritis

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**Introduction:** Takayasu arteritis is a rare, systemic, inflammatory vasculitis involving primarily the main branches of the aorta that most commonly affects women of childbearing age. In Europe and United States the incidence reported is one to three new cases per year per million population. The inflammatory process involving the walls of the concerned arteries causes thickening secondary to the inflammatory process. Other common consequences are narrowing, dilation and occlusion of the involved arterial portions resulting in a wide variety of clinical manifestations.

**Case report:** We hereby present the case of a 38 years old woman with no significant past medical history and without any traditional cardiovascular risk factors referred to our clinic for the assessment of two episodes of acute myocardial infarction occurred 5 and 4 years prior to the admission in our clinic. The first coronary angiography revealed critical left-main coronary artery and left anterior descending coronary artery sub-occlusion followed by aorto-coronary bypass surgery using a saphenous vein graft for the left main coronary artery and left internal mammary artery bypass for the left descending artery. The postoperative evolution was uneventful but ten months later the patient developed a similar episode and the coronarography revealed that the bypass using left internal mammary artery was non-functional, therefore a new bypass surgery using saphenous vein graft was performed with no postoperative complication.

Three years later, in our clinic, the physical examination revealed absence of left radial pulse, decreased left dorsalis pedis artery pulse and arterial systolic grade four bruits concerning the left carotid artery and grade III concerning the left subclavian artery, grade II bruit concerning the abdominal aorta and both femoral arteries. The systolic blood pressure difference between arms was 40 mmHg. Blood samples point out increased inflammation markers and the Doppler ultrasound confirms left subclavian steal syndrome, left external carotid artery and renal artery stenosis with secondary hypertension. At this point the diagnosis of Takayasu arteritis was made and the patient was started on 1 mg/kg prednisone and 400 mg hydroxychloroquine with further remission of the mentioned clinical findings and with no new arterial events.

**Discussion:** The particularity of this case is represented by the involvement of the coronary arteries, an uncommon first clinical manifestation of Takayasu arteritis.

### **Dynamics of endothelial dysfunction during therapy with unsaponifiable compounds avocados and soybeans in patients with cardiovascular diseases and osteoarthritis**

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**Objective:** To study the effect of unsaponifiable compounds of avocado and soybean (ASU) and compare it with the effect of diclofenac sodium on the state of endothelium in patients with cardiovascular diseases (CVD) and osteoarthritis (OA).

**Methods:** 60 patients were included in the study: group 1 (n=30) – patients who received ASU 300 mg 1 tablet per day (paracetamol was recommended for treatment of pain syndrome), group 2 (n=30) – patients who received diclofenac sodium when it was required (pain syndrome) – the individual dose and the dose is titrated according to a patient's condition. The diclofenac sodium was prescribed to the patients together with pantoprazole at a dose of 40 mg per day. There were no authentic sexual, age and clinical differences between the groups. All patients with previous Q-wave myocardial infarction (as main clinical models of atherosclerosis) had instrumental characteristics that confirm the presence of areas of akinesia in the Echo-CG. For all patients in groups the history of cardiovascular disease was collected, also the assessment of arterial dysfunction by using a certified device Angioscan and clinical evaluation of the course of a osteoarthritis (WOMAC scale) was made.

**Results:** At the start and at the end of the study all indicators of endothelial function corresponded to the presence of CVD. Significant positive correlation of moderate strength between the intensity of pain (WOMAC scores) and augmentation index ( $r=0.3$ ,  $p<0.05$ ), which is indicator of stiffness of the arterial wall of the patient, as the intensity parameter of the pathophysiological processes of atherosclerosis. In the patients of group I the stress index (Bayes) decreased by 12%. For the 3 months of observation for the patients in group I the augmentation index decreased by 18.3% (at the start – 15,9, 13). However the patients in group II had negative dynamics of stress index and the augmentation in

the analysis of endothelial dysfunction. Reduction in the intensity of endothelial dysfunction with added piascledine to the basic treatment of cardiovascular disease and osteoarthritis can be useful for long-term therapy of osteoarthritis in patients with cardiovascular diseases.

**Conclusions:** Therapy ASU for 3 months in patients with osteoarthritis and CVD leads to decrease in the indices of stress and augmentation. This may confirm a positive effect of the drug on endothelial status of the patient.

### **Dynamics of the systemic inflammatory response during therapy with unsaponifiable compounds of avocados and soybeans in patients with cardiovascular diseases and osteoarthritis**

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**Objective:** To study the dynamics of systemic inflammatory response during therapy of unsaponifiable compounds of avocado and soybean (ASU) in patients with a combination of cardiovascular diseases (CVD) and osteoarthritis (OA).

**Methods:** The study included 30 patients with previous Q-wave myocardial infarction as the main clinical models of atherosclerosis. CHF 2-3 FC according to NYHA is noted in 16 cases. The average age is  $64.5\pm 3.7$  years (26 women). The intensity of the pain WOMAC is  $672,3\pm 23,7$ ; functional failure is  $587,5\pm 17,4$ . Radiographic changes corresponding to stage III OA according to Kellgren–Lawrence have been identified in 70% of cases, the rest cases are stage II. Therapy CVD corresponds with National Guidelines. All patients received ASU in the dose of 300 mg, 1 tablet per day (with pain syndrome paracetamol will be offered). All patients had instrumental characteristics, indicating the presence of areas of akinesia in the Echo-CG. In patients from all groups history of cardiovascular diseases was collected and clinical evaluation of the course of osteoarthritis (WOMAC scale) was estimated. Quantitative determination of the level of cytokines TNF-a, IL-1B, IL-6, receptors to IL-2, CRP in serum was performed by solid-phase chemiluminescence immunometric analysis with enzymatic label using the test systems of the "DPC" on an automated analyzer "Immulite" (DPC, USA).

**Results:** Clinical evaluation of the dynamics of osteoarthritis for 3 months found decrease in the intensity of pain on WOMAC almost by 60% of the baseline, and the degree of functional disability by 39.4% ( $p=0.03$ ). The decrease of proinflammatory markers in serum in all patients was observed. The level of TNF-a decreased about 32.8% ( $p=0.05$ ). The concentration of IL-1b decreased by 33.3% ( $p=0.04$ ). The concentration of receptors for IL-2 decreased by 33.4% ( $p=0.03$ ). The concentration of C-reactive protein decreased within 3 months of the study by 42.3% ( $p=0.03$ ).

**Conclusion:** Therapy ASU patients with a combination of osteoarthritis and CVD leads to the significant decrease in markers of systemic inflammatory response by 30–40 % for 90 days of therapy.

## Lung involvement in patients with rheumatoid arthritis

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**Objective:** We aimed to determine the value of pulmonary complaints, physical findings and instrumental methods for indication of lung involvement in patients with rheumatoid arthritis (RA).

**Methods:** Patient group included 70 persons (female – 63, male – 7) with RA, aged from 24 to 83. Only 10% of them presented clinically manifested lung injury associated with RA. Patients with other pulmonary diseases were excluded. Investigation contained physical examination, lung X-ray, high resolution computed tomography (HRCT), single photon emission computed tomography (SPECT) of the lungs, external respiration function (ERF), and diffusing lung capacity for carbon monoxide (DLCO).

**Results:** Physical findings were nonspecific and not expressed. Pulmonary complaints were present in 65% of patients (dyspnea, cough, sputum); physical examination deviations were found in 40%. Lung abnormalities were detected by lung X-ray only in 10% (basal pneumofibrosis, local changes). HRCT findings were presented in 92% with varying severity: mild (bronchial obstruction – 40%, rheumatoid nodules – 10%), moderate (ground glass opacity – 60%, bronchial wall thickening – 20%, pleural exudates – 10%, branching linear structures – 3%); severe (lung arterial hypertension – 10%, bronchiectasis – 10%, emphysema – 5%). In 80% of cases SPECT demonstrated local hypoperfusion with two main patterns – bronchial obstruction and vasculitis. ERF analysis showed decrease of diffusing lung capacity in 40%, restriction – in 30% and bronchial obstruction in 70% of patients.

**Conclusions:** Comparison of clinical features and instrumental findings makes the evidence of subclinical lung lesions in patients with RA. So it requires the use of more sensitive instrumental methods HRCT and SPECT for early detection of lung involvement in RA.

## Abdominal pain as a sign of Takayasu arteritis

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**Introduction:** Takayasu's arteritis (TA) is a chronic inflammatory disease of large and medium sized arteries with a predilection for the aorta and its branches. It is a rare disease with unknown etiology with a 9:1 female predominance. Although the disease has a worldwide distribution, it appears to occur more often in Asian women.

**Case report:** We report a case of a 46 years old Caucasian woman, with a past medical history of smoking and varicose

vein surgery repair, admitted to the hospital with intermittent claudication of the right lower limb and ischemic ulcers of 2nd and 3rd toes of right foot. She also reported Raynaud's phenomenon in the 3rd, 4th and 5th fingers of the left hand associated with claudication of the left arm. Simultaneously she referred recurrent episodes of severe abdominal pain that worsened after meals, vomiting and a weight loss of 10 kg in the last 3 years. Cardiopulmonary auscultation, abdomen examination and femoral pulses were normal. She presented an absent right popliteal and pedal pulse, weak left popliteal pulse and absent left pedal pulse. Left humeral, radial and ulnar pulses were also absent. Right ankle-brachial index (ABI) was 0.17 and left ABI was 0.37. The laboratory findings were normal and the echocardiogram showed a patent foramen oval that did not explain the diffuse arterial disease. The abdominal and pelvic aortography revealed segmental occlusion of the superior mesenteric and right iliac artery. The arteriography of the lower limbs found multiple stenosis and occlusions. Doppler ultrasound of the upper limbs showed diffuse concentric thickening with multiple stenosis exceeding 50% of occlusion. The histological result of the thromboendarterectomy revealed large vessels vasculitis. She started immunosuppressive therapy with prednisolone (1 mg/kg/day) and later an anti TNF agent (infliximab). Abdominal pain and vomiting increased during hospitalization and she died 2 months later due to mesenteric ischemia.

**Discussion:** TA is a rare disease with a nonspecific initial clinical presentation. For that reason a diagnosis of Takayasu's arteritis can be extremely difficult. Establishing an early diagnosis is essential to the patient prognosis, since this disease is associated with high morbidity and mortality. In our case a TA diagnosis was established according to the American College of Rheumatology criteria, based on the patient symptoms, physical and imaging findings.

## Microscopic polyangiitis

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**Introduction:** Microscopic polyangiitis (MPA) is a rare (prevalence 1-3 cases per 100, 000), small vessel vasculitis associated with the presence of anti-neutrophil cytoplasmic antibodies (ANCA). Clinical presentation is typically non-specific, with constitutional symptoms being the main feature as well as arthralgia, skin rash, hypertension, seizures and ocular involvement. General laboratory findings include raised white blood cell count (WBC), normocytic anemia, elevated erythrocyte sedimentation rate (ESR), impaired kidney function and active urine sediment. Immunological screening frequently shows positive ANCA (80%), p-ANCA (60%) and c-ANCA (40%) without complement consumption. Definitive diagnosis is histological and the presence of small vessel vasculitis is consensually accepted as the hallmark of disease. The cornerstones of treatment are corticosteroids which may be associated with immunosuppression due to its steroid sparing effect. Prognosis is favorable with the majority

of patients achieving clinical remission and survival rate at 5 years is 75%.

**Case report:** We present the case of 79 years old woman with a history of weight loss, generalized myalgia, headache and recurrent corneal ulcers. Laboratory tests showed normocytic normochromic anemia, raised WBC and ESR (120 mm/h), altered kidney function and active urine sediment. To exclude cancer, gastroscopy, colonoscopy and thoraco-abdomino-pelvic CT were performed and did not show any relevant findings. Bone marrow aspirate was normal. Temporal arthritis was excluded by Doppler and temporal artery biopsy. Immunological screening showed negative c-ANCA and positive p-ANCA. Prednisolone (1 mg/kg/day) and azathioprine were started with gradual clinical and laboratory improvement which persisted after steroid tapering.

**Discussion:** MPA is a rare form of vasculitis and the differential diagnosis may be hampered by the paucity of clinical manifestations. Diagnosis is achieved through a combination of integrating symptoms, serological findings and excluding more common vasculitis and cancer.

## Arterial hypertension and complications of cardiovascular diseases in patients with rheumatoid arthritis

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**Objective:** To assess the characteristics of arterial hypertension (AH) and the risk factors of cardiovascular disease (CVD) in women with rheumatoid arthritis (RA).

**Methods:** The first group included the patients with rheumatoid arthritis (n=152) and the second one was without it (n=149). RA was diagnosed by the criteria ACR\EULAR 2010. The groups were comparable according to the age: the first – 54.9 (19-77) years, the second – 55.1 (20-77). The average duration of RA was 107 (4-381) months. 100% of patients had basic anti-inflammatory therapy; NSAIDs occasionally, 26% of them took glucocorticosteroids. Statistical data were obtained with the help of «Statistica» v 6.1 software.

**Results:** Patients with RA had AH in 73% of cases, 18% had primary AH. But AH was diagnosed only in 42% of patients from the second group (p<0.05). The blood pressure of patients with RA was SBP -142 (100-214)/DBP- 83 (60-122), in the second group – SBP 130 (98-174)/DBP 78 (56-109), (p<0.05). The increased blood pressure was revealed for the first time in 36% of cases after the patients had been diagnosed with RA, 34% had AH before they were diagnosed with RA, 35% of patients with RA had antihypertensive therapy. The patients with RA and AH had the following risk factors more often than the patients without RA: the decreased physical activity was more often in 1.1 times (94 and 82% respectively), abdominal obesity – in 1.3 times (81 and 64%), tachycardia – in 2.6 times (70 and 27%), the increased total blood cholesterol level – in 1.4 times (68 and 48%), sleep disturbance – in 1.5 times (30 and 20%), hyperglycemia – in 2.6 times (13 and 5%). The affected organs and early markers of atherosclerosis were left ventricle

hypertrophy, it occurred 1.7 times frequently in patients with RA (73 and 42% respectively in the first and second groups), lower limb arterial calcification (ankle-brachial index (ABI) >1.3) was 5.8 times more frequent (35 and 6%, p<0.05), stenosis of lower limb vessels (ABI<0.9) was registered only in 12% of patients with RA.

**Conclusions:** AH is 1.6 times more frequent in women with RA. Rheumatoid arthritis is supposed to influence on the AH development. Besides it is associated with the traditional risk factors such as decreased physical activity (p<0.05), tachycardia (p<0.05), the increased total blood cholesterol level (p<0.05), sleep disturbance (p<0.05), hyperglycemia (p<0.05) with the involvement of target organs (left ventricle hypertrophy, p<0.05) and early markers of atherosclerosis (ABI>1.3, p<0.05). The AH in patients with RA is characterized by the increased systolic/diastolic pressure (p<0.05).

## Two clinical cases, the same syndrome

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**Case reports:** Two women, one 28 years old and the other 40 years old, a shopkeeper and an administrative respectively. The first one had complaints of arthralgia and diffuse myalgia, of nocturnal and morning predominance, with a one year evolution. The second woman suffered from exuberant aphthous ulcers in the oral and genital mucosa, recurrent throughout a 2 year period, associated with arthralgia and myalgia. Both had a diagnosis of psychiatric illness, compatible with anxiety/depression. The first woman had a previous history of abortion during the first trimester of pregnancy (the placental histology revealed an extensive chorionic villus infarction). In the follow-up study, it is relevant to stress the negative results for  $\beta$ 2-glicoprotein, lupus anticoagulant, anti-cardiolipin and anti-dsDNA (anti-double stranded DNA) antibodies, and the positive results for the rheumatoid factor, anticitrulin antibody, antinuclear antibodies, anti-SSA (anti-Sjögren's-syndrome-related antigen A) and anti-SSB (anti-Sjögren's-syndrome-related antigen B). In the second woman the immunological study was completely negative, including HLA-B51 (human leukocyte antigen – B51). A biopsy was performed on the oral cavity ulcer, which revealed a polymorphous infiltrate, of plasmacytic predominance, with no signs of vasculitis and absence of microorganisms. In a more detailed anamnesis it was possible to identify symptoms compatible with xerostomia and xerophthalmia in both women. No other signs or symptoms were found. A scintigraphy of the salivary glands showed, in both, deficient uptake and elimination of the radiopharmaceutical, compatible with chronic parotitis and sialoadenitis. The salivary gland biopsy demonstrated aggregation of lymphoid cells. The first case is a primary Sjögren syndrome, while the second case is a secondary Sjögren syndrome.

## Big data and primary Sjögren syndrome: geoepidemiological characterization of 5027 patients recruited by the EULAR-SS Task Force International Network

Pérez-Alvarez R., Pérez-de-Lis M., Brito-Zerón P., Kostov B.A., Zeher M., Theander E., Gottenberg J.-E., Baldini C., Quartuccio L., Priori R., Kvarnstrom M., Kruize A., Hernandez-Molina G., Prapovnik S., Bombardieri M., Nordmark G., Isenberg D., Bartoloni E., Rasmussen A., Solans R., Valim V., Giacomelli R., Carsons S., Hammenfors D., Vollenweider C., Atzeni F., Mandl T., De Vita S., Wahren-Herlenius M., Sanchez-Guerrero J., Gerli R., Sivils K., Brun J.G., Mariette X., Ramos-Casals M., on behalf of the EULAR-SS Task Force

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**Objective:** To analyze the epidemiological, clinical and immunological characteristics of the largest international cohort of patients diagnosed with primary Sjögren syndrome (SS) according to the 2002 AE classification criteria.

**Material and methods:** The Big Data Sjögren Project is an international, multicentre registry formed in 2014 to take a "high-definition" picture of the main features of primary SS at diagnosis by merging international SS databases. International experts participating in the EULAR-SS Task Force were invited to participate. By January 2015, the database included 5027 consecutive patients fulfilling the 2002 classification criteria for primary SS (including probable SS, defined as fulfillment of 3 criteria pending the results of some diagnostic tests) from 9 European and 4 American countries. The main clinical features at diagnosis (time of criteria fulfillment) or at recruitment were collected and analyzed.

**Results:** The cohort included 4714 (94%) women (female:male ratio, 15:1), with a mean age at diagnosis of primary SS of 54.26 years (range, 10-97), of which 94.1% were Caucasian and 88.6% lived in European countries. The frequency of fulfillment of the 2002 criteria was: 94.4% for dry eye, 92.9% for dry mouth, 88.5% for positive salivary gland biopsy, 85.9% for positive ocular tests, 74.8% for positive oral tests and 70.9% for positive Ro/La autoantibodies. As a minimum of 4 of the 6 criteria are required for fulfillment, the percentage of diagnostic tests performed varied: Ro/La autoantibodies were tested in 99.5% of patients, ocular diagnostic tests (Schirmer's test and/or corneal staining) were made in 90.2%, oral tests in 76.7% and salivary gland biopsy in 72% of patients. With respect to criteria fulfilled, 7.5% fulfilled 3 criteria, 42% 4 criteria, 36% 5 criteria and 14.5% all 6 criteria. Patients carrying Ro autoantibodies were younger (52.91 vs 57.12,  $p<0.001$ ), had a higher frequency of positive ocular tests (88% vs 83%,  $p=0.001$ ), ANA (92% vs 80%,  $p<0.001$ ) and RF (60% vs 38%,  $p<0.001$ ) but a lower frequency of and positive salivary gland biopsy (81% vs 95%,  $p<0.001$ ). Patients carrying La autoantibodies were also younger (52.63 vs 55.39,  $p<0.001$ ), had a higher frequency of xerostomia (94% vs 90%,  $p<0.001$ ), positive ocular tests (89% vs 85%,  $p=0.003$ ), positive scintigraphy (75% vs 67%,  $p<0.001$ ), ANA (93% vs 86%,  $p<0.001$ ) and RF (68% vs 44%,  $p<0.001$ )

and also a lower frequency of positive salivary gland biopsy (82% vs 90%,  $p<0.001$ ).

**Conclusions:** In the largest cohort of primary SS patients diagnosed homogeneously according to 2002 AE criteria, the broad heterogeneity of clinical and analytical features observed emphasize that SS should be considered a systemic disease rather than a sicca-limited disease. Anti-Ro/SS-A and La/SS-B antibodies are detected in 71% of patients and are closely associated with the main clinical, diagnostic tests and immunological markers related to primary SS.

## Ethnicity-related differences in the clinical presentation of sarcoidosis: analysis of 175 patients from Spain

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**Objective:** To evaluate the influence of the main epidemiological features (age, gender and ethnicity) in the clinical presentation of sarcoidosis in a cohort of patients diagnosed at a Spanish urban tertiary teaching hospital.

**Methods:** Consecutive patients diagnosed with sarcoidosis between 1990 and 2014 in the Hospital Clinic of Barcelona (Spain). Sarcoidosis was diagnosed in agreement with the criteria proposed by the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) 1999 statement on sarcoidosis. Organ involvement was retrospectively determined in each patient (at the time of diagnosis and cumulated during the follow-up) using the 2014 WASOG organ assessment instrument.

**Results:** The cohort consisted of 175 patients, including 110 (63%) women and 65 (37%) men (female:male ratio 1.7:1), with a mean age at diagnosis of  $47.3\pm 15.5$  years (range, 16-92). Clinical features at the time of diagnosis mainly included pulmonary symptoms in 73 (42%) patients, cutaneous symptoms in 51 (29%), general symptoms in 50 (29%) and extrathoracic adenopathies in 21 (12%). In 20 (11%) patients, sarcoidosis was diagnosed in asymptomatic patients due to incidental radiological findings. Of the 175 patients, 41 (23%) were born outside Spain (16 in South America, 12 in Asia, 10 in Africa and 3 in other European countries). At diagnosis, non-Spanish-born patients had a lower mean age (40 vs 49 years,  $p=0.001$ ), a higher predominance of females (68% vs 54%,  $p=0.036$ ), and a higher frequency of musculoskeletal symptomatology (41% vs 25%,  $p=0.031$ ) compared with Spanish-born patients. With respect to the cumulative organ-specific involvement, non-Spanish-born patients had a higher frequency of pulmonary (100% vs 90%,  $p=0.027$ ) and ocular (17% vs 7%,  $p=0.05$ ) involvement compared with Spanish-born patients. Age, pulmonary and ocular involvement were significant independent variables in the adjusted multivariate analysis.

**Conclusion:** Age, gender and ethnicity play a significant role in the presentation of sarcoidosis and the variations in these factors may aid early diagnostic suspicion, the search for histopathological confirmation and the prompt introduction of the appropriate therapy.

## Diagnosis of systemic diseases in patients presenting with sicca syndrome using a minimally-invasive minor salivary gland biopsy: prospective evaluation of 200 patients

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**Objectives:** Sicca syndrome is a clinical presentation that is common for several systemic diseases that may infiltrate the exocrine glands. The most frequent disease is Sjogren's syndrome (SS), but other systemic diseases such as sarcoidosis, amyloidosis of IgG4-related disease may also infiltrate salivary glands. The aim was to analyze the safety and usefulness of a new diagnostic tool for investigating minor salivary glands (minimally-invasive biopsy technique) in patients presenting with sicca syndrome suspecting a systemic disease.

**Methods:** We present a prospective analysis of 200 patients presenting with a sicca syndrome (defined by the presence of xerostomia and xerophthalmia, with positive results for ocular tests and/or parotid scintigraphy) in whom a minimally-invasive biopsy of minor salivary glands was carried out at a single center. For all biopsy samples, a cumulative focus score of lymphoplasmacytic infiltration was evaluated (Chisholm Mason score, CMs), together with investigation of other infiltrative processes caused by granuloma, amyloid, positive IgG4 cells or lipids. Adverse events were recorded on a questionnaire immediately after the procedure and 7 days thereafter.

**Results:** All biopsies but 2 disclosed salivary gland tissue. Histopathological diagnosis was available in 189 cases (158 women, 31 men, mean age 59 years): 44% of patients showed a non-specific chronic sialoadenitis (NSCS) (CMs=1-2), 21% focal lymphocytic sialoadenitis (FLS) diagnostic of primary Sjögren syndrome (CMs=3-4), 12% chronic atrophic sialadenitis (CAS) (CMs unclassifiable), 18% normal glandular tissue (CMs=0) and other diagnosis in the remaining 4% (1 case of amyloidosis, 1 of sarcoidosis, 6 of lipoid infiltration and 1 salivary oncocytic cystadenoma); no patient had IgG4-related disease. The higher mean age was found in patients with CAS (69 years), followed by those with NSCS (59 years), those with FLS (57 years) and those with a normal result (54 years) ( $p<0.001$ ). A higher frequency of FLS was found in patients with positive immunological markers including RF, anti-Ro, anti-La, hypocomplementemia and cryoglobulins ( $p<0.05$ ). The percentage of patients diagnosed with Sjögren

syndrome varied according to the concomitant systemic features: 13% of patients presenting with an isolated sicca syndrome had FLS in comparison with 32% of those who present with extraglandular involvement ( $p<0.05$ ). Only 28 patients (14%) reported transient adverse events recovered completely during the first 24h: 7 mild paresthesias, 11 mild pain and 10 minimum local hematoma. Of the 29 patients that were receiving antiaggregant/anticoagulant therapies, only 3 (10%) showed local side effects.

**Conclusions:** Minimally-invasive biopsy of minor salivary glands is a simple, safe, and reliable tool for the diagnosis of infiltrative systemic diseases of exocrine glands, principally Sjögren syndrome but also amyloidosis and sarcoidosis. We found no case of IgG4-related disease, suggesting that this disease is extremely rare in Caucasian patients presenting with sicca symptoms (in contrast to Asian patients).

## Osteitis deformans: diagnostic challenge

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**Introduction:** The osteitis deformans or Paget's disease of bone (PDB) was first described by Sir James Paget in 1877. It is a chronic disease of unknown etiology, characterized by localized changes in bone turnover, which is increased in several areas of the skeleton, mainly in the spine, pelvis, femur, sacrum and skull. The PDB can cause bone pain and deformity, secondary osteoarthritis, hypervascularization which is sometimes warm to touch, increased risk of fracture and also sarcomatous degeneration in 1% of cases. The diagnosis is made by characteristic changes in radiographic and biochemical evaluation. The bone scintigraphy is useful to determine the extent of the disease.

**Case report:** We present the case of a 66 years old male, engineer, with diagnosis of hypertension, dyslipidemia, benign prostatic hypertrophy and prior sigmoidectomy for diverticulitis. The patient referred in the last 6 months the beginning of low back pain and right omalgia, with mechanical rhythm. Palpation of these sites was painful and exacerbated by movements. The radiographs of the painful areas were complemented by computed tomography and magnetic resonance imaging of the lumbar spine and bone scintigraphy, all of them favorable to the diagnosis of Paget's disease. The patient presented involvement of the skull base, the proximal half of the right humerus, left collarbone, sacrum, iliac bone, L2 – L5 and left patella. Laboratory tests including blood count, renal function, calcium, phosphorus and protein electrophoresis were normal; alkaline phosphatase was 206 U/L (45-129), total procollagen type 1 (P1NP) was 453 ng/ml (N=0) and beta-cross laps (B-CTx) 1.72 ng/mL, PTH was 97 pg/L (14-72). Because of the presence of polyostotic PDB in risk locations, the patient was treated with zoledronic acid, calcium and vitamin D.

**Discussion:** We describe the main clinical, laboratory and imaging findings of the PDB. An update treatment of this condition is presented.



## Vascular injuries in Behcet disease from the Madrid's community 3rd health care zone

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**Objectives:** Behcet disease (BD) is a multisystem pathology, chronic and of unknown cause, characterized by a relapsing course and evolving buds. It's been classified among the systemic vasculitis with strong capacity to affect all size arterial and venous blood vessels, so that, most of the clinical disease manifestations derived from this ailment. The BD is globally spread, nevertheless, is more frequent with countries related to the former "Silk Road": Iran, Iraq, Uzbekistan, Turkmenistan, China and Turkey and less recurrent on Northern Europe and United States of America. It's been estimated Turkey as the highest incidence country with 80-730 cases in each 100.000 habitants. Spain shows low incidence rate with 5-10 cases of each 100.000 people. The vascular disease (VD) on the BD, according to published case series, has 14,3% prevalence more common in men. The superficial venous thrombosis is the more frequent implicated sign followed by the deep venous thrombosis and then the arterial disease. The VD is one of the main causes of morbidity and mortality in the Behcet disease, principally pulmonary artery aneurysm with mortality rates up to 25%, reason why we report our experience on it.

**Methods:** We performed a retrospective review of the BD diagnosed patients clinical records in the different Príncipe de Asturias Hospital services, located in Alcalá de Henares, belonging to the 3rd health care zone of the Madrid's community analyzing from 1988 to 2015. After that we classified the patients according to the presence of vascular injury, venous or arterial.

**Results:** The BD was suspected on 33 patients during the reviewed period; from this only 29 met with the international recognized diagnose criteria. The VD was present in 24,1% of cases, 5 of these were women (71,4%) and just 2 men (28,6%). Regarding the involvement distribution, 85,7% had venous disease being predominant the deep venous thrombosis, with 14,3% of arterial disease and 14,3% having both.

**Conclusions:** The BD diagnostic was conducted on 29 patients during the time period studied. The VD was present in 24,1% of cases, of these, only 28,6% were men. The main event was the venous involvement, being 85,7% of deep venous thrombosis cases and only 14,3% superficial vein thrombosis. Venous and arterial involvement was evident in only one patient. Once established the thrombotic event 100% of the patients received standard dose anticoagulation. Given the high morbidity and mortality of vascular involvement in BD it is important to maintain clinical suspicion and early diagnosis. The approach to the prevention of venous thrombotic events at the BD is control, rather than systemic inflammation primary anticoagulation. However, if venous thrombotic events occur, they should be treated with standard dose anticoagulation.

## Comparison of clinical and antidestructive effects of rituximab in rheumatoid arthritis

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**Objective:** To compare clinical and antidestructive effect of rituximab (RTX) in patients with rheumatoid arthritis (RA).

**Material and methods:** Clinical and radiological study of 61 patients (pts) with RA (mean disease duration 10.1±7.7 years, mean DAS28 6.3±0.94, RF-positive 87%, ACCP-positive 93%) treated with RTX (1000 mg x2 or 500 mg x2). Clinical effect was assessed by EULAR criteria; radiological progression by SVH method.

**Results:** Patients were treated by different doses of RTX had good response. Good clinical results were registered in 29.7% (remissions – 14.6%) after 48 week of receiving 2 courses of RTX; good and satisfactory results in 85.3%. Whole group achieved a significant slowing of radiological progression in joint damage. After 48 weeks of treatment progression of articular destruction was absent in all pts in clinical remission, in 83% of pts with low disease activity, and in 43% of pts with moderate activity. Narrowing of joint space was more pronounced than bone destruction – 32% and 25% respectively. Clinical and antidestructive effects often did not coincide. Noteworthy, RTX treatment slowed joint damage in 54% of pts without clinical improvement. There were no significant correlations between clinical outcomes and doses of RTX. The high-dose use of RTX (1000 vs 500 x2) was associated with a significant slowing radiographic progression.

**Conclusions:** Clinical and antidestructive results did not always coincide which suggests different mechanisms of clinical and antidestructive effects of anti-B-cell therapy. The therapeutic effect of different doses of RTX was practically the same but the antidestructive effect of higher doses was significantly greater.

## Evaluation in a local hospital in southern Spain of patients diagnosed of systemic lupus erythematosus

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**Objectives:** Systemic lupus erythematosus (SLE) is an unknown autoimmune disease, multisystem etiology, primarily affects women of childbearing age. Among the most common clinical manifestations its known there are skin and joint commitments and from an analytical point of view are frequent the hematological and immunological alterations. Our goal with this study was to analyze the characteristics of the main clinical and laboratory alterations of 26 patients with diagnosis of systemic lupus erythematosus in our hospital.

**Methods:** We carried out a descriptive and retrospective analysis by reviewing the medical records of 51 patients coded as

"suspected SLE" in our hospital in a period of one year (February 2014 – February 2015), 10 were excluded for the lack of sufficient data for our analysis. We analyzed demographic variables (age, sex), clinical (acute or chronic cutaneous lupus, scarring alopecia, oral ulcers, arthritis, serositis, involvement renal and neurological) and analytical (hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia, ANA, anti-DNA, anti-SM, antiphospholipid antibodies, hypocomplementemia, direct Coombs test in the absence of anemia hemolytic). Data were entered and analyzed in an Excel spreadsheet developed for this study.

**Results:** A final sample of 41 patients with suspected SLE was obtained. 83% were women and 17% men, with a median age of 59 years. It is 23.5% of women under 50 years. With respect to clinical features, up to 81% of patients had joint involvement, followed by involvement cutaneous mucosa, present in 57%. Seven patients reported episodes of serositis (pleuritis/pericarditis) either at the time of diagnosis, or consisted in personal history. Respect to laboratory abnormalities noted that renal impairment, defined as proteinuria of 500 mg/24h and/or hematuria was observed in 15% of cases being referred to the referral hospital to assess pathological study. From the point of view highlights hematologic leukopenia and lymphopenia, present in the 42% of patients, followed by thrombocytopenia (19.2%) and, finally, hemolytic anemia (3.8%). Immunologically, in 100% we would demonstrate the presence of antinuclear antibodies (ANA), a high percentage of cases showed positive anti-DNAs (88.5%), however the anti-Sm were only present in a 11.5%. Moreover, hypocomplementemia (C3, C4, CH50) was observed in 27%.

**Conclusions:** In our sample, as the scientific literature on the subject says, it highlights the predominance of females, although most of them were older than 50 years. The most common clinical manifestation in our patients was the joint involvement followed by skin involvement mucosa. There was no case with alopecia or registered neurological involvement. Renal disease was present in a non-negligible percentage but it couldn't be confirmed by biopsy. From an analytical point of view it is necessary to highlight the presence of ANA in total patients with a high percentage of positivity of anti-DNA and low anti-Sm.

## Rheumatoid arthritis and venous thromboembolic events

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**Background:** Patients (pts) affected by rheumatoid arthritis (RA) present an increased risk of venous thromboembolism (VTE). It is important to determine risk factors of VTE in pts with RA (standard and associated with disease) for prevention of thrombosis. The gold standard for thromboprophylaxis is vitamin K antagonists (warfarin). However warfarin has a number of disadvantages. That is why in recent years new oral anticoagulants (NOAC) were synthesized. In contrast to warfarin NOAC are used in fixed doses, don't need routine monitoring, keeping diet, react with few amount of drugs.

**Objective:** To estimate efficiency and tolerability of dabigatran etexilate in pts with RA.

**Material and methods:** 187 patients (F: 152, M: 35) with confirmed RA were analyzed, 53,8±12,8 y.o., duration of the disease 12,2±10,8 years. Patients were grouped in 2 arms: 27/187 (14,4%) pts with VTE on enrollment or with history of prior VTE; and 160/187 (85,6%) pts without prior VTE. 16 pts had indications for anticoagulant therapy (F:14, M:2), 56,2±10,2 y.o., BMI 29,3±7,2 kg/m<sup>2</sup>, duration of disease 5 [2;14] y. Disease activity was expressed as DAS28 score. All pts were examined for risk factors of thrombosis including antiphospholipid antibodies (aPL) and markers of genetic thrombophilia. Dabigatran etexilate in dose 110mg bid was used for prophylaxis in these pts. Follow-up period was 1 year (48 weeks). Doppler ultrasound control was done on 0, 24, 48 weeks of taking drug.

**Results:** 13/16 pts had VTE after RA was diagnosed, 2/16 before the beginning of disease, 1/16 had antiphospholipid syndrome without VTE. Duration of RA to the time of thrombosis was 54 [16;180] months. 12/16 pts had VTE in the setting of high activity of RA. 1/16 patients had thrombosis associated with operation (ankle fusion). 1/16 pts had aPL. 11/16 were diagnosed genetic thrombophilia: 2/16 in the factor V Leiden, 2/16 in prothrombin gene, 9/16 in MTHFR gene. In coagulogram prolongation of APTT 40±7,8 sec and thrombin time 131±64 sec were noted. Cases of bleeding were not registered; there was 1 recurrence of thrombosis associated with being in sitting position for more than 12 hours.

**Conclusions:** It is needed to assess the risk of thrombosis in patients affected by RA and to take prophylactic measures if needed. Despite of prolongation of APTT and thrombin time dabigatran etexilate did not cause bleeding in patients with RA, 1 case of thrombosis was registered associated with long-time being in sitting position.

## Adrenal insufficiency due to antiphospholipid syndrome in a patient with MTHFR C677T mutation

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**Introduction:** The antiphospholipid syndrome (APLS) is characterized by thrombosis in the presence of antiphospholipid antibodies. APLS can be primary or secondary when coexists with another rheumatological disease, commonly with SLE. Although it is a rare complication; adrenal hemorrhage can be seen in APLS patients. In this report we present a 21 years old male patient with MTHFR homozygous C677 mutation, who developed adrenal insufficiency secondary to APLS associated bilateral adrenal hemorrhage.

**Case report:** A 21 years old male patient was admitted to our clinic with the complaints of fatigue, dizziness and abdominal pain. His past medical history revealed MTHFR homozygous C677 mutation which was established 7 years ago after an acute deep venous thrombosis in the left popliteal vein. Two years later from anticoagulant withdrawal, right femoral vein thrombosis had

occurred. With unfractionated heparin therapy, thrombocytopenia with new onset of thrombosis in the right lower extremity had been detected and the diagnosis of heparin induced thrombocytopenia was confirmed. B2 glycoprotein-1 antibody was positive. He was diagnosed with APLS after mixing studies and put on acetylsalicylic acid plus warfarin treatment with target INR range. There were no findings rather than skin hyperpigmentation and abdominal tenderness at right upper quadrant in his physical examination. He had hyponatremia with hyperkalemia and 2 to 3 fold elevated liver enzymes. Hepatobiliary US and portal vein Doppler US revealed thrombosis in two of three hepatic veins with ascites. Adrenal CT was performed due to a very low basal cortisol level with high ACTH level and bilateral adrenal hematoma was detected. Anti-nuclear and anti-ds DNA antibodies were positive therefore APLS diagnosis was accepted as secondary to SLE. Warfarin was started and he was discharged with immunosuppressive treatment consisting of prednisolone, hydroxychloroquine and azathioprine.

**Discussion:** It is not known either mutation that causes thrombophilia such as MTHFR C677T is more frequent in APLS patients. There are only a few reports about adrenal hemorrhage in APLS patients with mutations that cause thrombophilia but these patients have no diagnosis of SLE. It should be kept in mind that; if symptoms and findings like fatigue, hyperpigmentation, hypotension and electrolyte abnormalities consistent with adrenal insufficiency in a patient with APLS, bilateral adrenal hemorrhage should be strongly suspected.

## Severe reactive thrombocytosis in a patient with microscopic polyangiitis

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**Introduction:** Reactive thrombocytosis rarely exceeds platelet counts of 700x10<sup>3</sup>/μl. Platelet counts exceeding this value are usually considered secondary to chronic myeloproliferative disease (CMD). In the absence of CMD, an extreme thrombocytosis warrants thorough investigation for the presence of severe underlying disease, as malignancy, complicated pyogenic infections or inflammatory rheumatic diseases.

**Case report:** We report the case of a 65 years old woman presenting for undulating fever, weight loss and inferior lower limb arthralgia. Laboratory findings showed severe thrombocytosis of 925x10<sup>3</sup>/μl, leukocytosis (22.3x10<sup>3</sup>/μl), moderate anemia (hemoglobin levels between 9 and 7.5 g/dl), marked inflammation (ESR 88 mm/h, CRP 20 mg/dl, ferritin 287 ng/ml). We note also moderate hypoalbuminemia and mild proteinuria (about 700 mg per day). The presence of inflammation, the absence of splenomegaly, a normal LAP score, the lack of JAK2 V617F mutation and the bone marrow biopsy excluded the diagnosis of a CMPD, especially essential thrombocythemia. A normal procalcitonin level, multiple negative blood culture and the absence of a localized infection excluded also an infectious disease. A malignancy was ruled out by normal upper and inferior digestive endoscopy, as well as thoracic and abdomino-

pelvic CT scan. A left crural monoparesis appeared during hospitalization. The cerebral CT scan was normal. The presence of marked inflammation associated to renal impairment and mononevritis raised the suspicion of a small vessel vasculitis. The highly elevated cytoplasmic anti-neutrophil perinuclear antibody titers confirmed the diagnosis. She was treated with high-dose corticosteroids and cyclophosphamide, resulting in immediate resolution of fever and prompt physical improvement.

**Discussion:** Even in the presence of 'atypically' high platelet counts one should consider the possibility of reactive thrombocytosis. Although the small vessel vasculitis are a very rare entity, in a certain clinical context, we should take into account this diagnosis also.

## Comorbidity: renal dysfunction in patients with rheumatoid arthritis

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**Objectives:** The aim of present study is to evaluate the prevalence and associations of renal dysfunction in patients with rheumatoid arthritis (RA), to investigate whether comorbidities (insulin resistance, dyslipidaemia, hyperuricaemia, arterial hypertension) can influence on renal function of these patients.

**Material and methods:** 107 patients with RA (according to the 1987 revised American College of Rheumatology criteria for RA) at different stages of the disease were enrolled to this cross-sectional study. Risk factors for renal dysfunction were recorded or measured for all participants. The relationship between measures of glomerular filtration, laboratory and clinical parameters of inflammatory activity of RA and the presence of comorbid diseases (vascular atherosclerosis, arterial hypertension, hyperuricemia, insulin resistance) was evaluated. Assessment of renal function was carried out by determining the glomerular filtration rate (GFR), using the formula CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration), which is the adjusted formula MDRD (Modification Diet Renal Disease) and allows evaluating the GFR, including patients with preserved renal function. Correlations between GFR and other variables were analyzed by Pearson or Spearman test as appropriate. Linear regression was used to test the independence of the associations between GFR and other variables.

**Results:** In this RA cohort, mean (SD) age was 70,1±10,0 years, the average age of the onset of RA was 65.6 years. Patients were predominantly women (71%). Duration of RA in patients of clinical group was ranged from 1 to 34 years old, averaged 4.4 years. 61.7% of patients had a reduced GFR between 90 and 60 ml/min/1.73m<sup>2</sup> and 28% had a GFR of <60 ml/min/1.73m<sup>2</sup>. Multivariable analysis revealed significant associations between GFR and age (p<0.00001), female sex (p<0.003), serum uric acid (p<0.005) and the onset of the disease for elderly ≥65 years (p<0.0005). P<0.05 was statistically significant.

**Conclusions:** Renal dysfunction in RA is quite common and associates with such risk factors as advanced age, female sex, level of serum uric acid. According to this, all patients with RA

should undergo regular monitoring of their renal function using GFR predictive equations, while specific subgroups, such as older female patients with hyperuricemia may need particularly intensive monitoring.

## Effect of vitamin D on bone mineral density in dialysis patients

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**Objectives:** Vitamin D deficiency is associated with decreased bone mass in the general population. The effects of vitamin D on bone mass in hemodialysis patients remain to be understood. The aim of this study was to determine the relationship between vitamin D and bone mineral density (BMD) in hemodialysis patients.

**Methods:** In a cross-sectional study 90 hemodialysis patients, serum vitamin D3 was measured. All patients underwent bone densitometry of the lumbar spine and total hip. Vitamin D deficiency is defined as a 25OHD level <10 ng/mL and vitamin D insufficiency is defined as a 25OHD concentration between 10 and 30 ng/mL. Statistical analysis was performed using the Windows SPSS 19 package.

**Results:** 58 male and 32 female were included. The mean age was 53±14.6 years. The duration of hemodialysis was 3.94±1.99 years. Adequate exposure to sunlight was found in 61% of cases. 27 patients benefit from vitamin D supplementation. BMI values was 25.8±4.7 kg/m<sup>2</sup>. The average rate of vitamin D was 15.8±11.8 ng/mL. Vitamin D levels were higher in men (18.9 ng/mL) than women (10.1 ng/mL) (p<0.001). Insufficiency and deficiency on vitamin D were found respectively in 41.1% and 44.4% of cases. The mean of BMD was 0.854±0.152 g/cm<sup>2</sup> in the hip and 1.155±0.218 g/cm<sup>2</sup> in the lumbar spine. A positive correlation was observed between vitamin D and femoral BMD (r=0.239, p=0.025). However, no correlation was found between vitamin D and lumbar BMD.

**Conclusions:** Our study showed that vitamin D deficiency is common in hemodialysis patients. Several studies have demonstrated that low vitamin D level is a risk factor decrease of cortical BMD in the presumed healthy adult. A positive correlation between vitamin D and femoral BMD was observed. We suggested that correction of hypovitaminosis D in hemodialysis patients may increase femoral BMD and reduce risk of osteoporosis.

## Effects of diabetes and weight on bone markers in dialysis patients

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**Objective:** Osteoporosis is frequent in hemodialysis patient. The effect of diabetes on bone turnover markers in hemodialysis patients is unclear. The aim of this study was to determine the effect of diabetes on bone metabolic markers in regular hemodialysis (HD) patients.

**Methods:** A prospective study included 90 patients under hemodialysis (HD) therapy over a one year period. Blood samples were collected after at least 10h of fasting just prior to the HD session. Bone turnover markers including bone-specific alkaline phosphatase (BAP) and serum carboxy-terminal telopeptides of type 1 collagen (CTX) were measured. Both statistical and descriptive analyses were performed.

**Results:** In total, 90 patients were included in the study. The mean age was 53±14.7 years, with 64% men and 36% women. The body mass index was 25.8±4.7 kg/m<sup>2</sup>. The weight was 68.3±13.5 kg. Medical history of diabetes was noted in 38 cases. Diabetic nephropathy was found in 30 cases. The mean age of onset of HD therapy was 50.1±14.8 years. The mean age of onset of nephropathy was 48.4±15.1. The average rate of BAP was 26.8±27 ng/mL. Mean CTX values (2.49±1.51 ng/mL) were 6.25 times higher than the normal range. Negative correlations were found between weight and bone turnover markers: BAP (r=-0.265; p=0.015) and CTX (r=-0.382; p=0.000). Negative correlation was also observed between BMI and CTX (r=-0.347; p=0.001). Patients with history of diabetes had lower serum CTX levels (1.97 ng/mL) than patients without history of diabetes (2.87 ng/mL) (p=0.05). However, diabetes had no effect on BAP levels.

**Conclusions:** Our findings suggested that CTX levels are remarkably lower in hemodialysis patients with diabetes. This effect of diabetes on serum CTX was observed also in healthy subjects. Moreover, serum CTX correlated negatively with both BMI and weight.

## Propylthiouracil-induced vasculitis — a case report

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**Introduction:** Propylthiouracil is a drug commonly used to treat hyperthyroidism, and in a small percentage of cases is associated with adverse reactions like agranulocytosis, aplastic anemia, lupus-like syndrome and vasculitis. The diagnosis of drug-induced hypersensitivity vasculitis is mainly suggested by clinical findings and history of an offending drug, and usually its discontinuation is enough for resolution of the signs and symptoms. Sometimes, in the presence of more severe cases, immunosuppressive therapy is necessary.

**Case report:** The authors describe the case of a 45 year-old woman, with hyperthyroidism, anxiety disorder and fibromyalgia, undergoing treatment with diazepam, amitriptyline, cyclobenzaprine and propylthiouracil, who presented in the Emergency Room with cutaneous necrotic lesions with an erythematous halo, painful to touch, with about a 2 cm diameter, in both zygomatic areas and left ear, and progressive worsening, and also multiple painful erythematous papules in both legs. In the lab tests there was a mild leukopenia with 12% of atypical lymphocytes and an IgM monoclonal gammopathy. The patient was admitted in the ward with the presumed diagnosis of drug-induced vasculitis – propylthiouracil, and all the drugs discontinued. During the hospital stay there was a good evolution with remission of the cutaneous lesions, normalization of the blood panel, chemistry panel, viral serologies and autoimmune blood testing without changes.

The patient was discharged, and therapy with propylthiouracil suspended. She is currently followed in an Internal Medicine consult.

**Discussion:** The authors pretend to alert for the importance of considering drugs as a cause for cutaneous adverse reactions, and sometimes severe systemic manifestations. A careful clinical and pharmacological history is vital for a correct diagnosis and prompt therapy.

## Dermatomyositis and polymyositis: importance of the first signs of disease

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**Case report:** Female patient, 53 years old, irrelevant past clinical history, attends the emergency service with a 3 month history of a generalized rash with pruritus, predominantly in the trunk and upper limbs, extending to the face (close to the scalp), thighs and knees, associated with lip swelling, asthenia, muscle fatigue, difficulty elevating the arms above shoulder level, with impact in the daily activities. Physical examination showed a V shaped rash in the upper torso and a papular violaceous rash in the knees, lateral region of thighs, upper limbs, and nose. Blood test revealed a myoglobin of 312 ng/mL with no other abnormalities. After admission, the patient presented with mild heliotrope and muscle weakness of the pelvic and shoulder girdles. The initial study revealed increased enzymes of muscle lysis and positive anti-nuclear antibodies (reactive 1/160). With the clinical suspicion of dermatomyositis, the patient was submitted to a muscle biopsy (triceps muscle) that revealed atrophy of type II muscle fibres and perifascicular atrophy, necrosis, regeneration and hypertrophy of muscle cells. Skin biopsy showed: hyperkeratosis, acanthosis and epidermal atrophy, interface dermatitis, perivascular infiltrate of lymphocytes, dermal edema and deposit of mucin. Electromyography at rest revealed slight spontaneous activity (P waves and fibrillation) and in volunteer effort: motor units with myopathic features consistent with a framework of dermatomyositis<sup>1</sup>. Echocardiogram was normal. She underwent upper digestive endoscopy with no changes. Treatment with prednisolone was introduced, 1 mg/kg/day, with rapid improvement of skin lesions, muscle symptoms and normalization of the seric muscle enzyme. Functional rehabilitation was also started. The patient continues regular follow-up as an outpatient in the autoimmune diseases clinic.

**Discussion:** The correct interpretation of the clinical and analytical changes in an early stage enabled a fast diagnosis and a rapid initiation of therapy, minimizing the impact on the patients' general health and quality of life.

## Dermatomyositis in a patient with a renal mass

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**Introduction:** The objective of this case report is to demonstrate a case of dermatomyositis in a patient with a renal mass and

highlight the association of dermatomyositis with some specific malignancies. This diagnosis was confirmed after thorough medical workup in our clinic. Furthermore, all the other possible causes of dermatomyositis were ruled out.

**Case report:** 76 years old Caucasian male presented to the emergency department of our clinic complaining of progressive muscle weakness with fatigue and dysphagia. Symptoms had started approximately 1 month ago. Moreover he had a red flat rash on the face and erythema of the knuckles with a raised scaly eruption. Physical examination revealed muscle power 2/5 in upper limbs and 3/5 in lower limbs with no atrophy. Deep tendon reflexes were normal and the patient had difficulty getting up from a chair. Laboratory findings included CPK 9433 U/L, ESR 35 mm/h and ferritin 875 ng/ml. Magnetic resonance test revealed a mass in left kidney that had calcifications. The intravascular administration of a contrast agent showed rich vascularization. Muscle biopsy indicated that it was an inflammatory myopathy. Due to poor response in corticosteroids, cyclophosphamide and gamma globulin were also administered. After 5 days of treatment his muscle weakness was significantly improved. Finally, the mass on the left kidney was scheduled for surgical removal.

**Discussion:** The inflammatory myopathies, such as dermatomyositis, polymyositis and inclusion body myositis typify a large group of potentially treatable causes of muscle weakness. The prevalence of inflammatory myopathies is estimated at 1 in 100,000. Muscle weakness is often preceding the characteristic rash of dermatomyositis. Numerous studies have shown that, the incidence of malignancies appears to be higher in patients with dermatomyositis. Available experimental evidence regarding this association and the underlying mechanisms is limited. The most common associated malignancies are colon cancer, ovarian cancer, breast cancer, melanoma and non Hodgkin lymphoma. In clinical practice, older patients who are diagnosed with dermatomyositis, should be carefully examined and screened for potential associated malignancies.

## Evaluation of the efficacy of drug therapy of obesity in patients with knee osteoarthritis

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**Objectives:** Osteoarthritis (OA) and obesity – some global problems in the modern world, resulting in poor quality of life and disability. The aim of the study – to evaluate the impact of body weight loss on the clinical manifestations of knee OA and quality of life in women with knee OA and obesity, taking orlistat.

**Material and methods:** The study included 50 women, aged 45-65 years, with knee OA stage II-III by Kellgren-Lawrence and obesity (BMI > 30 kg/m<sup>2</sup>). Patients were randomized into 2 groups. Patients from group 1 (n=25) were taking orlistat 120 mg (1 capsule) 3 times a day during 6 months alongside with low calorie diet and exercise. Weight loss interventions in group

2 (n=25) were limited only to low calorie intake and physical exercise. The following parameters were monitored during 6 months on a monthly basis: anthropometric (BMI), functional index WOMAC and health related quality of life based on EQ-5D questionnaire.

**Results:** Weight loss in patients taking orlistat was 10,1% (mean 10,4 kg). Proportion of patients losing  $\geq 5\%$  of body mass from baseline was 44% (11 patients), 56% (14 patients) lost  $>10\%$  of body mass compared to baseline. In patients from group 2 mean weight loss was 1% (mean 1 kg). Pain intensity (WOMAC scale) in patients from group 1 reduced by 52%, which was significantly more ( $p < 0,05$ ), than in the group 2 demonstrating only 20% reduction. Similar trend was registered in functional impairment scale: repeated evaluations showed consistent improvement to a greater extent in group 1 as compared to group 2 ( $p < 0,05$ ) (by 51% and 18%, respectively). Summarized WOMAC index decreased in both groups after weight loss (by 51,5% and 19% respectively), but was statistically significantly lower in orlistat group ( $p = 0,006$ ). Besides weight loss was associated with improvement of knee OA, and thus, with the improvement of health related quality of life, more evident in group 1 with greater weight loss – EQ-5D (0,24) as compared to group 2 (0) ( $p < 0,001$ ).

**Conclusions:** Results of this study demonstrate that weight loss only by 10% in patients with obesity and knee OA thanks to orlistat resulted in significant improvement of clinical manifestations of knee OA: reduction of pain intensity and improvement of knee function. Weight loss and improvement of knee OA manifestations also favors the improvement of health related quality of life based on EQ-5D questionnaire, thus weight loss therapy should be considered in management of obese OA patients.

## Non traumatic hemarthrosis in patients on anticoagulant treatment

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**Objective:** To describe the characteristics of patients presenting with non traumatic hemarthrosis (NTH) linked to the use of anticoagulant therapy (AT).

**Methods:** Retrospective case series of patients discharged from the 12 de Octubre Hospital (Madrid) between January 1999 and July 2014 diagnosed upon discharge with “non traumatic hemarthrosis”. Only patients on AT were included. We registered several demographic variables, comorbidities (after I. Charlson), indication and type of AT, other drugs, clinical variables (location, treatment, evolution) and laboratory findings. Data was analyzed with SPSS v. 15.0 software.

**Results:** 8 cases were included. 78% were women, mean age of 76 years (range 62-91). They all presented with comorbidities (mean number 2.6; range 1-4) the most common being hypertension and heart failure (62.5 and 50%). 75% had previous joint pathology. All patients were in treatment with acenocoumarol. The most common cause

for receiving AT was atrial fibrillation (65%), followed by pulmonary thromboembolism and mechanical heart valves (12.5% each). None of the patients were taking antiplatelet agents. The hemarthros affected most commonly knees (50%) and shoulders (37.5%). 50% of the patients had acenocoumarol overdose (mean INR 4.9; range 1-11.9) and 50% had thrombopenia, which was mild in all cases ( $>100,000/\text{microL}$ ). 62.5% of patients had an abnormal renal function on admission (mean Cr 1.64 mg/dL; range 0.4-3.1). In 37.5% the joint was evacuated, in 50% conservative treatment was used. AT was restarted in 63%, mean time off the drug 4.5 days (0-20 days). All patients were discharged alive, being the mean hospital stay of 13.8 days. Complete functional recovery of the joint was reported in 71% of cases.

**Conclusions:** There is little data in literature on AT linked NTH, limited to small series of 3 cases max. We present a series of 8 cases that confirms the findings observed previously. They are old age patients with associated comorbidities, most of them with previous joint diseases, and receiving acenocoumarol for atrial fibrillation. The NTH often affects shoulders or knees, and can occur with INR within the therapeutic or supratherapeutic range. It may require arthrocentesis, although sometimes it is sufficient with watchful waiting. Mortality due to NHT is exceptional, but sometimes it involves loss of joint function and/or long hospital stays. In most patients AT can be restarted once the problem is solved.

## Vogt-Koyanagi-Harada syndrome: a case report

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**Introduction:** Vogt-Koyanagi-Harada syndrome is an inflammatory disease of unknown etiology with multisystemic manifestations, namely ophthalmic (bilateral diffuse uveitis, accompanied by an exudative retinal detachment), dermatologic, neurologic and auditory manifestations.

**Case report:** A 47 years old female, previously healthy, presented with headache, photophobia, bilateral red-eye and diminished visual acuity. The patient had been previously treated with antiallergic and anti-inflammatory medication without symptoms resolution and had done a brain MRI, orbit MRI and angio-MRI that only revealed changes consistent with an orbit inflammatory pseudo-tumor with multicompartimental and diffuse characteristics (myositis, cellulite and inflammation of the nerve sheath). Ophthalmology evaluation revealed bilateral papilitis and panuveitis (uveitis with positive Tyndall, retinal and disc edema and retinal detachment). Clinically without other relevant symptoms and signs, namely fever, neurological signs, oral ulcers or other cutaneous signs or hearing disturbances. The patient was then hospitalized with the diagnostic hypothesis of a panuveitis with a possible systemic cause (infectious or autoimmune disease). Laboratory investigations revealed an increased erythrocyte sedimentation rate and a positive HLA B51. Serological viral studies were negative. Cerebrospinal fluid (CSF) showed no pleocytosis or oligoclonal bands. CSF culture and viral PCR assays were

negative. Optical coherence tomography confirmed disc edema and glassy heterogeneity. Retinal macular architecture maintained. Fluorescein angiography revealed peri-foveal and marked peri-papillary diffusion, without signs of vasculitis. The patient was treated with topical corticosteroids and intravenous methylprednisolone (1 g/day for 5 days), which was then switched to oral prednisone (1.5 mg/kg/day), with good clinical response. She was referred to an Internal medicine and Ophthalmologic outpatient care for reevaluation.

**Discussion:** The authors present this case of incomplete Vogt-Koyanagi-Harada syndrome as it is an uncommon pathology which is important to recognize and treat early in the course of the disease to improve its prognosis. It also highlights the importance of a holistic view of the patient as well as an interdisciplinary collaboration for a better diagnosis and patient care.

### Effects of infliximab on pancreas tissue of methotrexate treatment rats

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**Objectives:** Tumor necrosis factor (TNF) plays an important role in the pathogenesis of immune-mediated inflammatory disease, such as rheumatoid arthritis (RA), ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis and psoriatic arthritis. Tumor necrosis factor (TNF)- $\alpha$  antagonists infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GOLI) and certolizumab pegol (CZP) have been widely used for the treatment of RA. TNF inhibition results in down-regulation of abnormal and progressive inflammatory processes, resulting in target organ damage.

**Methods:** Animal experiment: for the control group, only isotonic saline solution (an equal volume of methotrexate) was administered by intraperitoneal injection. For methotrexate (MTX) group, the animals received an intraperitoneal single dose injection of MTX (emthexate-s, 50 mg ampule) at a dose of 20 mg/kg and were sacrificed 5 days after MTX injection. Only one single dose of 7 mg/kg INF (remicate) was administered intraperitoneally to INF group. One single dose of 7 mg/kg INF was administered intraperitoneally to MTX+INF group. After 3 days a single dose of 20 mg/kg was administered intraperitoneally to MTX group. All animals were sacrificed 5 days after MTX injection. All groups were sacrificed under anesthesia with ketamine hydrochloride (ketalar, 50 mg/kg, intramuscularly). The liver tissues were then removed from the animals and immediately stored at -80C° until analysis.

**Results:** Pancreatic parenchyma and trabecular structure is quite properly observed. The amount of insulin and somatostatin have observed that as the healthy group. In our study pancreatic toxicity, acinar vacuolization and necrotic cells were observed in the Langerhans islets and acinar cells. We founded atypical Langerhans islets and amyloid deposits accumulation in the Langerhans islets. We show cell damage in the in the Langerhans islets and acinar cells with somatostatin, and insulin to decrease the cytoplasmic expression.

### Complex assessment of pain in knee osteoarthritis

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**Objectives:** Osteoarthritis (OA) considered to be a nociceptive model. Recent data suggest that central nervous system can take place in mechanisms of chronic pain (CP) in OA. J. Hochman examined 80 pts with knee OA. 34% pts used pain quality descriptions suggestive of neuropathic pain (NP). M. Imamura revealed generalized hyperalgesia in pt with OA even above deep structures. Some trials revealed decreased pressure pain thresholds (PPT) on spreading areas and temporal summation to repeated stimulation. We aimed to investigate the typical features of CP in knee OA with the help of rheumatological and neurological examination.

**Material and methods:** 89 women with knee OA (58 $\pm$ 5,4 years) and CP (<3 months) were examined. Duration of pain, its intensity (VAS), BMI and quality of life were taken into consideration. NP scales (PainDETECT and DN4) were used. Pts passed through neurological examination – no somatosensory deficit was found. But in sensitive sphere primary hyperalgesia (in the damaged knee) and also referred hyperalgesia (RH) in the intact region were revealed. Additionally PPT and temporal summation (wind-up) were assessed in 46 pts. Nociceptive pain was assessed with the by WOMAC and structural changes by X-ray and US. Examination of emotional disturbances by HADs was included.

**Results:** The pts were divided into two groups in accordance with presence of RH. 41,5% pt had RH, in 58,5% RH was absent. No significant differences between groups were seen in age, BMI, duration of pain, quality of life and the level of structural changes. The presence of RH correlated with intensity of pain, high level of NP scales, high level of WOMAC and depression. The presence of RH characterized by often described NP descriptors. All pt had statistically lower PPT in sites near the knee and also in intact site compared with 23 healthy controls. Wind-up data showed no differences between groups. But the intensity of pain on the first stimuli and sequential 10 stimuli was statistically higher compared with controls.

**Conclusions:** CP is a complex of mechanism of pain: nociceptive and central. Central mechanisms of pain are characterized with absence of neurological deficit and absence of correlation with the level of structural changes in joint. This type of pain is characterized with sensor NP phenomena, spreading of the region with pain – RH, and decreased PPT. The qualitative assessment of pain in knee OA give the opportunity for differentiate and pathogenic treatment.

### Acute adult Still disease in an African patient

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**Introduction:** Adult Still disease (ASD) is a rare disorder characterized by fever, rash and arthritis. The diagnosis is of exclusion and difficult due to the long list of differential diagnosis.

**Case report:** 34 year old black woman, from S. Tomé e Príncipe (Africa), presents with a six month history of fever and arthralgias, initially migratory that progressed to multiple symmetrical joint involvement. The patient also referred a skin rash on trunk and upper limbs and sore throat. In the outpatient clinic infectious disease was excluded the autoimmune disease screening was negative (ANA, anti-CCP, RF). Because of the persistent high fevers and debilitating joint symptoms, she was then admitted to our Internal Medicine Department. The initial exam revealed signs of arthritis on both wrists and shoulders, maculo-papular rash, which worsened with fever or after hot water bath. The lab results showed anemia 10,7 g/dL (MCV 86 fL), leukocytosis 12 900/uL, neutrophils 73,7%, thrombocytopenia 111 000/uL, ESR 47 mm/h, CRP 14,8 mg/dL ferritin of 1600 (Ref. 291) (glycosylated 6%), tryglicerides 241 mg/dL and fibrinogen 292 mg/dL. Infectious causes were excluded. Adult Still disease was admitted and prednisolone 40 mg/day was started with good clinical and analytical response. She was discharged completely asymptomatic. Two weeks later there was a recurrence of the condition, due to irregular medication compliance. She then started 60 mg of prednisolone with resolution of all symptoms. The diagnosis of ASD was made based on Yamaguchi criteria (3 major and 3 minor criteria).

**Discussion:** Adult's Still disease is very uncommon (0,16 cases per 100 000 people). It is important to exclude other rheumatologic diseases in order to make an accurate diagnosis. Not all patients respond in the same way to immunosuppressive therapy, for an optimal response to treatment it is important to assess the pattern of the disease.

## Do we detect more pulmonary arterial hypertension in systemic sclerosis with DETECT algorithm?

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**Objective:** To compare the number of patients identified in the screening of pulmonary arterial hypertension (PAH)-systemic sclerosis (SSc) by the new DETECT algorithm (a multivariable two-step decision tree) with the current European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines (based mainly in echocardiographic parameters).

**Methods:** We applied the current ESC/ERC guidelines for detection of PAH and the DETECT algorithm to all SSc patients followed in our tertiary hospital. We excluded those with previous PAH, interstitial lung disease (ILD), renal failure or treatment with inhibitors of endothelin and those without echocardiography or sufficient parameters to apply the DETECT.

**Results:** We followed 30 SSc-patients in our hospital but 2 were excluded for previous PAH, 2 for ILD, 1 for treatment with bosentan for digital ulcers, 1 for renal impairment, 4 for insufficient variables to apply the DETECT and 2 for

not having echocardiogram. Thus, 18 patients entered the study (mean age of 56.9±13.6 years; 13 limited SSc [75%], 3 SSc sine scleroderma [15%] and 2 diffuse SSc [10%], mean disease duration of 9±6.6 years; 2 with dyspnea [11%]). When we applied the current ESC/ERC guidelines no patients were identified as probable or possible-HAP by the echocardiography (6 patients [44%] without tricuspid regurgitation included). When we applied the DETECT, the average score obtained in the first step of the algorithm was 311.3±12.6 and echocardiography were recommended in 16 patients (80%). In the second step, 2 patients were positive in the screening and right heart catheterization (RHC) was recommended for confirmation of PAH. Patient 1 was 69 years old, limited SSc with symptoms onset in 1999, current class II dyspnea, without telangiectasias or anti-centromere antibody (ACA). Diffusing capacity for carbon monoxide (DLCO) was 73.4% predicted and the right atrium area (RAA) was normal, with tricuspid regurgitate jet velocity (TRV) of 2.6 m/s. Patient 2 was 64 years old, limited-SSc with onset in 2011. She had telangiectasias but no dyspnea. ACA were positive. DLCO was 82% predicted and the RAA was normal, with TRV of 2.4 m/s. These patients have not yet done a RHC to confirm HAP, but are closely follow-up in our centre.

**Conclusions:** The new DETECT algorithm selected more patients to RHC to confirm PAH than current ESC/ERC guidelines. However, in our study, PAH could not be confirmed because patients have not yet done a RHC.

## Absence of symptomatic pulmonary arterial hypertension in patients with mixed connective tissue disease in northwestern Spain after a long follow-up period

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**Objectives:** Mixed connective tissue disease (MCTD) is a rare entity characterized by high titres of anti-RNP antibodies and selected clinical features of other connective tissue diseases (CTD): systemic sclerosis (SSc), rheumatoid arthritis, polymyositis and systemic lupus erythematosus. Patients with MCTD were classically considered in a high risk for pulmonary arterial hypertension (PAH), one of the most frequent causes of death in this disease. However, the true prevalence of PAH in MCTD is still unknown, ranging between 3.4% and 23.4% in different series. Hence, guidelines for the screening of PAH in CTD have not been able to establish recommendations with sufficient evidence level. Our aim is to determine the cumulative incidence of symptomatic PAH in patients with MCTD in northwestern Spain after a long follow-up period.

**Methods:** We reviewed the medical records of patients with at least one positive antiRNP determination in high titre between Jan 2006 and Dec 2012 in EOXI Vigo (a tertiary hospital with an area of 370,000 habitants). Those patients who met Kanh's or Alarcon-Segovia's classification criteria for MCTD were selected.



Clinical, analytical, capillaroscopy, echocardiography and right heart catheterization (RHC) data were collected. PAH was defined as mPAP >25 mmHg on RHC and likely-PAH as PASP >30 mmHg or dilation of the right cavities on echocardiogram. Follow-up time period was considered as the time between the first clinical assessment for suspected-CTD and the last evaluation before Dec 2014.

**Results:** 89 patients had antiRNP in high titres, but only 16 (18%) met criteria for MCTD, mean age 53±12.9 years, 15 women, mean follow-up of 11.8±8.5 years. All of them had Raynaud's phenomenon and 5 (31%) also met criteria for SSs. Only 1 patient reported dyspnea during follow-up (MCTD with interstitial lung disease). None of them showed other symptoms or signs of PAH. 9 patients (56%) had at least 1 capillaroscopy: 1 scleroderma pattern, 7 nonspecific pattern and 1 normal pattern. 7 patients (43%) had at least one echocardiogram, all with normal right cavities, normal or undetectable PASP; in any case RHC was made. 2 patients (13%) died during follow-up, for reasons not related to MCTD.

**Conclusion:** No patients with MCTD in northwestern Spain had symptomatic PAH after a mean follow-up longer than 10 years.

## A case of reactive arthritis

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**Case report:** A 44 years old male, previously autonomous in his daily life activities. No previously known pathological conditions or usual medication. No known food or drug allergies. The patient sought medical care due to the development of inflammatory signs in several joints, with 3 days of evolution. He described pain, swelling and heat that affected the extensor surface of the right foot, the left ankle and the left shoulder. Before these complaints appeared, the patient also detailed lumbar and hip joint pain of inflammatory characteristics, with 15 days of prior evolution. He denied every other complaint asked, including fever, other affected joints and the presence of additional inflammatory signs on other locations. Upon further questioning, it was discovered that before the initial onset of hip joint pain, the patient did have other relevant signs and symptoms. He presented a urethral discharge, dysuria and bilateral red eye, all of them self limited. The joint pain started shortly after. At physical examination, inflammatory signs were apparent on the previously mentioned locations. Swelling, heat and pain were easily perceived. Left hip joint passive active and mobilization elicited pain, as it did for the left shoulder, but there were no other inflammatory signs in these particular locations. Patrick sign was absent and Schober's test was normal. No other abnormalities were noted. Routine blood work only revealed increased inflammatory markers. The patient was admitted under the suspicion of a reactive arthritis (previously named Reiter's syndrome). During the hospital stay, several other exams were conducted. Further serologic testing revealed positive immunoglobulin G and M (borderline) for Chlamydia pneumoniae. No other infectious agents were detected. Autoimmunity was also negative. Imaging studies ruled out

joint destruction and osteomyelitis, only showing a probable left sacroiliitis. The patient was treated with doxycyclin for 7 days, and was started on non-steroidal anti-inflammatory drugs. Some improvement was obtained, but in the end it was not enough to control the inflammation, and particularly the pain. Oral systemic corticosteroids were introduced, with fairly good results, improving the pain control and overall reducing the inflammation of the joints. After significant clinical and symptomatic improvement, the patient was discharged, under referral to posterior outpatient follow-up.

## Application of the 1997 American College of Rheumatology revised criteria and 2012 Systemic Lupus International Collaborating Clinics classification criteria in a Spanish Systemic Lupus Erythematosus Register

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**Objectives:** The present study was undertaken to apply the SLICC-12 criteria and compare them with ACR-97 in an adult European study population. ACR-97 and SLICC-12 criteria were applied to individuals with a fair SLE suspicion, referred to internal medicine specialists at our unit.

**Methods:** A descriptive, retrospective study was conducted. We examined the medical records and ancillary files of adult patients who were coded as "suspected SLE" and were admitted at our center for outpatient care from February 2014 to February 2015. We evaluated epidemiological, clinical and analytical variables. We compared the diagnosis of SLE with the ACR and the SLICC classification criteria. A descriptive statistical analysis was performed.

**Results:** 51 medical charts coded as "suspected SLE" were found and 10 of them were excluded for having a lot of missing data that compromise the analysis development. Hence, the medical records of 41 subjects were included in the study. 83% were females and 17% males, with a median age of 59 years old. 22 patients were classified as SLE (53.7%) based on ACR-97 criteria and 19 patients (46.3%) did not meet enough criteria and were classified as not having SLE. However, based on SLICC-12 classification criteria, 26 of the subjects (63.4%) would be classified as SLE, because they met 4 criteria (including one immunologic criterion) and 15 of them did not meet the criteria (36.6%). There were no patients with lupus nephritis proven by biopsy at the moment of diagnosis.

**Conclusions:** All patients who met the ACR-97 classification criteria met the SLICC-12 criteria as well. SLICC-12 criteria classified a 9.8% more of patients with SLE. Therefore, it is more sensible. These results are congruent with the literature. So to accomplish increased sensitivity and specificity figures, a combination of criteria sets for clinical SLE studies should be considered. Any patients had lupus nephritis confirmed by biopsy with ANAs and anti-DNA being that this technique is not available in our hospital.

## The method of differential diagnosis of edema syndrome in patients with systemic lupus erythematosus

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**Objectives:** It is known that the edema syndrome in patients with systemic lupus erythematosus can be caused by both renal and cardiac damage. The purpose of our research: to assess the usefulness of the N-terminal fragment of brain natriuretic peptide (NT-proBNP) in the differential diagnosis of edema syndrome in patients with systemic lupus erythematosus.

**Material and methods:** We examined 80 patients with systemic lupus erythematosus – 74 women (92,5%) and 6 men (7,5%), the average age –  $40,7 \pm 11,9$  years, duration of the disease –  $8,9 \pm 7,5$  years. All participants conducted ECG, echocardiography with Doppler, staging and functional class of heart failure. We determined the level of NT-proBNP for all patients by enzyme immunoassay. NT-proBNP values more than 125 fmol/ml allow to diagnose a heart failure with a high degree.

**Results:** 16 patients with systemic lupus erythematosus (20%) had edema syndrome. 8 patients of them had only renal damage: in 5 cases – rapidly progressive lupus nephritis, in 3 – nephritis with nephrotic syndrome. All of these patients had normal value of NT-proBNP ( $40,1 \pm 34,4$  fmol/ml). 4 patients with heart failure and without renal damage had an increased value of NT-proBNP ( $283,6 \pm 79,3$  fmol/ml). Another 4 patients with a renal damage and heart failure had an increased value of NT-proBNP: 2 of these patients had nephrotic syndrome and heart failure combined with increased value of NT-proBNP ( $867,5$  fmol/ml and  $310,5$  fmol/ml). Thus, edema syndrome in these patients was of a mixed origin – cardiac and renal. Two other patients had a combination of heart failure and nephritis with minimal urinary syndrome. They had an increased value of NT-proBNP ( $415,5$  fmol/ml and  $218,5$  fmol/ml). We consider that in this case, edema syndrome was due to heart disease and heart failure.

**Conclusions:** Thus, the determination of NT-proBNP may be used for differential diagnosis of edema syndrome in patients with systemic lupus erythematosus. Increase of NT-proBNP can be a reliable criterion for heart failure in patients with systemic lupus erythematosus.

## Others

### The relationship between serious illness risk and serum lactate levels in intensive care unit patients

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**Objectives:** Patients with life-threatening disorders are hospitalized in the intensive care unit. Sepsis, acute renal failure, gastrointestinal bleeding and pneumonia are the most common types of serious diseases. Early diagnosis and treatment of these diseases can reduce the high rates of morbidity and mortality in intensive care units. There are some laboratory parameters currently used for early diagnosis. Serum lactate level is one of these parameters. In particular, high level of lactate in patients with sepsis is an important indicator of disease severity. In the current study, we investigated the relationship between lactate levels and acute renal failure, sepsis, GIS bleeding, pneumonia and other diseases.

**Methods:** Overall 229 intensive care unit patients meeting the inclusion criteria were enrolled into the study. Among these 27.1% had sepsis, 52.4% ARF, 10.5% gastrointestinal bleeding, 21.8% pneumonia and 41% were diagnosed with other diseases. Some patients had more than one diagnosis. Mortality rate was around 50%.

**Results:** Lactate levels in patients who died were significantly higher than those in healed patients ( $p < 0,05$ ). On admission, mean lactate concentration were significantly higher in patients with sepsis than any other diagnosis ( $p < 0,05$ ). On mid-treatment and discharge, the average values of lactate in sepsis were higher, but not significant, as compared with others diagnoses ( $p > 0,05$ ). Patients with an increased lactate concentration displayed a 1.49-fold increased risk of developing sepsis ( $p < 0,05$ ). Mid- lactate concentration was significantly higher in patients with ARF and GIS bleeding as compared with other diagnoses ( $p < 0,05$ ). Length of hospital was significantly shorter in patients with gastrointestinal bleeding than in patients with any other diagnosis ( $p < 0,05$ ). Average lactate levels in patients with pneumonia were found to be similar with other patients. Mean length of stay was significantly longer in patients with pneumonia ( $p < 0,05$ ).

**Conclusion:** Our results suggest that lactate concentration not only is associated with mortality, but also with clinical progression in critically ill patients diagnosed with sepsis or any similar severe disorder.

### State of ventricular diastolic function and cerebral blood flow in patients with chronic obstructive pulmonary disease amid the pathology of cardiovascular system

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**Objectives:** To examine the cardiorespiratory system, cerebral hemodynamics, to evaluate the nature and frequency of arrhythmias in patients with the chronic obstructive lung disease (COPD) secondary to the chronic heart failure (CHF).

**Material and methods:** The study involved 103 patients with COPD, the average age of  $56,8 \pm 5,7$  years affected by CHF. The assessment of the frequency and nature of arrhythmias of all patients was based on the results of daily monitoring of ECG, echocardiography with estimation of ventricular diastolic function (echocardiography), external respiration function (ERF), cerebral hemodynamics due to the data of ultrasound (US) of the head and neck vessels as well as the functional class of CHF on the scale of the clinical state assessment (CSAS).

**Results:** Clinically, the majority of the observed patients had CHF of functional class II. The average score of CSAS by the examined patients was  $5,7 \pm 1,3$  points, which were corresponding to functional class II of heart failure. The evaluation of ERF revealed a significant reduction in forced vital capacity (FVC) and Tiffno index (FEV1/FVC) whose values made up  $56,8 \pm 2,3\%$  and  $67,6 \pm 2,6\%$ , respectively. When analyzing the nature and frequency of arrhythmias, the average heart rate was  $73,0 \pm 1,6$  per minute, the daily number of supraventricular arrhythmias  $447,4 \pm 177,6$ , the daily number of PVCs  $362,9 \pm 153,4$ . According to the results of echocardiography the revealed ventricular diastolic dysfunction showed itself in the duration reduction of the phase of isovolumic relaxation of the left and right ventricles, the value of which were  $69,2 \pm 5,4$  ms and  $67,4 \pm 4,3$  ms, respectively. Analyzing the ultrasound of head and neck vessels showed a reduction the blood flow velocity in the left and right middle cerebral and the common carotid artery (MCA, CCA) were  $82,7 \pm 3,3/78,4 \pm 2,7$  cm/s and  $59,0 \pm 4,4/62 \pm 3,5$  cm/s, respectively. Correlation analysis showed a significant positive correlation between the frequency of supraventricular arrhythmias and Tiffno index ( $0.52$ ,  $p < 0.05$ ), supraventricular arrhythmias with the CSAS ( $0.65$ ,  $p < 0.05$ ), isovolumetric relaxation of the left ventricle and the speed rates of MCA and CCA ( $0.51$  and  $0.58$ ,  $p < 0.05$ ).

**Conclusion:** Patients with the chronic obstructive lung disease secondary to the chronic heart failure revealed diastolic dysfunction of both ventricles, disturbance of intracerebral hemodynamics and frequent supraventricular arrhythmias.

### Comparison of arterial blood pressure measurement with oscillometric and Doppler ultrasonography for ankle-brachial index

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**Objectives:** Peripheral artery disease (PAD) is associated with atherosclerosis and increased risk of cardiovascular events and

mortality. The ankle-brachial index (ABI) measured by Doppler ultrasound is a screening test for the diagnosis of PAD, but this method is time consuming and requires expert. We investigated the relationship between the ABI values calculated with Doppler ultrasound and oscillometric blood pressure measurement in healthy subjects.

**Material and methods:** A total of 53 healthy subjects (25 male, 28 female) were enrolled to the study. All subjects four extremities Doppler ultrasound and oscillometric blood pressure examined and ABI were calculated. All parameters were correlated statistically.

**Results:** The average ages of all subjects  $43.2 \pm 6.8$  years. The average of all subjects Doppler ultrasound and oscillometric blood pressure were right brachial ( $109.3 \pm 13.1$ ,  $115.7 \pm 12.4$  mmHg), left brachial ( $108.7 \pm 13.9$ ,  $115.7 \pm 14.1$  mmHg), right tibialis anterior ( $117.5 \pm 19.7$ ,  $128.3 \pm 16.8$  mmHg), and posterior ( $122.2 \pm 19.7$ ,  $126.7 \pm 19.7$  mmHg), left tibialis anterior ( $116.5 \pm 19.0$ ,  $128.8 \pm 18.2$  mmHg) and posterior ( $119.2 \pm 18.9$ ,  $127.5 \pm 16.9$  mmHg) respectively. There was a significant correlation between these measurements ( $r=0.774$ ,  $r=0.891$ ,  $r=0.813$ ,  $r=0.858$ ,  $r=0.780$ ,  $r=0.844$ ,  $p<0.001$ ) respectively. There was a significant correlation between Doppler and oscillometric ABI ( $r=0.333$ ,  $p=0.015$ ).

**Conclusion:** This oscillometric devices are seem useful, simple and timesaving as an ABI screening method.

## Parotid gland swelling – a case report

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**Introduction:** There are various causes of bilateral parotid gland enlargement, some of the possible causes including lymphoma, HIV disease, mumps, sarcoidosis, Sjogren's syndrome. The achievement of differential diagnosis leads to a correct and quick diagnosis and can prevent the complications due to delay of the specific treatment.

**Case report:** We present the case of a 66 years old male patient reported to the Internal Medicine Clinic complaining of polyarthralgia, cough, mucopurulent expectoration, dry mouth and parotid hypertrophy (the onset of symptoms – about 4 weeks ago). On clinical examination: sweating, dry eye and mouth, laterocervical lymph, global diminished lung vesicular murmur, crackles lung sounds, nodular erythematous eruption on pretibial surface of lower extremity. Routine hematological investigations, investigation for HIV tests, mumps, Coxsackie and Epstein-Barr virus were done. Were requested ophthalmologic and pulmonology consultation. There were performed CXR, spirometry, chest tomography, bronchoscopy, abdominal ultrasound and ultrasound of the parotid glands. The bronchoalveolar lavage brought into discussion sarcoidosis and Sjogren's syndrome. Diagnosis was decided by the parotid gland biopsy, histopathological aspect being conclusive for lymphoproliferative disorder (diffuse large B-cell lymphoma secondary to extranodal marginal zone B-cell lymphoma (MALT)).

**Discussion:** As shown in the medical literature, in the early stages the non-Hodgkin lymphoma of the parotid gland has an excellent prognosis and minimal morbidity. The particularity of the case emerges from the lack of the specificity of symptoms, which can leads to the delay in establishing the diagnosis and specific treatment.

## Ultrastructural hallmarks of cell death in diabetic nephropathy

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**Objectives:** According to recent data from the World Health Organization, 9% of the adult global population was affected by diabetes mellitus (DM) in 2014. It is known that approximately a quarter of diabetic patients develop renal affection, DM being among the leading causes of kidney failure. Moreover, those diabetic patients who develop renal impairment have a mortality rate of about 40 times higher than those without proteinuria. From ultrastructural point of view, DM causes changes triggered by partially clarified intimate cellular mechanisms. As the ways conducting kidney cell depletion are still a debated issue, our aim was to study renal tissue damages specific to diabetic nephropathy in terms of an immunohistochemical research carried out on human renal tissue.

**Material and methods:** The data were selected from medical records of patients who died between 2007-2014 in Colentina University Hospital. The study was conducted on human autopsy samples; the research group comprises 43 renal tissue samples of patients with clinical or pathological confirmation of diabetes or prediabetes, whereas the control group contains 6 renal tissue samples of patients without diabetes or renal impairment. Immunohistochemistry on paraffin-embedded samples was performed and used antibodies for the anti-apoptotic protein Bcl2, APAF (apoptotic protease activating factor), CD95 (Fas receptor/apoptosis antigen 1), caspase-1 and caspase-9.

**Results:** Our research results show that the studied molecules are reliable markers of cell death in human renal tissue, confirming the loss of balance between cell death and cell proliferation in favor of cell death in diabetic renal disease and also identifying proofs for mechanisms of apoptotic cell death in the renal structures in diabetic human kidney samples.

**Conclusions:** Cell death mechanisms depend on the cellular context and the death-inducing stimuli. The involvement of specific death molecules may be dependent on a specific tissue region. The role of the caspases may differ in pathologic or normal states.

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## Comparison of cases of pulmonary hypertension diagnosed in a specialized medical office: group 1 and group 4

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**Objective:** Comparison of the main clinical cases of pulmonary hypertension data on group 1 and 4 diagnosed in a monographic medical office.

**Methods:** Prospective descriptive analysis of clinical parameters in patients with pulmonary hypertension of group 1 and 4. For analysis we have used the statistical package SPSS 20.0.

**Results:** We have analyzed a number total of 19 patients from group 1 (average age 56.5 years, 31-84) and 13 in the group 4 (average age 71.2 years, 23-83). There is a clear predominance of women in both groups (94.7% and 76.9%). There is a clear prevalence of cardiovascular antecedents of group 4 (hypertension 76%, atrial fibrillation 30.7% and heart failure 46.1% of cases). In both groups the majority of the patients belong to a functional class III (52.6% group 1 and 53.8% group 4) and the initial symptom and main reason for inquiry was breathlessness followed the discovery in echocardiography. The average PSAP in group 1 was far superior to the one presented in group 4 (78.4 mmHg and 58.2 mmHg, respectively). In terms of cardiac catheterization, a 68.3% of group 1 underwent the procedure (PAPm 52.8 mmHg and PcP 13.6 mmHg) and 69.2% of group 4 (PAPm 38.7 mmHg and PcP 18.1 mmHg). The reasons for the non-realization of cardiac catheterization were mainly comorbidities. In terms of treatment, in group 1 63.2% received anticoagulant therapy while in group 4 were all anticoagulated. On 73.7% of group 1 received diuretic therapy while group 4 was 76.9%. On 30.8% of group 1 received treatment with prostanoids (20.3% inhaled iloprost and 10.5% epoprosterenol IV) and none at the group 4. Endothelin antagonists were equally used in group 1 (47.4% bosentan) and 4 (38.5 bosentan and 7.7 ambrisentan). The use of PDE5i in group 1 was higher (21.1% sildenafil) than in group 4 (7.7% tadalafil). In terms of mortality, this was substantially higher in group 1 (38.8%) with in relation to group 4 (15.4%).

**Conclusions:** Pulmonary hypertension is a little known entity, and not very well treated. There are specific treatments of utility in certain cases that increase the capacity and tolerance to daily activities. Clinical characteristics of both groups are very similar, emphasizing the age at diagnosis in patients of group 1. In our series of cases there is a significant number of cases of group 1 and 4, many of them in specific treatment with adequate tolerance and activity. Mortality in both groups is high, being considerably higher in group 1. This makes necessary the early identification and specific treatment with intent to modify as much as possible the evolution of the disease.

## Pulmonary hypertension in a monographic medical office of a secondary level hospital

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**Objective:** Analyzing patients' clinical data referred to our monographic medical offices of pulmonary hypertension since the beginning of the same until May 2015.

**Methods:** Prospective descriptive analysis of the clinical features of patients with a presumptive diagnosis attending monographic inquiry of pulmonary hypertension. For statistical analysis we used the software package SPSS 20.0.

**Results:** The total number of patients studied was 91, of which a total of 14 ruled out the presence of pulmonary hypertension. In our series, we have observed a larger number of patients belonging to group 1 with a 28.4% (19 patients) of cases, followed by the group 2 with a 23.8% (16), the groups 3 and 4 with 13.2% each (13); and 5 with 8 patients (8.8%). In 10 patients in the study when they were in studio. The middle ages turned out to be 67 years old and there was a higher prevalence among women (81.3% or 74 women). We have observed that most of the patients presented a functional class II (44%) and III (46.2%) at the beginning of the study. The main reason for consultation, with almost 50% of the cases, was the echocardiographic finding, followed by dyspnea in 41 patients (45.1%) and edema in 5 (5.5%) and the most frequent symptom in all groups at the beginning was breathlessness (in 94.3% of the cases). In echocardiogram we obtained an average PAPs of 63.4 mmHg and 37.5% out of patients who underwent such proof presented pericardial effusion. 39 patients out of total, were performed a right heart catheterization with a PAPm of 42.9 mmHg, a PCP of 17.9 mmHg and a 11.9 UW. More than 60% of the patients were anticoagulated and under treatment with diuretics. In addition, a 22.7% was in treatment with inhaled iloprost, 9% with epoprostenol, 63.4% with bosentan, 9% with ambrisentan, 18.8% with sildenafil and 4.5% with tadalafil. 27.2% out of total was in treatment with combination therapy.

**Conclusions:** Pulmonary hypertension is a rare pathology and underestimated many times, it is necessary to increase awareness of this entity to better management and specific treatment in selected cases. The clinic of debut is difficult to evaluate since in many occasions the information is the appearance of difficulty in breathing that is very unspecific but to bear in mind in certain populations. In our series of cases there is a greater number of cases of pulmonary hypertension in group 1, which is not in accordance with the studies where the predominant group is 2. This may be due to the confluence of the patients with diagnosis of pulmonary hypertension in our medical offices that are derived from other specialties without a clear diagnosis of group. It is necessary to establish strategies for the identification of patients with pulmonary hypertension and possibilities of specific treatment, since it is a little-known entity and with effective treatment in some cases.

## Intestinal microbiocenosis in patients with different phenotypes agammaglobulinemia

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**Objectives:** Primary immunodeficiency with a- and hypogammaglobulinemia are infectious and autoimmune clinical phenotypes. The purpose was to study of intestine microbiota condition at the patients with different phenotypes of a- and hypogammaglobulinemia.

**Methods:** The intestine microbiota condition was estimated by the excrement bacteriological inoculation, the respiratory hydrogen test with lactulose, by the maintenance definition of the short chain fat acids AI in excrements using GLC, and by a method of cytofluorometry PBMC was phenotyped. 11 patients were examined, 4 – with autoimmune (AP), 7 – with an infectious phenotype (IP) of the AP.

**Results:** It was revealed more significant increase of opportunistic pathogenic water producing microflora at the patients with AP:  $143.8 \pm 53.4$  ppt, at the patients with IP –  $131.8 \pm 46.5$  ppt, more significant decrease in quantity of bifido- and lacto bacterium was established at the patients with IP on the average group –  $2.1 \times 10 \pm 1$  Ig. During GLC in the AP AI was lowered in the area of distinctly negative values (IP it was lowered to the direction of weakly negative ones). At the AP case the increase of cytotoxic cells number was not accompanied by the reduction CD4+ lymphocytes: IRI- $1.2 \pm 0.1$ , unlike the patients with IP- $0.6 \pm 0.1$ . TLR4 expression strengthening at the patients with AP ( $63 \pm 8\%$ ) in comparison with the norm ( $20 \pm 4$ ) and the patients with IP ( $21 \pm 3$ ).

**Conclusion:** The noted distinctive features can become the basis for the forecast of a course and the differentiated introduction of additional therapeutic means of treatment of primary a- and hypogammaglobulinemia.

## Prescription and adequate monitoring of intravenous fluid therapy in a tertiary hospital

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**Objectives:** The rational use of intravenous fluid therapy (IFT) is important in both treating and preventing iatrogeny in admitted patients. By analyzing renal function, blood ionogram, clinical signs of fluid overload and the monitoring of hydric balance/urine output, we aimed at characterizing and evaluating the correct use of IFT in the infirmaries of our hospital.

**Methods:** We selected a day in June 2015 to organize a cross sectional study in which data was collected by means of our computerized information systems in respect to patients undergoing IFT in various medical and surgical wards. The following parameters were analyzed: patient demographics, fluid being administered, creatinine levels, arterial pressure, blood ionogram values, presence of pulmonary/peripheral edema and hydric balance/urine output monitoring.

**Results:** From a total of 187 patients analyzed 92 (51,3%) were undergoing IFT. The volume administered ranged from 500 to 3000 ml per day. The most frequently used was sodium chloride at 0,9% (52%) followed by polyelectrolyte solution (41%). The chosen fluids had glucose (at 5%) in 42% of cases. Two different fluids were use simultaneously in 11% of patients. All but 3 patients had a recent blood ion evaluation. Of the 7 patients who had elevated sodium values, one was being administered sodium chloride 0,9%. Those who presented reduced sodium level where either being administered saline or polyelectrolyte solution. In regard to potassium, the data revealed use of polyelectrolyte solution in 4 of the 6 patients with elevated levels and saline or 5% dextrose in 5 of 6 who presented reduced levels, although potassium chloride was added in most. Acute kidney failure was observed in 20% of patients undergoing IFT. Urine output and/or hydric balance was monitored in 22,8%, edema was observed in 13% and hypertension in 16%. Oral administration of food and water was possible in 88% of patients and only 8,7% presented vomiting or diarrhea.

**Conclusions:** Despite the limitations of a cross sectional study, we observed that a large percentage of patients admitted to our medical or surgical wards undergo IFT. The level of fluid overload vigilance and the adequacy of the chosen fluid are lacking and some if not most patients should undergo hydration per os, thus preventing fluid overload as well as iatrogeny. To prevent this, we need to implement stronger guidelines and protocols, focusing on both the correct initiation and the continuous monitoring necessary for an adequate and safe IFT.

## Pyogenic hepatic abscess in the caudate lobe

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**Introduction:** Pyogenic hepatic abscesses are infrequent (2.3 cases per 100,000 populations, occurring most in the fourth to sixth decade of life, with male predominance), but challenging conditions since the presenting symptoms are atypical, differential diagnosis manifold and there is no common consensus on therapeutic approaches. Etiology: the main cause is bacterial invasion, mostly from the portal and biliary tracts. *E. coli*, Streptococcal, *Pseudomonas* species or mixed bacterial and fungal infections are predominant in Western countries; *Klebsiella pneumoniae* is common in East Asia. Despite many advances, the mortality remains high (31-50%). Detained treatment invariably ends fatal, especially in case of an abscess rupture. Despite the fact that hepatic abscesses were known since Hippocrates era, the drainage options have only been developed in the last century. Management: the therapy includes antibiotics and catheter drainage under the guidance of ultrasonography or computed tomography. New approaches as percutaneous needle aspiration under sonographic guidance have been described as safe, effective, and low-cost procedures. Laparoscopic or open surgical drainages are to be considered when the abscess is not amenable to percutaneous approach. Caudate lobe abscesses: PLAs in the caudate lobe are extremely rare, but exquisitely

challenging because they can submerge as a silent infection until they rupture or leak into the lesser sac. Most patients suffer from epigastric pain until it exacerbates and causes septic shock. Literature search with MEDLINE, Cochrane, EBM and Google research machine revealed solely 1 methodic paper on EUS use and 5 case reports. Management of caudate lobe PLAs is not easy because of their anatomic location (proximity to the stomach, embedded in hepatic parenchyme and with its own independent arterial and venous supply) and limited to either strictly conservative or more aggressive, surgical ways. Any minimally or invasive approach is associated with significant risks. Drainages and aspirations are mostly unsuccessful. Surgical debridement is therefore considered earlier than in case of otherwise located abscesses. However, they are more frequently accompanied by hemorrhage, peritonitis, fistula formation etc. **Conclusions:** Despite the unspecific findings in the clinical and laboratory investigation, a clinician should consider a PLA as a differential diagnosis, with or without presenting symptoms (anorexia, fever, nausea and abdominal pain, etc.), particularly if hypoechoic hepatic mass has been found on radiological imaging. Due to the rarity of PLAs, optimal diagnostics and management are still elusive, basics for guidelines and classifications are vague and the literature regarding this topic is insufficient.

### **Peculiarities of cardiorenal syndrome in patients with chronic obstructive pulmonary disease**

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**Objective:** To study the peculiarities of cardiorenal syndrome in patients with chronic obstructive pulmonary disease (COPD).

**Material and methods:** 300 patients (76,3% men, mean age 68,5±9,9 years; 23.6% of women, average age 66±10,1 years) with an established diagnosis of COPD I-IV. Glomerular filtration rate (GFR) was calculated by CKD-EPI. The data are presented as M±SD.

**Results:** The initial degree of GFR reduction (89-60 ml/min/1.73m<sup>2</sup>) was marked in 37.3% of the patients, moderate GFR decrease (59-45 ml/min/1.73m<sup>2</sup>) was identified in 26.7% of patients. Significant GFR reduction (44-30 ml/min/1.73m<sup>2</sup>) was observed in 3.3% of patients. Only 4.3% of the patients had the diagnosis of "CKD of I-III degree" proved earlier, which is almost 7 times as low as that of the data received. The frequency of the GFR decrease was significantly increasing with the age both in men (p<0.05) and women (p<0.05). End-systolic dimensions of the left ventricle in group 1 was significantly lower as compared to group 3 (34,1±0.3 mm and 36.5±0.2 mm, respectively; p<0.05). Interventricular septum (IVST) in group 3 was significantly higher than that in group 1 and was 13.6±0.4 mm as compared with 11.7±0.2 mm (p<0.05). IVST in group 3 was 13,3±0,2 mm as compared to 11.4±0.3 mm in group 1, (p<0.05). Negative correlation of medium strength between the thickness of the posterior wall (PWT) and GFR (r=-0,286, p<0.05) was established. End-diastolic and systolic volumes of left ventricle in patients of

group 2 (138,9±5,7 ml of 52.5±3,4 ml) and group 3 (148.6±7,9 ml of 54.1±3.8 ml) were significantly higher than in group 1 (121,4±3.3 ml, 43,1±1.5 ml; p<0.05). LV myocardium mass (LVM) in patients of group 2 (345±19,1 g) and group 3 (378±15.1 g) was significantly higher than in group 1 in patients with COPD (308±13,1 g; p<0.05). Negative correlation of medium strength between GFR and LVM (r=-0,309; p<0.05) was established. The same relationship was noticed for LV mass index (LVMI) in group 1 it was 171,4±3.8 g/m<sup>2</sup>, which is significantly lower than that in patients of group 2 (188,6±9,2 g/m<sup>2</sup>; p<0.05), in group 3 LVMI was 225±9.1 g/m<sup>2</sup>, which is significantly higher than that in groups 1 and 2 (p<0.05). Negative correlation between LVMI and GFR was established (r=0,356; p<0.05).

**Conclusions:** Revealed a high prevalence reduction GFR among patients with COPD, having a close relationship with the severity of the underlying disease and combined with changes in LV geometry and mass increase of the LV myocardium, which, as we know, leads to increased risk of adverse cardiovascular events. The above determines the need for control GFR in patients with COPD.

### **Should medical students practice cardio-pulmonary resuscitation for educational purposes on the newly dead following cardiac arrest?**

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**Objectives:** At a cardiac arrest I witnessed a doctor encouraging a medical student to practice CPR after time of death had been declared. This raises ethical issues that will be explored.

**Methods:** Using ethical principles the dilemma was analyzed. The focus was on the four principles of medical ethics, virtue ethics, utilitarianism and deontology.

**Results:** For consent to be valid the patient must have capacity, be sufficiently informed and freely given. It can be argued that death means the person has now become an object and therefore exempt from the ethical principles and consent is not required. If consent were to be obtained from the next of kin post death, the conversation could be difficult and inappropriate. All acts performed should be beneficial to the patient. The act of practicing CPR on the dead is not beneficial to the patient. However, it is also causing no harm. Patients should receive the best possible care, including access to well-trained doctors who perform CPR. If practicing CPR on the dead is the best way to teach then it should be undertaken. A utilitarian would argue practicing CPR on the newly dead is appropriate to further skills with the consequence of saving future lives. A deontologist would suggest we treat people as individuals, not just for our own gain. If students are practicing on the newly dead to further skills, the body is being used for their own education. Virtue ethics focuses on an individual's character. If CPR is practiced on the newly dead without consent, this could indicate that the student and educator do not have integrity and lack compassion. Conversely, a doctor who does not wish to practice CPR could be seen as unconscientious.

**Conclusions:** Although a utilitarian would argue that the benefits for society as whole outweigh those of the individual,

the deontological approach focuses on the individual being paramount. One's own character is also important. There are many other acceptable ways of teaching CPR skills and we should not place responsibility on the patient before death or the relatives after to make a decision. CPR during a cardiac arrest is undignified. This should not be furthered by practicing on the newly dead. One option is to introduce a card similar to that of the Donor Card in the United Kingdom, which states a person consents to be used to practice CPR after their death. This may be required with increasing number of medical students. There needs to be clarity from regulatory bodies.

### Smoking cessation as a part of our daily practice: Do we do it properly?

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**Objectives:** Smoking, as a major risk factor for many chronic diseases, is a worldwide public health problem. Asking about smoking and advising about cessation should be an important part of a patient-doctor encounter. However, in busy medical clinics this important step may be overlooked. We aimed to determine the nicotine dependence level of the adult patients in a university hospital internal medicine outpatient clinic and to evaluate the appropriateness of smoking cessation counseling.

**Methods:** This is a cross-sectional study conducted between October 2014- May 2015 in department of internal medicine of a university hospital. Adult patients seen at the general internal medicine clinics were asked to fill a questionnaire about smoking habits, doctors' questioning about smoking status and advices about smoking cessation. Data were analyzed by descriptive statistics and Pearson Chi-square test was used where appropriate.

**Results:** A total of 512 patients with a mean age of 39±14 years (17-64 years) and 64.6% females completed the questionnaire. 145 of them (27.7%) were active smokers. The mean age of the current smokers was 39±12 years (18-63 years) and 52.1% were female. According to Fagerström test for nicotine dependence, 33.8% were high-dependent smokers. 135 (95.1%) of the smokers told that they were asked about the smoking status during doctor visit and 72.5% were advised to quit smoking. However, any method to quit smoking was discussed with only 41 (28.9%) of the smokers. The most common advice was to visit the smoking cessation clinic of the same hospital. The advice rate for smoking cessation did not change with regards to the dependence score. We also found that 61.3% of smokers had at least one smoking person living in the same house and that was statistically different from non-smokers (41%,  $p < 0.01$ ).

**Conclusions:** Smoking is a major risk factor for atherosclerotic and malignant diseases. Although asking about smoking was a common practice, advising about cessation and particularly, discussing methods for cessation were not a part of the doctor visit in many of the patient-doctor encounters. Smoking cessation counseling should be an indispensable part of the patient examination.

### Overutilization of proton pump inhibitors and H2 receptor antagonists in hospitalized medical patients

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**Objectives:** Proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2RA) are widely used drugs in the outpatient setting and in the hospital. The primary aim of the study was to determine the frequency of the use of PPI and H2RA in the medical wards. The secondary aim was to determine the utilization patterns of these drugs.

**Methods:** The study was performed retrospectively in a tertiary care university hospital internal medicine wards and medical intensive care unit (MICU). The medical records of the patients who were hospitalized between January 1st and December 31st, 2010 were retrieved. The frequency of the patients who used either an H2RA or a PPI any time during the hospital stay was calculated. Of those patients to whom these drugs were ordered, a random selection was performed and one fourth of the cases were included to create data set.

**Results:** In 2010, a total of 4730 patients were admitted to internal medicine wards and either a H2RA or a PPI was ordered for 2177 (50.3%) of them. Following a random selection process, the hospital records of 556 of these patients (25.5%) were evaluated. Majority of the patients (76%) were on PPI. While 90.3% of the patients who were hospitalized in wards used a PPI rather than a H2RA, 74.8% of the patients who were hospitalized in the MICU used a H2RA rather than a PPI ( $p < 0.001$ ). 95 patients were transferred from the MICU to internal medicine wards and 58 (61%) of them were switched from an H2RA to a PPI without a specific reason. Before hospital admission 8% of patients were on PPI and 5% on H2RA but during hospitalization and at discharge, utilization significantly increased, 76% and 79%.

**Conclusions:** There is a high rate of acid suppressive therapy usage among hospitalized medical patients and this leads to a similarly high rate of prescription at discharge. As overutilization brings along adverse effects and drug-drug interaction problems in long term, further studies are required to evaluate the appropriateness of the utilization of these drugs.

### Idiopathic inflammatory myopathies prevalence in Hospital University Severo Ochoa. Reality and experience against these entities

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**Objective:** Determine the clinical features and know the evolution and lines of treatment in patients with idiopathic inflammatory myopathies (IIM).



**Methods:** It is an observational and transversal study in which we have collected all the clinical records of patients diagnosed with myopathy and myositis from 1 January 1999 to 31 December 2013. After reviewing these stories, we obtained clinical and epidemiological information of these patients and checked if they met the diagnosis criteria set out in the literature for IIM. Obtained information about the treatment and evolution of these patients. We used Excel 2007 and SPSS version 20.0 to create a data base and perform the statistical analysis.

**Results:** From the initial search phase were gathered 27 clinical records that fulfilled the diagnosis of IIM. 22.2% was diagnosed in the last 5 years. The medium age at the diagnosis was 57.7, been mostly women (55.6%), 37% were smokers in the past and the most common symptom was muscle weakness which represented 88.8% above the 29.6% of skin involvement. Dysphagia was present in a 25.9% of patients, joint involvement in a 22.2% and Raynaud's phenomenon in a 7.4%. Pulmonary involvement occurred in 33.3% (9 patients) whose 6 had lung fibrosis; no evidence of cardiac involvement was found. Positive antibodies were found in 77.8% of patients. There were dermatomyositis (55.6%), polymyositis (29.6%) and antisynthetase syndrome (14.8%). 18.5% presented a malignant neoplasm at the time the diagnosis was made. All patients were treated with corticosteroids but 66.6% had other drug (18.5% – rituximab, 3.7% – infliximab and 3.7% – certolizumab). During the follow up, only 3 of the 27 patients died, 2 of them for lung disease and 1 in connection with oncological pathology. All deceased had more than 4 years of evolution of the myopathy. 14.8% of patients present episodes of recurrences that evolved favorably.

**Conclusions:** The importance of proper treatment and follow-up of these patients leads to a good control of the disease and fewer recurrences. The need for biological treatment, although promising studies have been made, remains unclear.

## Alcohol: do they know how much is too much?

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**Introduction:** The harmful use of alcohol causes 3.3 million deaths worldwide every year and is a causal factor in more than 200 disease and injury conditions. In such a setting, education towards healthy alcohol consumption habits is mandatory to reduce the negative effects of this substance's misuse. Presently, it is recommended by the World Health Organization (WHO) that the daily intake of alcohol shouldn't exceed 2 drinks (20 g) in men and 1 drink (10 g) in women. But how do our patients perceive what is a healthy alcohol intake and how do they perceive their own behavior in this matter? In order to shed some light on this matter, the present observational study is being performed on a small population of 322 patients taken from a family doctors' attributed list of patients (n=2000) from a small region of Alentejo, Portugal.

**Objectives:** Clarify what patient perceives as unhealthy alcohol consumption habits and compare whether it matches WHO recommendations. Also describe the population's present ethanolic habits in what refers to quantity and pattern of consumption.

**Methods:** From a 2000 patient list, a sample of 322 individuals was calculated (95% confidence level and a 5% confidence interval). Data collection was initiated in June 2015. Patients older than 16 years are systematically asked to enter the study until the desired sample number is reached. Each patient can only enter the study once. A questionnaire including the AUDIT-C is distributed before each consultation. Patients were asked to answer it by themselves and then deposit it in a box located outside the office. The results are to be inserted in a database using Microsoft Excel and statistical analysis shall be performed accordingly using SPSS.

**Results:** Though the study is still ongoing, it is expected that patient's set point for what is maximum advisable daily alcohol consumption will be greater than WHO recommendations. It is expected to see different patterns of consumption according to age, being younger groups more prone to binge drinking. We also expect heavier ethanol habits in male gender, though this may not be as evident in youngsters.

**Conclusions:** In spite of the limitations imposed by the sampling methods, the present study is still a valuable tool for accessing one's work in education on ethanolic habits. Health promoting events and actions can be tailored according to high risk groups, once results become available. Follow up and reevaluation after such measures would be interesting in order to verify their impact of such in our patient's health knowledge and daily habits.

## Nutritional risk screening in a regional hospital. Conut prognostic index

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**Objectives:** Undernutrition is a prevalent problem which increases morbidity and mortality, both surgical and medical field. There are many studies that have tried to develop screening tools for early detection of undernutrition. Of these, prognostic index Conut, establishes three risk situations: low (result from 0 to 4 points); moderate (result from 5 to 8 points); high (result from 9 to 12 points) based on three analytics scores (cholesterol, albumin and total lymphocytes) which are measured at patient's hospital admission. This index allows identifying patients with nutritional risk in an efficient way and applicable to all the patients admitted. It has a minimum cost and doesn't need to be developed by specialists. Our hospital, since 2004, has an analytic profile that allows the realization of this index during the hospital admission and facilitates patient stratification according to referred risk situation. The aim of this study is to know the PI value in determinations performed at our hospital and its prognostic implications in our patients.

**Methods:** A retrospective analysis of PI Conut's analytical requests made at the hospital from 2014 to February 2015 was completed. Data collected included age, sex, petitioner

department, mortality, hospital stay and PI. Statistical analysis was performed using SPSS for Windows.

**Results:** During this period 144 analyses have been performed at the hospital. Patients' age was  $69.2 \pm 14.1$  years, and 73,3% were males and 26,7% females. According to petitioner departments, PI requests were: 72.9% in ICU, 18,1% in internal medicine department, 4,9% in surgery and 4,2% in emergency department. The number of cases according to undernutrition degree was: 18 patients with low risk, 41 patients with moderate risk and 85 patients with high undernutrition risk. Average hospital stay was 9.4 days for low risk group, 17.7 days for moderate risk and 23.5 days for high risk group ( $p=0.002$ ). PI score in group of patients who died during hospitalization was 9.67, against 8.63 in non-died patients ( $p=0.117$ ).

**Conclusions:** CONUT seems to be an efficient tool for stratifying our population according to nutritional risk and identify those patients more vulnerable to increase the average hospital stay and mortality. Our hospital works in development of a multidisciplinary nutritional management in admitted patients. This procedure, based on undernutrition risk should allow minimizing malnutrition impact in our patients.

## Main causes of hospital admissions in the Brazilian Unified Health System

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**Objective:** To analyze the gender and age group more prevalent in the hospital admissions by the Brazilian Unified Health System (SUS), as main causes of these admissions.

**Methods:** Were used data of DATASUS, an online platform of Brazilian Ministry of Health data base, to evaluate gender, age group, global spending and main causes (classified by ICD-10, International Statistical Classification of Diseases and Related Health Problems of World Health Organization) of all hospital admissions in the year of 2014.

**Results:** Were found a total of 11,072,247 hospital admissions, resulting in a public spending of BRL\$ 13,214,965,279.65 (US\$ 4,404,988,425.55). As to gender, 41.1% were men and 58.9% were women. The prevalence of persons below 19 years old was 23.7%; 20-39 years old, 31.6%; 40-59 years old, 20.8%; over 60 years old – 23.9%. Regarding the main causes of hospital admissions, the first 5 causes account for 61.2% of all hospital admissions: 'pregnancy, childbirth and the puerperium' (20,7%), 'diseases of the respiratory system' (11%), 'diseases of the circulatory system' (10,1%), 'injury, poisoning and certain other consequences of external causes' (9,9%) and 'diseases of digestive system' (9,5%).

**Conclusions:** From the results obtained, we can provide information to managers of hospitals, in order to help them plan, more appropriately, health strategies by identifying the real needs in their hospitals, the profile of the population served and thus better organize the service of the units individually in order to allocate funds, human resources, and other actions to treat and rehabilitate such diseases more forcefully, for the well being full of users.

## Referrals percentage of the subspecialties of the internal medicine: an analysis from three Family Health Units of the Family Ribeirão Preto-SP, Brazil

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**Background:** The Family Health Strategy presents strategic features for the Unified Health System (USF), aimed at replacing a health care delivery system purely traditional to roll out a model that, in about 98% of cases, is resolved in this sphere. Studies show that among a population of 1,000 people aged superior to 15 years, about 250 will seek a primary health service and only 5 needs to be referral to medical specialties. Thus it is very important to diagnose the reality of our Health Units Family (USFs) on the subject discussed, so that this is a tool for managers to better organize the care provided in these USFs.

**Objective:** To analyze the profile of three USFs the northern region of Ribeirão Preto, highlighting the demographic profiles of users as well as the percentage of referrals to specialties.

**Methods:** This is a transversal observational study. Medical records of three USFs of Ribeirão Preto-SP, Brazil (USF Avelino Palma Neighborhood, USF Heitor Rigon Neighborhood and USF Estação do Alto Neighborhood) were analyzed, comprised between June/2011 and May/2012, in order to assess sex and range age of their patients, plus the percentage of referrals to medical specialties.

**Results:** The three USFs showed the prevalence of female patients (USF Avelino Palma: 59.4%; USF Heitor Rigon: 59.3%; USF Estação do Alto: 61.3%). As for the distribution by age groups, the USF Avelino Palma showed 45.13% of the population such as age above 41 years; in USF Heitor Rigon and USF Estação do Alto, 36.8% and 47.4%, respectively. The USF Avelino Palma sent 14.6% to medical specialties, while USF Hector Rigon and USF Estação do Alto, 6.4% and 4.5%, in that order.

**Conclusions:** Data regarding sex and age of the patients are in agreement with the literature. However, data regarding referrals to specialists are well above what the literature reports, that show the need for referrals to medical specialists in only 2% of the patients. Thus, there is a need to revise the parameters used in each USF, thereby providing reduced costs, as well as the waiting time for a new query, and consequently accelerating the process of resolving the problem.

## Immunosuppressed patients admitted to an intermediate care unit of internal medicine

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**Objective:** To evaluate morbidity and mortality in patients under pharmacological immunosuppression (IS) for autoimmune diseases (AID) or solid organ transplants (SOT).

**Methods:** Retrospective analysis of the admissions to an intermediate care unit (IC) of internal medicine over the last 5 years.

**Results:** There were 115 admissions of 86 patients (52 women, median age 59, all Caucasian), the majority (57%) being under double IS and 11% under corticosteroids only (prednisone  $\geq 20$  mg/day). The reason for IS was AID in 70 cases (rheumatoid arthritis – 29, systemic lupus erythematosus – 19, ANCA vasculitis – 9) and SOT in 45 (kidney – 32, lung – 9, heart – 3). In 67% of the cases it was at least the second admission on the previous year and 32% had been admitted to IC/intensive care on that period. The patients were admitted for infection in 53% of the cases, and in 13% – for other problems directly related to flares/disease progression or ARE complications (as 2 secondary thrombotic microangiopathies). They came mainly from the urgency department (25%) and internal medicine ward (16%). In 76% of the admissions infection was diagnosed (respiratory – 36, urinary – 24, intra-abdominal – 11), with septic shock in 14%. From 53 cases with microbiological isolation, 2/3 were multiresistant pathogens; there were 17 bacteremias, 1 fungemia, 4 aspergillosis, 3 pulmonary pneumocystosis and 1 disseminated strongyloidiasis. IS was altered or increased in 16% of the cases and plasmapheresis was performed in 4 cases. The stays in IC lasted an average of 4 days (with total average duration of admissions around 24 days), and 13% of the cases needed to be readmitted. There were 4 deaths in IC and a total of 30 during the same admission, with a 6-month mortality of 37% (19 AID patients and 13 SOT patients). Infection was significantly associated with mortality ( $p=0.031$ ), while the reason for IS was not.

**Conclusion:** Most of the immunosuppressed patients were admitted to IC for severe infection, with high short-term mortality.

## End-of-life care and the use of cardiopulmonary resuscitation in Europe – a survey of junior doctors' experiences

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**Objectives:** Attitudes to end-of-life decisions and the use of cardiopulmonary resuscitation vary internationally. After exploring these differences in a workshop at the European School of Internal Medicine in Latvia in January 2015, we designed a survey with the aim of comparing the School participants' experiences of end-of-life decision-making.

**Methods:** An online questionnaire was distributed to all 44 participants of the course, physicians in postgraduate training or in the first year following specialization in Internal Medicine or a related subspecialty. They were asked to describe who is responsible for making decisions about cardiopulmonary resuscitation in their clinical practice and whether patients and relatives are involved in these decisions. Other questions included whether the participants had any training in communication about end-of-life issues, whether they have access to palliative care

services and whether they use 'Do not attempt cardiopulmonary resuscitation' (DNACPR) orders in their usual practice.

**Results:** Of 44 course participants, 36 replied (82% response rate). Respondents came from 18 different countries. The majority (67%) stated they had received some training in communication about end-of-life issues, and most (76%) had access to palliative care services. 66% reported that anticipatory care planning commonly takes place in their country and 56% reported using DNACPR orders. Most (67%) reported routinely discussing resuscitation decisions with patients, and these discussions are more frequently carried out by training grade doctors (58%) than specialists (42%). Participants working in Northern and Western European countries had better access to palliative care services and reported commonly using DNACPR orders and anticipatory care planning. Participants from the South and East of Europe did not commonly use anticipatory care planning or DNACPR orders and reported limited access to specialist palliative care services.

**Conclusions:** Our data displays a marked variation in end-of-life care with more use of anticipatory care planning and palliative care services in Northern and Western Europe. This may be due to cultural or religious factors, inequalities in access to resources or differences in medico-legal practice. Despite the high response rate, there are limitations to our methodology as individual participants' experiences may not be representative of prevailing clinical practice in their country.

## A critical and evidence-based comparison of published guidelines on atrial fibrillation

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**Objectives:** To publish the methodology adopted to compare the guidelines on atrial fibrillation (AF) management during the 2014 European Summer School of Internal Medicine (ESIM).

**Methods:** The committee identified the three most-widely used guidelines on AF: Canadian Cardiovascular Society on AF guidelines (2010), AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation (2014) and European Society of Cardiology guidelines on AF (2010-2012). Focusing on the ED management of AF, 5 main practical clinical questions were identified: 1) selection of a rate or a rhythm control strategy, 2) selection of electrical or pharmacological cardioversion, 3) choice of drugs for pharmacological cardioversion, 4) choice of drugs for rate control and 5) management of anticoagulation in acute-onset AF. 45 internal medicine residents attending the course participated to the study, and were divided in 5 working groups. Each group was moderated by a senior tutor and evaluated the level of agreement of the indications between the three guidelines in each topic. Namely, it was expressly asked to report (a) whether

the GRADE system was used or not (b) differences on the strength of recommendations and (c) references cited.

**Conclusion:** ESIM 2014 group is actually analytically investigating the differences between the three selected documents to prepare an evidence-based paper aimed to compare current guidelines and providing less confounding indications to the internal medicine specialist working in the ED.

## Evaluation and management of pain by physicians in an internal medicine department

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**Background:** Pain is defined as the fifth vital sign by the World Health Organization. It is a very frequent symptom with multiple etiologies, and is seen in all aspects of medical practice. However, it is still underestimated by medical doctors, who fail to apply adequate control measures.

**Objectives:** Evaluation of the assessment and management of pain by medical doctors in an internal medicine ward.

**Methods:** A transversal observational study was made, through a questionnaire, answered by the medical personnel, characterized according to age, gender and years of professional experience (Group A <5 years, Group B 5-10 years and Group C >10 years). The evaluated parameters were: diseases most frequently associated with pain; qualitative and quantitative assessment of pain; preferred analgesics used and administration pathway; physiological variables that influence the choice of analgesic; familiarity with the WHO pain ladder; and indications for the use of morphine.

**Results:** There were 20 doctors included in this study, with an average age of 33.9 years old and female predominance (15/20). Concerning years of experience: Group A had 9 doctors; Group B – 5 and Group C – 6. Concerning etiology of pain, all doctors attributed it to neoplasia or osteoarticular disease. Regarding the questioning of patients about pain: 16/20 doctors always and 4/20 sometimes or according to the clinical setting. All the doctors characterized pain qualitatively and quantified it either by the visual analogical scale or by asking the patient. Only 12/20 doctors knew the WHO pain ladder. The most commonly used drugs for the control of pain were: paracetamol 20/20, anti-inflammatory drugs and tramadol in 18/20. Only 11/20 used fentanyl and 12/20 doctors used morphine. Preferred administration pathway was oral 20/20 or endovenous 19/20, followed by transdermic 14/20 and intramuscular pathways (9/20). The choice of analgesic was influenced by renal function 20/20, hepatic function 16/20 and age 13/20. Morphine was used mainly in intense pain, patients with neoplasia and agony.

**Conclusions:** There were no significant differences concerning the perception and treatment of pain concerning the years of experience. The pain scales are not widely used, but have proven benefits in terms of symptom control and quality

of care. Administration pathways tend to be transdermic, subcutaneous, or endovenous, and as such, more efficacious. Morphine is in use and part of everyday practice when controlling pain.

## COMPARTE program for the chronic patients care in Aljarafe. Comparative analysis of population

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**Objectives:** Since 2009 our Hospital-Health district has a program of assistance to the chronicity that uses a longitudinal model of attention between different levels, different health professionals and some specialties. This format aims to give answer to the health care of the chronic patients of Aljarafe. This program promotes inter-level assistance continuity with patient formal following after come home from hospitalization for a process of exacerbation. This attention has like argument lines the joint visit (primary physician/family nurse) at home in 48-72 working hours after arrive home, including review of patient drug treatment. Aljarafe has now counted approximately 280,000 inhabitants. 9 health areas depend on his health care of our Hospital. The aim of our study was to determine if there were differences in patient care included in the program according to the different health area, when went home from hospitalization.

**Methods:** A retrospective study of patients included in the COMPARTE program with some hospitalizations in 2014 from 2 different geographical areas: the town of San Juan de Aznalfarache (with 21663 registered inhabitants and proximity to our hospital, about 10 km) and the town of Pilas (with 13,837 inhabitants and 33.4 km to the Hospital). We study variables like age, sex, cause of inclusion in the program, number of hospitalizations, days of hospitalization, mortality in hospital, including in primary attention, visit within 48-72 business hours, joint visit and review treatment drug at home.

**Results:** We collected a total of 93 patients in the period analyzed: 57 from the town of San Juan (61.3%) and 36 patients from the town of Pilas (38.7%). The mean age was 78.7±10.1 years and without differences between locations. The gender distribution was 47.3% men and 52.7% women. The average hospitalization's days during 2014 was 10.4±8.4 days. The average number of hospitalizations was 1.34 (1-5 maximum revenue). In relation to the inclusion in the Program when patients went home, 66 patients were included in the Program in Primary Attention, 2 patients were not included and 25 patients died in the episode of hospitalization. Most of the patients (64.5%) were pluripathology in both locations, although the percentage of oncologic palliative patients included was higher in Pilas (33.3% vs. 10.5%). In connection with the visit at home, it was held in 48-72 working hours by 85% of patients from San Juan,

and 69.2% in Pilas. The visit was joint (doctor-nurse) in 50% of patients from San Juan, 30.8% of patients in Pilas. Revised drug treatment was made in 82.5% of patients in San Juan, compared with 57.7% of patients in Pilas.

**Conclusions:** We found differences in the care of patients that we thought to be related to the different profiles of professional activity, professional satisfaction, as well as physical distance to our hospital. We are evaluating now that differences and they will be the project of our next communication.

## An unusual case of acute meningitis

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**Introduction:** Ibuprofen-induced meningitis is a very rare disease, but it should be considered in patients with repeated episodes of aseptic meningitis, especially given the high consumption of this and other NSAIDs in our patients.

**Case report:** 65 years old male with previous history of non-Hodgkin lymphoma treated with chemotherapy 3 years earlier. 2 years before present admission, he was admitted in Internal Medicine with diagnosis of acute meningitis, with sterile cerebrospinal fluid culture; he received ceftriaxone and vancomycin and was discharged 10 days later with full recovery. 2 years later he was referred to the emergency room from allergology outpatient clinic, where he was being studied for suspected allergy to ibuprofen. After administration of 75 mg of ibuprofen, the patient complained of severe headache and chills. Temperature on admission was 39.3°C. A lumbar puncture was performed: CSF showed pleocytosis with 260 cells/mm<sup>3</sup> (81% neutrophils, 19% lymphocytes), normal glucose (87 mg/dL) and elevated proteins (133 mg/dL). Gram stain and culture of CSF were negative. After ibuprofen withdrawal, he was started on low dose steroids along with antihistamines, with good evolution and disappearance of the symptoms in less than 48 hours.

**Discussion:** Ibuprofen is the most common cause of drug-induced aseptic meningitis, although cases have also been reported with other NSAIDs. The real incidence of this condition is unknown, and experience to date is based on a few dozen cases reported in the literature. Clinical manifestations of ibuprofen-induced meningitis are similar to infectious meningitis, including fever, headache, photophobia and stiff neck. Laboratory findings are also similar, including pleocytosis in CSF with neutrophil predominance, elevated protein and normal or low glucose levels. The mechanism of drug-induced meningitis is unknown, although it is suggested that could be related to hypersensitivity mechanisms. Diagnosis of ibuprofen-induced meningitis is a diagnosis of exclusion; it should be suspected in patients with recurrent episodes of bacterial meningitis features but with sterile cultures and with a temporal relationship to the use of ibuprofen. The prognosis of this entity is good; there have not been described cases of death or serious neurological sequelae in the literature.

## Cardiorenal interaction in hypertensive patients with type 2 diabetes mellitus

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**Introduction:** Communication of cardiac and renal disease for a long time attracted the attention of internists, cardiologists and nephrologists. The mutual dependence of pathological processes of the cardiovascular system and kidneys, clinical predictability of outcomes allow to consider cardiorenal relationship as a continuous chain of events that make up a kind of vicious circle – cardiorenal continuum. The combination of diabetes mellitus (DM) and arterial hypertension (AH) in 10 times increases the risk of cardiovascular events and terminal chronic renal insufficiency compared to patients not suffering from hypertension. We suppose that AH in type 2 diabetes is part of the symptom, which is based on insulin resistance (IR). Therefore, studying the pathogenetic mechanisms of development of cardiorenal syndrome in type 2 diabetes combined with hypertension, we can assume significance as IR in violation of the structure and function of the heart and kidneys. Thus, the study of the relationships in cardiorenal hypertensive patients with type 2 diabetes is an actual interdisciplinary task, controlling the level of blood pressure (BP) control of carbohydrate and lipid metabolism will successfully meet the challenges of preventive and pathogenetic modern medicine.

**Objective:** To study the characteristics of cardiorenal interaction in hypertensive patients with diabetes mellitus (DM) type 2.

**Material and methods:** The study included 120 patients with AH stage I-III aged 40-65 years: 60 diabetic hypertensive patients (study group) and 60 non-diabetic hypertensive patients (control group). We performed ambulatory blood pressure monitoring, echocardiography, studied endothelial function, evaluated the artery stiffness, estimated renal function and metabolic parameters.

**Results:** A prognostic unfavorable changes of ambulatory blood pressure profile, a significantly higher incidence of left ventricular hypertrophy (LVH) were found in diabetic hypertensive patients in comparison with non-diabetic hypertensive patients. There were no patients with normal diastolic LV function in the study group. Increased pulse wave velocity (PWV) was noted in 83.3% diabetic hypertensive patients. More severe endothelial dysfunction, tubular and glomerular dysfunction were identified in diabetic hypertensive patients in comparison with non-diabetic hypertensive patients. Severe insulin resistance (IR) led to metabolic changes – glucose and lipid toxicity in diabetic hypertensive patients.

**Conclusions:** This study shows the presence of cardiorenal interactions and correlation relationship between IR and end-organ damage in hypertensive patients with type 2 diabetes. IR can be considered as an independent predictor cardiovascular and renal disease. Accordingly, IR correction will help us to optimize the results of treatment cardiovascular diseases and kidneys diseases in hypertensive patients with type 2 diabetes.

## Correction of endothelial dysfunction is an important goal for antihypertensive therapy in hypertensive patients with type 2 diabetes mellitus

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**Objective:** To evaluate the impact of combination antihypertensive therapy with lisinopril + amlodipine (Ekvator) on endothelial dysfunction in patients with arterial hypertension (AH) concurrent with type 2 diabetes mellitus (T2DM).

**Material and methods:** The trial enrolled 30 patients aged 40 to 65 years with AH stages II-III concurrent with T2DM. All the patients received combination antihypertensive therapy with lisinopril + amlodipine (Ekvator) for 24 weeks. Endothelial function was studied from serum and urinary metabolites of NO and endothelin-1 concentrations and occlusion test results. 24-hour blood pressure (BP) monitoring and echocardiography were performed; arterial elastic properties and renal function were investigated. The study was conducted in accordance with the guidelines of the law "On Circulation of Medicines" from 12.04.2010 № 61 and the principles of "Good Clinical Practice». It received permission of the Regional Ethics Committee to conduct a clinical trial – the approval of the protocol number is 192 – 2013 from 03.11.2013.

**Results:** After 24-week therapy all the patients achieved BP goals. Endothelial function was improved in hypertensive patients with T2DM: there were increases in both serum and urinary metabolites of NO production (by 122.8 and 65.8%, respectively) and decreases in serum and urinary endothelin-1 secretion (by 26.1 and 76.1%, respectively). The number of patients with normal microcirculation increased from 13.3 to 86.7% ( $p < 0.001$ ). There was significant improvement in 24-hour ABPM monitoring readings and reductions in the left ventricular mass index by 10.7%, proteinuria by 58% and albuminuria by 43.6%; the number of patients with increased pulse wave velocity along the elastic arteries declined by 30%.

**Conclusion:** 24-week treatment with the combined antihypertensive medication Ekvator is highly effective and safe for recovering endothelial function and improving the state of target organs in hypertensive patients with T2DM.

## "The final countdown" – experience of 3 years

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**Objectives:** The necessity of transplantable organs is growing over the last years. "Donor Hospitals" have a great importance in identification, signaling and maintenance of the viability of potential organ donors. The aim of the study: to describe 3 years of experience of an organ "Hospital Donor".

**Methods:** Retrospective study analyzing 13 patients who were admitted in intensive care unit (ICU) during the period between

01 January 2012 and 31 December 2014, and evolved to potential organ donors (POD). The sex, age, admission diagnostic in ICU, time occurred between the 2nd brain death tests, organ harvest, fluid therapy and vasoactive support used in POD maintenance were evaluated.

**Results:** Of the 13 analyzed cases, 30.8% were male with a mean age of 47.2 years. "Potential Organ Donor" was the admission diagnostic in 61.5% of cases. The causes of brain death were traumatic brain injury (TBI) (38.5%), spontaneous intracerebral hemorrhage (30.8%), brain infarction (15.4%), subarachnoid hemorrhage (7.7%) and post-cardiorespiratory arrest status (7.7%). The mean time occurred between the 2nd brain death test and organ donation was 6,41 h (min 2h; max. 15h). Mean fluid therapy necessities during the period between the 1st brain death test and organ harvest was analyzed: [0-4h], 487.8 ml/h; [4-8h], 598 ml/h; [>8h], 341.7 ml/h. The majority (84.6%) of POD needed vasoactive support in rising dosages over the time and all of them experimented a deterioration of their gas exchanges quantified by a drop in  $FiO_2/pO_2$  ratio.

**Conclusions:** Homeostasis of a POD is a difficult and demanding process in order to secure a good organ quality. The mean time occurred between the confirmation of brain death and organ harvest is primordial. In this period we can see a rapid deterioration of the POD over the time, so, is urgent to do every effort in order to ensure the quantity and quality of harvest organs.

## Erythrocyte sedimentation rate – marker of disease activity in systemic lupus erythematosus patients

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**Objectives:** The use of erythrocyte sedimentation rate (ESR) decreased in time, systemic lupus erythematosus (SLE) included, in favor of new available parameters. Our aim was to investigate the relation of ESR with disease activity in SLE patients, overall and on subgroups determined by specific organ involvement.

**Methods:** We prospectively included all patients fulfilling the 2012 Systemic Lupus International Collaborating Clinic (SLICC) SLE's criteria. Presence of acute or chronic infection was an exclusion criterion. Disease activity was assessed by the Systemic Lupus Activity Measure (SLAM) score in all patients. The SLAM score calculated without the item related to the ESR was also introduced as a variable. The ESR levels were categorized as follows: normal ( $< 25$  mm/h), mild (25-50 mm/h), moderate (51-75 mm/h) and marked ( $> 75$  mm/h) elevated.

**Results:** 125 patients (90.4% of female sex) were included with a mean age at inclusion of  $46.6 \pm 12.8$  years, respectively median (inf; sup) disease duration of 8.0 (1-37) years. Active renal, hematologic, neurologic, articular, cutaneous involvement was present in 19 (15.2%), 46 (36.8%), 11 (8.8%), 40 (32.0%), 37 (29.6%) patients at inclusion respectively. The SLAM score was significantly higher when elevated ESR: 3.7 (0-11) vs 6.7 (1-18) vs 12.4 (5-24) vs 14.4 (18-24) points ( $p < 0.05$ , Mann-

Whitney test). Univariate analysis (Spearman test) found a significant association between the ESR and SLAM score without ESR item in the entire lot and also in subgroups with specific active organ involvement ( $p < 0.05$ ). The multivariate analysis by logistic regression identified ESR as the only biological marker significantly correlated with disease activity as assessed by the SLAM score without item ESR,  $p$ -value 0.018 (variables: ESR, fibrinogen, C-reactive protein (CRP), complement C3, C4, anti-dsDNA and antinuclear antibodies by ELISA). The AUC (95% CI) for ESR as predictor of a high SLAM score without item ESR (more than 10 points) for the entire lot, respectively for subgroups with renal, hematological, neurological, articular, respectively cutaneous active involvement were impressively high: 0.86 (0.75-0.97), 0.96 (0.84-1), 0.91 (0.8-1), 0.96 (0.81-1), 0.98 (0.93-1), 0.95 (0.86-1) respectively.

**Conclusion:** ESR is positively correlated with SLE's disease activity overall the type of organ involvement.

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## A case with hyperamylasemia thought to be associated with prednisolone use

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**Introduction:** Steroids are commonly used agents in the endocrine practice. Adrenal and pituitary insufficiencies are the most common indications for their use. Amylase is primarily produced in the pancreas, and is also secreted by several other sites including salivary glands and fallopian tubes. Thus, lipase levels are more specific for pancreatic injury. An elevated amylase in association with normal serum level of lipase is not consistent with the diagnosis of pancreatitis.

**Case report:** A 20-year old male was admitted with the previous diagnosis of prolactinoma. His pituitary adenoma had been removed surgically, and in addition to a daily dose of cabergoline, he had received replacement therapies with thyroid and steroid hormones (5 mg/day of prednisolone) due to postoperative hypopituitarism. He was evaluated for serum amylase by mistake, which was found to be high. Despite no abdominal pain, gastroenterology was consulted and no obvious etiology of hyperamylasemia was defined. The normal lipase levels were also not indicative of a pancreatic pathology. The daily dose of prednisolone was gradually tapered, and amylase concentrations dropped following the cessation of therapy. Although, cabergoline was considered the reason of hyperamylasemia firstly, the improvement of hyperamylasemia after withdrawal of the steroid strongly suggested that the use of prednisolone was responsible.

**Discussion:** Hyperamylasemia is a condition commonly encountered in the internal medicine practice. Various medications are associated with elevated amylase levels. Pulse methylprednisolone has been associated with hyperamylasemia in a case report, and after cessation of the steroid an apparent decrease of serum amylase levels has been reported in a dog study, despite increased lipase concentrations. There is no

knowledge in the literature that the hyperamylasemia may develop from the use of steroids. Interestingly, methylprednisolone has been associated with elevated lipase levels. However, the steroid-induced hyperamylasemia and its regression after the discontinuation of the offending drug proposed that prednisolone may be the causal factor for the increase in amylase. Further prospective studies should be carried out to clarify the aforementioned relationship.

## Cardiovascular risk assessment in patients with chronic hepatitis C and various degrees of glucose tolerance

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**Objectives:** Chronic hepatitis C is a major health problem worldwide and has been associated with cardiovascular disease. We aimed to evaluate cardiovascular risk in patients with chronic hepatitis C and various stages of glucose tolerance and the relationship between inflammatory markers, represented by adipocytokines, and cardiovascular risk in these patients.

**Material and methods:** This cross-sectional and observational study, held in the N.C. Paulescu National Institute of Diabetes, Nutrition and Metabolic Diseases, Bucharest, included a total of 161 patients in different stages of glucose tolerance. We followed anthropometric indices (weight, height, waist circumference, BMI (body mass index)). The biochemical parameters followed were fasting plasma glucose, glycosylated hemoglobin, lipid profile, liver profile, blood counts, cytokines (adiponectin, IL-6, leptin, resistin and TNF- $\alpha$ ). For each patient the cardiovascular risk was calculated using the UKPDS software (The United Kingdom Prospective Diabetes Study). Insulin resistance was determined by using HOMA-IR (Homeostasis model assessment of insulin resistance). MetS (metabolic syndrome) was defined according to the International Diabetes Federation.

**Results:** The average of age was  $53.1 \pm 8.3$  years and 48% ( $n=82$ ) representing men. MetS was present in 64.9% ( $n=111$ ) of patients included in the study. Of the 171 patients in 38% ( $n=65$ ) had type 2 diabetes, 8.2% ( $n=14$ ) IFG (impaired fasting glucose), 8.8% ( $n=15$ ) IGT (impaired glucose tolerance) and 45% ( $n=77$ ) NGT (normal glucose tolerance). The mean duration of diabetes was  $8.5 \pm 4.2$  years and mean duration of liver disease  $4.9 \pm 2.5$  years. Using UKPDS-CHD score, show that 31.6% ( $n=54$ ) and 8.8% ( $n=15$ ) of patients had moderate and high cardiovascular risk. The average concentrations of pro-inflammatory cytokines (TNF- $\alpha=15.9$  pg/ml, IL-6=17.5 pg/ml, leptin=18.9 ng/ml and resistin=23.1 ng/ml) were higher in patients who had a cardiovascular risk calculated by software UKPDS-CHD greater than 30 ( $p < 0.001$ ). In these patients have experienced a high level of TNF- $\alpha$ , which correlates with the degree of inflammation specific chronic hepatitis C, and insulin resistance.

**Conclusions:** The results of this study indicate that patients with chronic hepatitis C associate a higher cardiovascular risk.

These data may be important to identify and treat cardiovascular disease as early as possible in patients with various stages of glucose tolerance.

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## Hemorrhagic blisters as presentation feature of bullous pemphigoid

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**Introduction:** The aim of this work was to reinforce the need for recognition of skin signs as a clue for proper early clinical diagnosis.

**Case report:** We present the case of a 64-year-old male patient living in a long-term care facility because of severe incapacity following an ischemic stroke with cognitive and motor impairment including impaired communication by not being able to speak or to follow commands. He was admitted to an internal medicine ward with the diagnosis of dehydration and urinary tract infection. He presented with multiple skin blisters with serous, purulent and hemorrhagic content, some already ulcerated, they were mainly located in the upper, lower extremities, neck and oral cavity, the biggest were 3 cm diameter he had them for at least one month and had made previous treatment with antibiotic. They didn't appear to cause pain. He was diagnosed clinically with bullous pemphigoid, a skin biopsy was made that confirmed the diagnosis. He responded well to treatment with prednisone. Some of the blisters were colonized with methicillin resistant *Staphylococcus aureus*.

**Discussion:** The proper recognition of skin signs was the clue for proper diagnosing and treating this patient. Internist should be alert, recognize and distinguish between different skin manifestations of systemic diseases.

## Hospital detoxification unit in an internal medicine service. What do we know about our patients?

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**Objective:** The aim of this study was describe the characteristics of the patients admitted to the hospital detoxification unit (HDU) over 3 years.

**Methods:** Prospective study of patients admitted between September 2010 and December 2013. Medical records were reviewed. SPSS program was used to perform the statistical procedure.

**Results:** 227 patients were admitted to the HDU. 175 (77%) patients were men, with average of 44,6 years (23-82) without significant differences between sex. Alcohol was the main drug to detoxify (55,5%), methadone withdrawal 18,8%, decrease methadone dose 7% and cocaine and heroin withdrawal 5,7% and 5,3% respectively. Methadone withdrawal patients had a higher unemployment rate (64%). 29% alcohol detoxification patients were pensioners. 22 patients (9,7%) applied for voluntary discharge. 28 patients had to be readmitted, 10 of them to treat the same drug. 205 patients were smokers (1-102 pack of cigarettes/year), 100% admitted methadone withdrawal patients were smokers. 160 patients (70,5%) drank alcohol, those admitted for alcohol detoxification (73%), for methadone withdrawal (18,7%) and for decrease methadone (42,8%) drank more 100 g ethanol/day. 46% of detoxification alcohol patients and 40% methadone withdrawal lived with partner or children. Hepatitis B virus infection was diagnosed in 17 patients (7,8%), 25 (11,5%) were immune for VHB, and 86 (39%) had hepatitis C infection.

**Conclusions:** The mean age is similar in both sexes and the main drug to detoxify was alcohol. Methadone withdrawal shows a lower economic stability with important incidence on smoking. Patients admitted in HDU were very serious alcohol drinkers. When comparing the actual with previous figures we observe that the incidence of hepatitis virus B and virus C infection are lower than 20 years ago, and patients had a better social integration with more family support. A best knowledge of our patients can help us to provide better assessment and treatment. The patients admitted in HDU have a better economic and social stability compare to 20 years ago. Smoking and drinking are risk factors for our patients and these factors are undervalued.

## HFE gene mutations, iron overload and hypertriglyceridemia

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**Objective:** To evaluate the degree of association between different mutations of the HFE gene (mHFE) and biochemical iron overload (IST>45%) and triglycerides (Tg).

**Methods:** A descriptive, cross-sectional study of 839 ambulatory patients with an alteration of iron metabolism (elevated ferritin or IST). Determination of mHFE for hereditary hemochromatosis was performed for all them at the Hospital Infanta Leonor (April 2008 – April 2012). Variables such as age, sex and biochemical determinations (glucose, IST, ferritin, iron and lipid profiles) were evaluated. Subsequently, quantitative and qualitative variables were studied with a bivariate analysis using Student "T" test and Chi square, respectively. Two groups (IST higher and lower than 45%) were compared. With the bivariate statistical association variables, a logistic regression analysis



was performed to assess the degree of phenotypic independent association with IST>45%.

**Results:** The mean age was 53.5±15.4 years, with 34.8±15.3% and 475.8±359.6 ng/dL average values of IST and ferritin, respectively. 78% of the patients included were male. IST>45% was found in 20.5% of patients. Findings show that 86% of men had IST>45%, whereas only 15% of women (p=0.005). Elevated ferritin (>370 ng/dL) was observed in 58% of the cases. The following mHFE were founded: C282Y homozygotes (HH) (1%), H63D/C282Y heterozygotes (Hh) (6%), H63D Hh (30%), H63D HH (10%) and S65C Hh (1%). 40% of the patients showed no mHFE. The presence of C282Y HH and C282Y/H63D Hh with IST> 45% was observed in 77% vs 22% (p=0.001), respectively. Elevated values of Tg was associated with an IST>45% (190 mg/dL vs 136 mg/dL, p<0.0001). By performing the logistic regression analysis, the presence of mHFE (OR 2.99; p=0.003) and the Tg elevation >180 mg/dL (OR 4.26; p=0.001) remained as independent factors associated with an IST>45%.

**Conclusions:** Iron overload is more frequent in men and in patients with hypertriglyceridemia, suggesting an interaction between iron metabolism and triglycerides. "Classical" mutations on HFE gene with elevated penetrance (C282Y HH and C282Y/H63D Hh) present the highest association with the iron overload phenotype. The observed ferritin increase has not been associated with the genetic determinations. When iron overload is observed without known genetic mutations, DIOS (dysmetabolic iron overload syndrome) should be considered which appears in patients with metabolic syndrome and/or insulin resistance.

## Living with cavernomatous transformation of the portal vein – a clinical case

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**Introduction:** It's a rare cause of either portal thrombosis or hypertension in the adult, resulting from the formation of collateral vessels with hepatopetal flow around the obstruction area in individuals without underlying liver disease. It can result from direct injury of the portal vein with formation of thrombus, congenital malformation of the portal system, procoagulant factors or it can even be idiopathic. The first manifestation can be intestinal ischemia and infarction, digestive bleeding or cholangitis. Treatment can be conservative, endoscopic or surgical. Anticoagulation remains controversial.

**Case report:** Female patient, 29 years old, chronically treated with prednisolone for systemic lupus erythematosus (SLE) with no apparent disease activity and without concurrent antiphospholipid syndrome. She has a twin sister that is healthy. The study of thrombophilia showed heterozygosity for MTHFR and PAI-1 polymorphism, without hyperhomocysteinemia. She also has chronic anemia, iron deficiency by esophageal varices and reflux oesophagitis secondary to gastro- and splenectomy made at the age of 12 due to cavernomatous transformation of the portal vein. Multiple admissions in the hospital were made for upper gastrointestinal bleeding. Now

she is admitted by constitutional symptoms such as asthenia, anorexia, dizziness and one episode of melena stool. In the initial assessment, anemia of 6.8 g/dL was documented; an upper endoscopy was made that indicated extensive ulceration of esophageal mucosa, with low output bleeding and varicose veins. An infusion with terlipressin, proton pump inhibitor was started. Prophylactic ciprofloxacin, transfusional support and supplementation with intravenous iron were also administrated. Abdominal ultrasound revealed mild prominence at the level of intrahepatic bile ducts of the right and left lobes, with decreased flow of the hepatic right branch, thickening of the gallbladder's wall and perigallbladder varicose veins, with cavernomatous transformation of the porta vein. Clinical improvement. Maintains follow-up consultation.

**Discussion:** Serve this case to remember that although rare it should be taken into account. If well controlled and with tight follow-up, prognosis is good.

## Altered iron metabolism, head trauma and atrophy of hippocampus and corpus callosum among alcoholics

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**Objectives:** Ethanol causes brain damage and altered iron metabolism. Various studies have pointed out a relationship between iron-mediated oxidative alterations and hippocampal damage in different settings. Although ethanol itself may lead to iron-mediated oxidative damage, repeated head trauma may also be a contributing factor. This study was performed in order to analyse the relationship between the previous history of head trauma and areas of corpus callosum and hippocampus.

**Methods:** Hippocampal and corpus callosum areas were assessed by magnetic resonance (MR) among 34 heavy alcoholics admitted to the Internal Medicine Service, who underwent MR study for different reasons (Seizure after withdrawal, trauma, and suspicion of Wernicke's encephalopathy). In addition, sideremia, transferrinemia and ferritinemia were determined in 32 heavy alcoholics.

**Results:** We found that there was an inverse relationship between serum ferritin (high levels were found in 78% of patients) and hippocampal areas, especially with left hippocampus (rho=-0.43; p=0.014). Moreover, patients with high ferritin levels showed smaller callosal (t=2.96; p=0.006) and left hippocampal area (t=3.36; p=0.002) than those with normal ferritin levels. In addition, patients who had suffered head trauma showed smaller callosal areas than those who did not (Z=2.15; p=0.031). Callosal area and hippocampal areas were also related to mean corpuscular volume and some variables associated with liver dysfunction, but, by multivariate analysis, ferritin was the sole variable independently related to left hippocampal area.

**Conclusion:** Therefore we conclude that increased ferritin and previous history of head trauma may be related to brain atrophy in alcoholics.

## Laryngeal papillomatosis in a patient with dysphonia, a case report

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**Introduction:** Description of a case of recurrent laryngeal papillomatosis (RLP) in patients with dysphonia and tests performed to reach the diagnosis and treatment.

**Case report:** 75 years old male with a history of chronic laryngitis, diabetes mellitus, hypertension and smoker was admitted because of dysphonia of long evolution. Laryngeal fibroscopy shows an exophytic neoplasm of anterior and posterior right hemilarynx with good mobility. Biopsy to rule out malignancy, reported tissue fragments with vascular connective tissue axis lined by acantósic squamous epithelium, focal keratoses and coliocitos type cytopathic changes without dysplasia is requested; Compatible with squamous papilloma with no evidence of malignancy. In CT nodule pedicle neck that protrudes from subglottic region it was observed hemilarynx right. Resection of the lesion with CO2 laser is performed. A year later presented recurrence of the injury, which holds the right vocal cord and obstructed glottis and subglottis. Tracheostomy and new laser excision is performed. 4 months after exophytic papillomatous lesion protrudes through the tracheostomy is observed, requiring new laser surgery. Currently the patient remains with smaller papillomatosis that glottis or subglottis unobtrusive, staying exophytic lesion in the tracheal stoma and requiring periodic excision every 4-6 months.

**Discussion:** The RLP infection human papillomavirus (HPV) types 6 and 11 virus can be transmitted mainly through sexual contact or when a mother with genital warts transmits it to her baby during childbirth. Treatment with antivirals and interferon is ineffective; the CO2 laser resection is the main treatment. It tends to grow back after surgery, surgery 1 or 2 times a year as needed.

## DRESS syndrome – a case report

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**Introduction:** The drug reaction with eosinophilia and systemic symptom (DRESS) is a severe idiosyncratic drug-induced reaction. Rapid diagnosis is crucial as prompt withdrawal of the offending drug is essential for treatment, while the potential role of corticosteroids remains controversial.

**Case report:** A 78 years old woman with known history of seizures, multiple cardiovascular risk factors, hypertensive cardiopathy and stage 3 chronic kidney disease, was presented to the emergency department with fever and macula-papular pruriginous rash, medicated with ciprofloxacin and a venothropic drug in the previous couple of days for a post-traumatic inferior limb cellulitis. This patient was already on carbamazepin, allopurinol, omeprazol and furosemide medication for a long time. The

laboratory investigation revealed peripheral eosinophilia and lymphocytosis, acute kidney injury (AKI), citocholestatic hepatitis and elevated CRP. All possible offending drugs were suspended and antibiotics were escalated as high-fever persisted. There wasn't any microbiologic agent isolated from the cultures or serologic evidence of virus infection. The rash and AKI resolved, but with laboratory evidence of increasing injury at the hepatic level. Abdominal echography excluded any surgical complications. Patient was submitted to hepatic biopsy which result is not yet known.

**Discussion:** The DRESS syndrome is a difficult diagnosis entity, both the multiorganic involvement, as the poor specificity of the changes found. In this particular case the diagnosis was particularly difficulty because the exposure to multiple potential drugs.

## Smoking as risk factors for chronic non-communicable diseases among the working population of the Ryazan region (according to MERIDIAN-RO study)

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**Objective:** To estimate the frequency of smoking and its association with chronic non-communicable diseases (NCD) among the working population of the Ryazan region according to MERIDIAN-RO study.

**Material and methods:** The MERIDIAN-RO study was conducted as a prospective cross-sectional with retrospective part and included a survey using a standardized questionnaire, the study of biochemical samples and ECG. In a study from 2011 it included 1,622 people (1220 – in a city, 402 – village), aged 25-64 years (mean age 43,4±11,4 years), of which, 42.6% were male, 53.8% – female. The data are standardized by age and sex. In studying the association used the method of multiple logistic regressions. The unadjusted values are presented as odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** The incidence of smoking in the MERIDIAN-RO study was 35%, including in the city – 35.6%, in rural areas – 33.6% (p=0.138). Smokers among women were 22.9%, among men – 49.2% (p=0.0001). With age, there was a decrease smoking among females (from 33,1% aged 25-34 years, to 7.9% aged 55-64 years, p<0.05), while among men this dynamic was not observed (45.6% aged 25-34 years, 56.5% aged 55-64 years, p>0.05). Surveyed individuals, who were divorced, smoked more likely than persons who are married (42.1% vs. 36.0%, p=0.05). In the group of higher education and completed secondary education the prevalence of smoking was 35% and 34.7% respectively, while those with incomplete university and vocational school were smoking prevalence at 47.2% and 56.5% (p=0.046). In the study of the association between the most common NCD and smoking it found that active smoking significantly influenced the development of diabetes mellitus (OR 1.05, 95% CI 1,01-1,08), hypertension (OR 1.23, 95% CI 1,11-1,37), CKD (OR, 1.04; 95% CI 1,01-1,07) and combined points – chronic cough/bronchitis/COPD (OR 1.23, 95% CI 1,04- 1.46). Passive smoking increases the risk of

chronic cough/bronchitis/COPD (OR 1.09, 95% CI 1,02-1,16). Links Smoking with a combined point of CAD/myocardial infarction/stroke has been not received (OR 1.06, 95% CI 0,60-1,86). Adjustment for age, sex, education, obesity and hypertension demonstrated this relationship (OR 1.02, 95% CI 1,01-1,22).

**Conclusions:** The prevalence of smoking among the working population of the Ryazan region was 35.0%, and significantly higher in men was observed, as well as those with incomplete higher and secondary education. Active smoking was associated with the development of the most important NCD: diabetes, hypertension, CKD, chronic cough/ bronchitis/COPD and coronary heart disease/myocardial infarction/stroke. Passive smoking was associated only with chronic cough/bronchitis/COPD.

### Study of the patient safety culture in health professionals of a Spanish internal medicine service (preliminary results)

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**Objectives:** The efficient management of the Services is an essential aspect of a good practice and healthcare quality. One of the fundamental characteristics of the management is the safety. We the internists must be leaders in the field of the management and the patient safety culture to minimize errors and adverse effects. The Agency for Healthcare Research and Quality (AHRQ) designed the Hospital Survey on Patient Safety Culture to assess staff views on patient safety culture in hospital settings. The purpose of this study was to examine the safety culture of one of the Spanish hospitals where the most important service is that of Internal medicine.

**Methods:** The Spanish version of the AHRQ questionnaire on patients' safety was distributed among the health professionals and auxiliary personnel working at the "Los Montalvos" Hospital (a part of the University Hospital of Salamanca, Spain) during a period of 10 months. The survey provided an evaluation of the global level (from 0 to 10) of the perceived safety climate. The strengths and opportunities for improvement were analyzed, following the scheme and criteria proposed by the AHRQ, in order to guide the measures to improve the safety culture in the future.

**Results:** Only preliminary results of our survey (those regarding the nursing staff of the Internal medicine service) are included in this abstract. 20 surveys (40% response rate) were analyzed. 50% estimated the global patient safety level between 6 and 8. 95% reported less than 2 events of threat to the patients' safety during the last year. We stood out as positive dimensions: "Teamwork within hospital units/services" and "Supervisor/Manager expectations and actions promoting safety within hospital units/services". We identified as weaknesses: "Endowment of personnel", "Teamwork between units/services", "Safety perception" and "Support of the management in the safety of the patient". The opportunities for improvement perceived related to the endowment of personnel, to the pace of work

and to the need for a most proactive attitude on the part of the hospital management.

**Conclusions:** Strengths and weaknesses of the safety climate in one Spanish hospital have been identified and they will be used to design appropriate improvement strategies. We propose to encourage internal reporting and discussion of errors and to pay attention to the organization and pace of work of the staff.

### The internist teacher: adaptation of Peyton's four-step approach applied to chest radiography interpretation for Spanish medicine students

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**Objective:** The medical internist for his/her extensive training and global vision of the diseased person is the ideal teacher to instruct the future doctors. Clinical teaching is a decisive part of medical education. The Peyton's four-step method has been widely validated in skills-lab training of medical students, allowing them to practice procedures on mannequins. This method has not been applied to the learning of not manual skills as it is the interpretation of chest radiography. The aim of our work was to adapt the didactic Peyton's four-step method to the practical teaching of medicine, in groups of students, for the interpretation of the chest radiography.

**Methods:** The research team adapted the model of Peyton as follows: First step: The internist teacher described an X-ray chest image. Second step: The teacher repeated the description of the chest radiography explaining the systematic approach previously employed. Third step: The teacher invited every student to identify in an orderly manner each of the chest structures on the radiography, as he himself explained in step 2. Fourth step: Every student described without help at least one chest radiography. A check list for evaluation of the fourth step was elaborated as well as a satisfaction questionnaire. The method was applied to groups of 5 students.

**Results:** Our adaptation of the Peyton's approach was applied in 50 medicine students. More than 93% was "fairly satisfied" or "very satisfied" with the method. 84% of the students agreed totally with that repetition helped them in the reflection process of describing the radiography. Only 4 students demonstrated to feel bad when they had to describe their findings in front of their companions. 100% felt capable of describing an X-ray image by themselves and they all would recommend the method to other students. Each of the items of the checklist was assessed by at least 80% of the students.

**Conclusions:** We have adapted the Peyton's four-step approach to the peer education of medical students receiving practical instruction during the last years of their degree, applied to the interpretation of the chest radiography. The students demonstrated high levels of satisfaction with the method. According to the results obtained in the evaluation checklist our adaptation of the method can be considered as a useful tool to learn how to properly interpret chest radiographies.

## Mesenteric panniculitis

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**Introduction:** Mesenteric panniculitis is a chronic inflammatory process, rare and involving the adipose tissue of the mesentery. The etiology is unknown and has been suggested, among other things, autoimmune disease, trauma or cancer.

**Case report:** We describe a case of a 74 years old patient, male gender. With history of hypertension, dyslipidemia, pacemaker carrier, stroke, dysphagia, Parkinson's disease, depressive syndrome, multiple hospitalizations for pneumonia. Usually treated with omeprazole, bisoprolol, levodopa + benserazide, paroxetine, betahistine, permixon, clorazepate dipotassium, melperone hydrochloride, furosemide, rasagiline, acetylsalicylate lysine, simvastatin and vitamin D3. Admitted for worsening of the usual pattern of dyspnea with productive cough with 1 day of evolution, recurrent episodes of abdominal pain and acute urinary retention. At the physical examination he was prostrate, pale, hemodynamically stable, with no changes to the heart and lung auscultation; abdomen painful on palpation, with defense and palpable bladder globe, without peripheral edema. Analytically with normocytic and hypochromic anemia with 11.4 g/dL hemoglobin; leukocytosis 13.2 with neutrophilia 11.8 and C-reactive protein 9.1 mg/dL; normal renal function; total bilirubin 1.6 mg/dL; direct bilirubin 0.44 mg/dL. Urine and blood culture negative. CT of the chest, upper abdomen and pelvis: 5 mm calcium caliceal calculation in the right kidney, unobtrusive. No ureterohydronephrosis. Catheterized bladder, "empty". Signs of nonspecific mesenteric panniculitis, particularly in the upper left quadrant. Cardiomegaly and pacemaker. Densifications of the lung parenchyma in the middle lobe and both lower lobes, with diffuse distribution suggestive of acute pneumonic inflammation/infection. Upper endoscopy and colonoscopy unchanged. Admitted, therefore the diagnostic mesenteric panniculitis, community-acquired pneumonia and acute urinary retention.

**Discussion:** Mesenteric panniculitis is a benign disease, with nonspecific clinical. Although the definitive diagnosis is histological, the findings of computed tomography are allowing specific diagnosis.

## Alcohol consumption modulates the association between the rs1746661 in the irisin gene and HDL-cholesterol in a Mediterranean population

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**Objectives:** Irisin has recently been described as a novel myokine, which reduces visceral obesity and improves glucose metabolism in mice. Thus, polymorphisms in the gene encoding irisin,

fibronectin type III domain containing 5 (FNDC5), may be associated with type 2 diabetes mellitus (T2DM), blood pressure and dyslipidemia in women with T2DM. Our aims were to analyze the association between FNDC5 gene variant and plasma lipid levels, as well as their modulation by alcohol consumption.

**Methods:** We analyzed the participants in the PREDIMED-Valencia Study (n=1094, aged 67±7 years), a randomized controlled trial aimed at assessing the effects of the Mediterranean diet (MedDiet) in the prevention of CVD. Plasma lipid were measured and rs1746661 (G/T) FNDC5 variant was determined. Alcohol consumption was measured by validated questionnaires. We calculated alcohol intake (in g/d) for each individual on the basis of the type and amount of alcoholic beverages consumed.

**Results:** The genotype frequencies of FNDC5 rs1746661 polymorphism were 63.5% TT, 31.4% GT and 5.1% GG. A recessive association was observed with HDL-cholesterol levels: TT 48.5 mg/dL and G carrier 52.6 mg/dL (p=0.045). This polymorphism was not associated with total cholesterol, LDL-cholesterol or triglycerides. 43.4% of the population not consumed alcohol. To analyze the HDL levels as alcohol consumption we detected TT 51.7 mg/dL and G carrier 52.4 mg/dL (p=0.786) in nondrinkers, and TT 45.8 mg/dL and G carrier 52.9 mg/dL (p=0.019) in drinkers.

**Conclusion:** Our results suggest that the association between FNDC5 polymorphism and HDL-cholesterol is modulated by alcohol consumption.

## Genetic variation in the hepatic uridine diphosphate-glucuronyltransferase gene, bilirubin levels, type 2 diabetes and all-cause mortality in a Mediterranean population

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**Objectives:** The hepatic uridine diphosphate-glucuronyltransferase (UGT1A1) gene encodes hepatic uridine diphosphate-glucuronyltransferase, which is a major enzyme in bilirubin (BIL) conjugation and in regulation of BIL levels. Several works have observed consistent associations between some UGT1A1 polymorphisms and plasma BIL concentrations. Perception of BIL has undergone a transformation, although BIL has well-documented neurotoxic effects in infants, current evidence indicates mildly elevated BIL is associated with protection from type 2 diabetes(T2D), cardiovascular disease(CVD) and all-cause mortality in adults. However, more studies are needed to increase the evidence level. Our aims were:1) to analyze the association between genetic variants at the UGT1A1 gene and plasma BIL levels; 2) to estimate the association between the most relevant of these variants and T2D, CVD incidence and all-cause mortality in a high cardiovascular risk Mediterranean population.

**Methods:** We prospectively analyzed the participants in the PREDIMED-Valencia Study (n=1094). PREDIMED is a multicenter randomized trial aimed at assessing the effects of the Mediterranean diet (MedDiet) in the prevention of CVD. Participants were high cardiovascular risk subjects (aged 67±7 years) who fulfilled at least one of two criteria: T2D (47% at baseline) or 3 or more risk factors. We identified 44 CVD cases and 48 deaths after a median 5 years follow-up. Multivariable Cox regression models were fitted to estimate the risks. BIL levels were not available in the PREDIMED participants and were measured in similar sample of the PREDIMED PLUS participants (n=100) recruited in the same field center. Polymorphisms in the UGT1A1 gene (n=32) were determined with the HumanOmniExpress Illumina assay.

**Results:** Several polymorphisms were associated with BIL levels. The rs6742078(G>T), which has been previously discovered as the top ranked SNP in a GWAS of total BIL, was strongly associated with BIL levels in our population (0.50±0.13 mg/dL in GG (44%), 0.61±0.25 in GT (46%) and 1.06±0.41 in TT (10%); p=4.2x10E-8). We selected this polymorphism to analyze the association with T2D, CVD and total mortality in the PREDIMED participants. We did not obtain significant associations between the rs6742078 polymorphism and T2D (p=0.48), CVD incidence (p=0.98) or total mortality (p=0.23).

**Conclusion:** Although the rs6742078-UGT1A1 polymorphism is strongly associated with BIL levels, this SNP is not associated with a reduced risk of the analyzed diseases in this Mediterranean population.

## A challenging case of inflammatory myopathy

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**Introduction:** Inflammatory myopathies are the largest group of potentially treatable myopathies and constitute a heterogeneous group of disorders – dermatomyositis, polymyositis, necrotizing autoimmune necrotizing myositis and inclusion-body myositis.

**Case report:** A 60 years old woman is diagnosed with chronic liver disease of unknown etiology (primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis, overlap syndrome?) after an exhaustive complete study in 2010. Currently in Child-Plugh C stage, treated with oral corticosteroids and in liver transplant list. Also medicated with simvastatin. She has a first hospital admission for the study of a chronic dry cough – diagnosis of a pulmonary hypersensitivity pneumonitis/extrinsic allergic alveolitis, but no known allergen. After a month, she is again hospitalized – clinical picture: subacute onset of decreased muscle strength in the inferior limbs and asthenia. During hospitalization, she presented with worsening encephalopathy, liver cytolysis (transaminases >1000 U/L) and muscle cytolysis (creatinine kinase >50000 U/L and myoglobin >12000 U/L). Treated with pulses of methylprednisolone and acetylcysteine infusion for 72 hours, but no response. The muscle-biopsy showed severe signs of necrotic fibers likely associated with necrotizing myositis of probable autoimmune etiology. The patient evolved with rapid

deterioration and multiorgan dysfunction, was transferred to the intensive care unit and passed away.

**Discussion:** We describe and discuss a case of a rare combination of diseases (hepatic liver disease, interstitial lung disease and inflammatory myopathy).

## Frailty in pluripathological patients. Clinical characteristics and associated factors

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**Objectives:** The aim of this study is to know the prevalence of frailty in a sample of pluripathological patients (PP) in a hospital scope –including from the hospitalization and the consulting room, as well as to establish clinical-epidemiological characteristics, comorbidities and associated factors.

**Material and methods:** We conducted a cross-sectional multicenter study through weekly prevalence studies. We included the PP who were identified in the studies and that had signed their consent. Those who were carrier of metallic devices, had an amputation or were in the agony stage were excluded. Demographic, clinical, analytical and comprehensive assessment variables were surveyed and we determined whether each one of them met the Fried and cols frailty criteria. We carried out a descriptive study of the clinical characteristics of the patients with frailty, as well as a bivariate analysis in order to know the main risk factors associated with its presence. The analysis of the data was carried out by means of SPSS statistics 20.0.

**Results:** A total of 214 PP that belonged to the Hospital Universitario Virgen del Rocío and the Hospital San Juan de Dios (Bormujos) were included (58.3% male, average age 77.3 years old). 64% of them (138 patients) met frailty criteria. Among the patients with frailty, the average age was 78.4±7.2 years old, 50.7% of them were female. The category of PP more frequent was the A category: cardiovascular (88.3%), the average of the pluripathology categories was 2.8±0.9 and of comorbidities, 6±2.1 per patient. The number of chronicle prescription medicines was 9.6±3.4. Average Barthel 54.1±28 and PROFUND index 8.2±4. The factors associated with frailty were: female sex (50.7% vs 22.4%; p=0.000), age (78±7.2 vs 71±8.4), institutionalization (6.8% vs 0%; p=0.020), need for a carer (54.6% vs 9.9%; p=0.000), category G: chronic anemia or neoplasia (21.4% vs 11%; p=0.050), category H: life-limiting osteoarticular disease (16.8% vs 2.7%; p=0.003), category E: neurological diseases at the expense of categories E2: neurological disease with motor deficit (5.1% vs 0%, p=0.049) and E3: neurological disease with cognitive impairment (11.7% vs 2.7%; p=0.028), category A1: heart failure (68.6% vs 47.7%, p=0.003), the presence of delirium in the last hospitalization (18.3% vs 2.7%, p=0.001), degree of dyspnea (NYHA and/or MRC), oxygen therapy at home (25.4% vs 11.3%, p=0.017), PROFUND index (8.2±4.1 vs 3.1±3.2, p=0.000), BARTHEL functional scale (54.1±28.7 vs 90.1±15.7, p=0.000), as well as low muscle mass (26.5±9.5 vs 32.4±1.8, p=0.000) and less total body water (40.2±9.5 vs 43.5±9.1, p=0.002).

**Conclusions:** We noticed high frailty prevalence in our sample of pluripathological patients included in the study, up to 64%. Frailty was associated with heart failure, chronic neurological diseases, neoplasias/chronic anemia, life-limiting osteoarticular diseases, certain typical symptoms of advanced stages of chronic diseases, with the functional limitation and with a worse scale PROFUND.

## Severe multiorgan involvement in systemic sclerosis

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**Introduction:** Systemic sclerosis (SSc) is a multisystemic autoimmune disease with microvascular involvement and activation of fibroblasts associated with fibrosis. The severe multiorgan involvement most often occurs early in the course of disease.

**Case report:** We present the case of a 69 years old man admitted to a hospital because of syncope. He complained about weakness, weight loss (10 kg in 6 months), arthralgia, dysphagia, retrosternal heartburn, gastroesophageal regurgitation with years of evolution and Raynaud phenomenon in the winter months with ischemic digital ulcers. He had anemia diagnosed 2 months earlier with occult blood in the stool positive. On exam stood out sclerodactyly, thickening and changes in skin pigmentation and telangiectasia. Blood tests showed: Hb 10.7 g/dL, MCV 77.6 fL, MCH 24.3 pg, creatinine 1.40 mg/dL, iron 22 ug/dL, ferritin 29.9 ng/dL, transferrin 4%, total iron-binding capacity 490 ug/dL, vitamin B12 161 pmol/L and folic acid 4.76 nmol/L. Upper gastrointestinal endoscopy showed esophageal candidiasis, sliding hiatal hernia and gastric antral vascular ectasia ("watermelon stomach") and colonoscopy showed colon angiodysplasia and diverticula of sigmoid colon. CT angiography of the thorax excluded pulmonary thromboembolism and showed ectasia of the arterial pulmonary trunk and its main branches, dilation of the thoracic esophagus, diffuse ground glass with cylindrical bronchiectasis, inflammatory process secondary to aspiration events and pulmonary emphysema. Respiratory function tests showed decreased diffusing capacity of the lung for carbon monoxide (39% of predicted value) and desaturation in effort. The immunological study showed positive antinuclear antibodies, centromere pattern 1/1280, and autoantibodies associated with SSc (CENP-A and CENP-B antigens) strongly positive.

**Discussion:** The authors made the diagnosis of SSc with multiorgan involvement: pulmonary (interstitial lung disease), gastrointestinal (esophageal candidiasis, "watermelon stomach", angiectasis and colon diverticula, iron deficiency anemia, malabsorption syndrome with vitamin B12 and folic acid deficiencies), renal (chronic kidney disease), vascular (Raynaud phenomenon and probably pulmonary hypertension) and skin (sclerodactyly and telangiectasia). It is necessary to invest in identifying risk factors that can predict the multiorgan involvement of this pathology; as well as specific organ-system damage for a close monitoring of these patients and the early begin of appropriate therapy.

## Palliative care in Egypt: the experience of the Gharbiah Cancer Society

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**Objectives:** The need for palliative care in middle and low resources countries, including Egypt, is emerging. The Gharbiah Cancer Society (GCS) is a nonprofit, nongovernmental hospital, located in Tanta, the Capital of the Gharbiah governorate in the mid-Nile Delta. The Society provides acute care to patients with cancer including surgery, chemo-, and radiotherapy. Review of 9 year-data of Gharbiah population-based cancer registry from 1999 to 2007 revealed 3480 cancer cases/year, with age standardized rate (ASR) of 161.7/100,000 for males & 120.8/100,000 for females. About 70 % of cases present in advanced stages (III&IV) with liver cancer the most frequent cancer in male and breast cancer as the most frequent cancer in females. The GCS started a comprehensive palliative care services in April 2011 with 10-bed inpatient unit and 6 days/week outpatient clinic. All palliative care equipment was provided by public donations.

**Methods:** Through collaboration with National Cancer Institute, Bethesda, Maryland and the San Diego Hospice and the Institute for Palliative Medicine and Middle East Cancer Consortium, a fellowship training program was developed for a medical oncologist in palliative medicine and End-of-Life Care training course for nurses.

**Results:** The program succeeded in convincing local health authorities to increase the recommended opioids dose and to allow more physicians to prescribe opioids for cancer pain. In a period of 24 months, symptom management and palliative care were provided to 195 patients with advanced malignancies. The opioids consumption was increased by 30 folds.

**Conclusions:** The major challenges for the program were inadequate public and health professionals' awareness of palliative care services and lack of vehicles and finances to cover home visits. The initial results of the program warrant allocating more resources for coverage of a large number of trainees and instituting a home visits program.

## Prognostic value of physical function test in elderly hospitalized patients

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**Objectives:** To discern if physical function test are better mortality predictors than muscle mass in elderly hospitalized patients, we analyzed the prognostic value of muscle mass malnutrition and compared it with physical muscle function tests, including the six-minute walking test (6MWT) and hand grip strength.

**Methods:** We included the ankle brachial index (ABI) to assess arterial disease, related to muscle atrophy due to hypoperfusion.

We also analyzed the relationship of ABI with malnutrition, physical function tests and survival. We studied 310 hospitalized patients older than 60 years. To assess nutritional status, we determined BMI, triceps skin fold and mid-arm muscle area; we performed a subjective nutritional assessment; and evaluated the degree of inflammatory stress. We assessed physical function by hand grip strength and 6MWT. We evaluated arterial disease by ABI.

**Results:** 41 patients died during hospitalization; 269 were discharged and followed for a mean 808 days, reaching a mortality of 49%. Muscle malnutrition was frequent and was related to mortality, but the best predictors were physical function tests: inability to perform the 6MWT and low handgrip strength.

**Conclusions:** Function tests were closely related to each other and correlated with nutritional data. Reduced ABI was related to impaired nutritional status, physical function tests and mortality.

### **Study of the perceptions, attitudes and uses of Spanish elderly chronic patients and caregivers on the Information and Communication Technology for health ("e-health")**

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**Objectives:** An increasing interest exists for the use of the new technologies when addressing the health problems of the elderly with chronic diseases and its implementation in our environment constitutes a strategic objective of the health system managers. But the attempt of implantation of tools that favor the development of the new ICT in any area must begin for knowing the opinions, uses and expectations of the potential users. The present work is orientated towards the study in our environment of the perceptions, attitudes and uses of the Spanish elderly chronic patients and/or their caregivers on the ICT for health.

**Methods:** We designed a questionnaire that was applied to non selected elderly patients (over 64 years) with chronic pathology and/or to their caregivers, assisted at the service of internal medicine "The Montalvos" of the University Hospital of Salamanca. The questionnaire was developed after 1) a bibliographical review; 2) adjustment of the items by the research team; and 3) a pilot test in a group of 10 patients/caregivers. The questionnaire (voluntary and anonymous) was administered in writing during the hospitalization period of the patients.

**Results:** An 18 items written survey was elaborated which has been applied up to the moment to 32 patients and 55 caregivers. The internet appears as an alternative source of information related to health issues in 12.5% patients and in 32.7% caregivers, though the confidence level that inspires this source is low when compared with the information obtained directly from health professionals. The surveyed individuals acceded for the most part to private webs (57.5%), being the obtaining of information about diseases the most frequent topic of search (46%). The lack of reliability of the information gathered from the internet was the major barrier that limited its use (63.2%). The access to

online social networks, e-health services and the use of health related "apps" (except for some telecare systems) was scarce.

**Conclusions:** The development and application of a specific survey has allowed us to know that in our Spanish environment there exists a low degree of utilization of the new ITC for health among the elderly patients and their caregivers. Demographic factors, socioeconomic development variables and the perception of lack of reliability of the new technology could be responsible for this finding.

### **The internist teacher: development of a method of structured reflection to instruct in diagnostic abilities to Spanish medical students**

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**Objectives:** Structured reflection is a method known to improve the diagnostic accuracy of the medical professionals when facing complex problems and of counteracting the possible errors produced by cognitive biases. The procedure consists, essentially, of the exposition of organized questions that guide the logical process of the diagnostic thought in the sense of confirming or of rejecting the intuitively proposed initial diagnostic hypotheses. Nevertheless, the method has not been applied, as far as we know, in medical students of our cultural and educational environment, being the development and implantation of this the aim of our investigation.

**Methods:** The research was carried out at the service of Internal Medicine "Los Montalvos" of the University Hospital of Salamanca (Spain). Firstly, we elaborated clinical cases related to common clinical problems in Internal Medicine and we prepared for every case a scheme of structured reflection leading to the establishment of the most plausible diagnosis based on the given information. Secondly, we prepared a program and a schedule of the working sessions of structured reflection to be implemented in the practical training of the students of the last three years of the degree of Medicine. Finally, the method was evaluated by means of satisfaction questionnaires.

**Results:** 8 clinical cases were elaborated, for consensus of the research team, each one with its corresponding scheme of structured reflection that included, in essence: the establishing of an initial diagnosis, the discussion on the information that would allow to support or to reject this diagnosis and the consideration of other findings that could be found in case the initial diagnosis was the correct one. This material was used in work sessions of five students, which included a period of individual reflection, followed by 20 minutes of guided group discussion. The survey showed a high level of global satisfaction (higher than 90 %) in all the investigated items both among students and professors.

**Conclusions:** We have elaborated a method of structured reflection to foster Spanish medical students' acquisition of diagnostic competence. This method shows now its applicability in the Spanish context with a high degree of satisfaction on the part of the participants (students and teachers) taking part in it.

## Palliative care in Republic of Macedonia

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**Objectives:** According to the World Health Organization palliative care is an active and complete care for patients with terminal illness. Control of pain, symptoms, and psychological, social and spiritual problems are of special importance. The purpose of palliative care is achievement of the highest possible quality of life of the patient and his family. Palliative care covers the period from the diagnosis of advanced disease until the end of the period of mourning for ailing loss. Palliative medicine implies adequate medical care for patients with active progressive and advanced disease, with limited prognosis, with a focus on care for the quality of life. The duration of palliative care can vary from a few years to weeks or days. Palliative care can take place in different environments. The aim of this study was to show types of patient who need palliative care in Republic of Macedonia, and the average time of their hospitalization.

**Methods:** A retrospective analysis of patients hospitalized in PHI Gerontology Institute 13 November Skopje – Hospice Sue Ryder for a period of 7 years.

**Results:** Development of palliative care in the Republic of Macedonia started in the 90's of last century by creating a national plan for palliative care. Later were open specialized institutions – Sue Ryder hospices, which provide palliative care to around 600 patients a year. The motive for hospitalization in this palliative care institutions usually are malignant diseases (73%). Most of them are malignant processes on digestive system (31,6%), urogenital system (26,3%), respiratory system (14,4%), breast cancer (12,4%), central nervous system (8,3%) and less common forms of malignant diseases. The average time of treatment was 98, 9 days (1-273).

**Conclusions:** In both hospices is performed one of the main characteristics of palliative care that is meeting the complex needs of the patients, treatment of pain and other physical, psychosocial and religious needs. Next steps for palliative care in Republic of Macedonia are improvement of the standards for palliative care, dispersion of the domiciliary palliative care and creation of day-care hospitals, introduction of palliative care in educational programs.

## Characteristics of patients treated with oral anticoagulation when they are hospitalized in internal medicine

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**Objectives:** Our first purpose is to describe the number of hospitalized patients with oral anticoagulation (vitamin K agonists), that are in therapeutic range. Secondly we will determine of those patients who are over optimal range, if it was due to change of medication. Which ones are hospitalized due to adverse effects of oral anticoagulants and those who are with new therapies to describe them.

**Methods:** It is an observational study. We collected patients from January 1st 2014 until December 31st 2014 which were hospitalized in the internal medicine service and who were previously treated with oral anticoagulation. The number of patients needed to have a significant test is 460, so an intermediate analysis was made of 230 patients.

**Results:** 230 patients were collect for the test, whose ages were between 55 and 101, medium age was 81. 115 were females and 115 where males. The cause of hospitalization were in the majority due to infections – 106, cardio-respiratory insufficiency – 81. For bleeding were only 17 patients and for other causes – 26. Bleeding complications were observed in 12 patients (urinary, skin hematoma, digestive and hemoptisis). From the 230 patients treated with oral anticoagulation, 214 are treated with classical anticoagulation, 16 with the new ones. The prior cause of anticoagulant is atrial fibrillation in 198 patients, then valvular prosthesis in 18 and venous thromboembolic disease in 12. About the therapeutic range of those treated with classical anticoagulation, 82 patients were in optimal range and 133 were not in optimal range (46 were under optimal range and 87 was over optimal range). 32 of all patients had previously changed the medication; the most common medication was antibiotics and corticoids.

**Conclusions:** Studies have already described that patients treated with classical oral anticoagulation are often out of therapeutic range even when have no other illness or complication. In Spain the prevalence of poorly controlled anticoagulation was 47%. Mean time in therapeutic range was 63.8% in cardiology clinics. What we wanted to describe is what happens with international normalized ratio control when an acute process is on course, when the patients have an infectious disease, a cardio-respiratory deficiency or and electrolytic disorder. Our study shows that the majority (57%) of the patients treated with classical oral anticoagulation are not in therapeutic range while they have an acute illness so they are not protected against thromboembolic disease.

## Association between diabetes mellitus and dementia in geriatric patients

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**Objectives:** Diabetes mellitus (DM), describes a group of metabolic diseases in which the person has high blood glucose either because insulin production is inadequate, or because the body's cells do not respond properly to insulin, or both. An estimated 387 million people have DM worldwide. The global prevalence is projected to be 4.4% by 2030. Dementia is type of cognitive dysfunction and is an overall term that describes a wide range of symptoms associated with a decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities. Dementia affects 36 million people and is rising in prevalence worldwide, especially among the elderly. Nearly half of the people over 85 years of age have dementia. The aim of the present study was to investigate the association between DM and dementia in geriatric patients.

**Methods:** A retrospective analysis of patients hospitalized in



PHI Gerontology Institute 13 November Skopje for a period of 5 years.

**Results:** In this period were hospitalized 1640 patients with an average age of 79.4 years. Analyzing their medical history we learn that among other diseases 401 patients were treated for DM, 425 patients were treated for dementia. Insulin-dependent were 44.6% diabetic patients, and 55.4% had diabetes treated with oral therapy. In the group of patients treated for dementia was included all types of dementia (Alzheimer's disease, vascular dementia, Lewy-body dementia, Parkinson's disease and Creutzfeldt-Jakob disease). Dementia diagnosis was determined during the follow-up period from hospital records indicating an admission associated with dementia or the use of prescribed dementia medications. Comparing DM and dementia we find that 23% of the patients who were treated with diabetes have some form of dementia.

**Conclusion:** Analyzing the data we come to conclusion that there is association between diabetes mellitus and dementia and that DM and its complications may increase risk for developing cognitive dysfunction, including all types of dementia among geriatric patients.

## Prognosis of recovering from acute confusional syndrome

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**Objectives:** Elderly patients hospitalized with an acute confusional syndrome (ACS) in an internal medicine department have higher mortality. The primary outcome of this study is finding if patients with ACS related to sepsis have more mortality than those with ACS due to other reasons.

**Methods:** We studied 119 patients hospitalized in an internal medicine department, 49 men and 47 women, with a mean age of 76 years; 47 with ACS and sepsis; 36 with ACS without sepsis and 36 with sepsis without ACS. We analyze comorbidities, characteristics of ACS (agitation, orientation, attention, mental status with Glasgow scale, hallucinations and abnormal thinking), the evolution of ACS the first and third day of hospitalization, and hospital mortality and later mortality. We also measure in those patients and in 27 controls levels of S100b, alfaTNF, IFN gamma, IL10 and IL6.

**Results:** 21 patients died during hospitalization, 9 (19,1%) in ACS and sepsis group, 7 (19,4%) in ACS group, and 5 (13,9%) in sepsis groups, but we did not find statistical difference. Patients with chronic obstructive pulmonary disease (COPD), peripheral vascular disease, proliferative syndromes, cirrhosis, comorbidities, more than 5 drugs intake, absence of fever, organ failure, desnutrition, frailty (measure with Canadian Study of Health and Aging), high score in Pfeiffer tests, decrease in serum bicarbonate and transferrin had more mortality. We also found that levels of S100b, alfaTNF, gammaIFN gamma, IL10 and IL6 were increased in patients compare with controls. And IL10 and IL6 were higher in patients with sepsis against confused. We did not find connection

between pro-inflammatory cytokines and S100b and mortality. The absence of recovery from the ACS was highly associated with mortality independent of the cause. Also if the patients only recover in some aspects of the ACS the mortality was higher.

**Conclusion:** We found statistical association between the improvement of mental status (awareness, orientation, agitation and attention) and decrease in mortality in patients hospitalized with an ACS due to sepsis or other cause

## Preventive education for adolescent-adult pertussis: development of an SEIR model and e-learning materials, and student comprehension of them

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**Objectives:** Outbreak of adolescent-adult pertussis became a matter of public concern in Japan. Health education for students to prevent outbreak of pertussis is important. Therefore, we have investigated preventive education of infectious diseases in school. In this study, we developed a pertussis simulation model and e-learning materials that students could easily understand.

**Methods:** Simulation model: we made an SEIR model. the definitions are as follows: N: total population, S(t): susceptible population, E(t): exposed population, I(t): infectious population, R(t): recovered population,  $N = S(t) + E(t) + I(t) + R(t)$ . E-learning materials: e-learning materials comprised 7 chapters, 1) structure and toxin of Bordetella pertussis (B. pertussis); 2) international epidemiology of pertussis; 3) prevention of droplet infection of pertussis; 4) diagnosis of adolescent-adult pertussis; 5) treatment of pertussis; 6) vaccination of pertussis; and 7) simulation model of pertussis. Assessment of e-learning materials: We performed a lecture with the materials for university students, and had a questionnaire about the materials.

**Results:** Simulation model: in the SEIR model, we drew simulation curves using differential equations.  $dS(t)/dt = -\beta S(t)I(t)$ ,  $dE(t)/dt = \beta S(t)I(t) - \alpha E(t)$ ,  $dI(t)/dt = \alpha E(t) - \gamma I(t)$ ,  $dR(t)/dt = \gamma I(t)$ ,  $\beta$ : rate of infection,  $\alpha$ : rate of attack,  $\gamma$ : rate of recovery,  $R_0$ : basic reproduction number =  $\beta N / \gamma$ . By using scroll box, students could change N, I(0),  $R_0$ ,  $\alpha$ ,  $\gamma$  and rate of immunization. E-learning materials: 1) Structure of B. pertussis and function of pertussis toxin, filamentous hemagglutinin and pertactin were explained. 2) Epidemiological data of pertussis among the United Kingdom, the United States and Japan were compared. 3) Risk of microorganism contamination by cough or sneezing was explained to prevent droplet infection of pertussis. 4) Clinical diagnosis, laboratory examination and serodiagnosis were presented to diagnose of adolescent-adult pertussis. 5) Effective antibiotics for B. pertussis were explained as recommended treatment of pertussis. 6) Bivalent, trivalent and tetravalent vaccine were described as vaccination of pertussis. 7) The SEIR simulation model of pertussis was explained. Assessment of e-learning materials: About 85-97% students answered that they understood about contents of the materials.

**Conclusion:** We developed effective e-learning material for prevention of adolescent-adult pertussis.

## Non-communicable diseases and related risk factors in young people: prevalence and trends

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**Objectives:** To study the prevalence and trends of the modifiable risk factors of non-communicable diseases (NCDs) among students in Kabardino-Balkarian Republic in the period of social and economic reforms in order to develop and implement of scientific-based guidelines to preserve and improve the health of students.

**Methods:** Since 1999 to 2011 four cross-sectional population-based studies of the university students of the Kabardino-Balkarian Republic were conducted. 613 boys and 929 girls were surveyed by the standard epidemiological methods. The average age of the surveyed students was  $20.7 \pm 5.8$  years.

**Results:** The study involved of students which is characterized by high frequency modifiable risk factors of NCDs: physical inactivity (76.3%), high levels of personal anxiety (41.8%) and reactive anxiety (28.9%), smoking (15.5%), excessive body mass (10.5%) and hypertension (5.7%). In 32.8% of students several risk factors were identified. During the study reducing of the prevalence of hypertension, high levels of personal anxiety and reactive anxiety and physical inactivity was found in 2005 compared to 1999 with subsequent increases in 2011, reducing the frequency of smoking and the number of students with one risk factor and increase – with a combination of several risk factors ( $p < 0.05-0.0001$ ).

**Conclusions:** The high prevalence of risk factors of NCDs and the negative trends among young people of the Kabardino-Balkarian Republic indicates the need for the creation and implementation of regional prevention programs. The low level of health of the examined students served as the basis for the development of health saving program intended to offer comprehensive assessment of students' health and their lifestyle with the follow-up analysis of the obtained data, development and implementation of educational, health-improving and prophylactic projects. The key to effectiveness of the preventive programs is to integrate the efforts of the educational and health institutions and the whole society. Early detection and prevention of risk factors of NCDs may suspend the development of chronic disease in adulthood.

## Comorbid pathology structure in somatic patients

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**Objective:** To study the structure and combinations of nosologies forming the comorbid pathology that caused death of the patients in the clinic of internal medicine.

**Methods:** 2751 fatal cases with final diagnosis consisting of 2 or more nosological units in the Municipal Clinical Hospital

of internal medicine were studied. Among the deceased there were 1035 (37,6%) males, 1716 (62,4%) females at the age of  $69,4 \pm 11,5$  and  $76,0 \pm 9,8$  ( $p < 0,001$ ), accordingly. The average age came to  $73,5 \pm 10$  years old.

**Results:** The cardiovascular diseases prevail in the comorbid structure: arterial hypertension (AH) and ischemic heart disease (IHD) were diagnosed in about 80% of the cases; cerebrovascular diseases were revealed in 70% of the cases. Post-infarction and atherosclerotic cardiosclerosis were revealed in 1641 (59,6%) cases. Wherein brain infarction in 92% of the cases goes together with AH, and in 83,8% – with the urinary system diseases, in 68,7% – with the chronic obstructive pulmonary disease (COPD), in 68% – with IHD, in 30% – with pancreatitis. Myocardial infarction combines with AH in 92% of the cases, in 75,4% – with the urinary system diseases, with COPD – in 71% of the cases, in 34% – with the diabetes mellitus, in 32% – with the cerebrovascular diseases. The urinary system diseases were diagnosed with the same frequency (72,7%): among them – the chronic pyelonephritis (74,3%), urinary stone disease and cystitis – in 63 and 64 cases (2,3%) accordingly. The diseases of the respiratory system were revealed in 73,3%, in 1977 cases (71,9%) they were represented by the COPD. Chronic pancreatitis (28,6%) and the gall bladder diseases (22%) were most frequently diagnosed among the digestive system pathologies (22%).

**Conclusion:** Thus, the most frequent pathologies participating in forming comorbidity in somatic patients are the diseases of the cardiovascular system of atherosclerotic genesis, COPD, and chronic diseases of the urinary system.

## Risk factors in patients with comorbidity

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**Objective:** To study the degree of incidence and the structure of risk factors (RF) in the patients with comorbidity.

**Methods:** Cross-sectional analysis to identify RF in the patients with comorbidity. The research includes 241 patients with comorbidity. Among them there were 146 males (60.6%; the average age of  $62 \pm 5.2$ ) and 95 females (39.4%; the average age of  $65 \pm 4.8$ ). Averaged Charlson comorbidity index was 3.2 points. The most frequent nosologies in the comorbidity structure were different forms of coronary artery disease (53%), chronic cerebrovascular disease (32%), chronic obstructive pulmonary disease (12.3%), osteoarthritis (15.2%), malignant tumors of various stages (9.5%) and benign prostatic hyperplasia (5.7%).

**Results:** The presence of risk factors was diagnosed in 87% of the patients. The existence of one of these risk factors was detected only in 4% of all the cases, the combination of 2 risk factors was in 27% of the cases, 3 or more ones were in 69% of the patients. Among the most frequent primary risk factors there was smoking (71.9%) with the index of smoking at an average of 144, alcohol abuse (23.8%) and obesity (54.3%) with average BMI  $32.6 \pm 2.7$ . Among the most frequent secondary risk factors there was arterial hypertension (87.6%), diabetes (23.3%) and dyslipidemia

(46.2%). At the outpatient stage there was correction of primary risk factors in none of the cases. Among 184 patients with arterial hypertension 151 patients (82%) received antihypertensive therapy. One third of them had only monotherapy. At the time of examination 12 (24.5 %) of 49 patients with diabetes had the disease decompensation (according to glycemic level). 7 patients received no hypoglycemic therapy at all. 59.2% of the patients received sulfonylurea medications, 16.3% of the patients received metformin, Combined hypoglycemic therapy was prescribed for only 10.2% of the patients. Only one in two patients with dyslipidemia received lipid-lowering therapy.

**Conclusions:** Most of the patients with comorbidity have risk factors. Most commonly they have the combination of three risk factors or more at the same time. At the outpatient stage there is correction of mainly secondary risk factors. The lack of timely correction of the primary risk factors is likely to affect the formation and progression of comorbid pathology.

### Sudden arrhythmias as a risk factor of cognitive disorders

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**Objective:** To examine the peculiarities of psycho-emotional and cognitive disorders in patients with sudden-onset arrhythmia.

**Material and methods:** 48 patients was observed with a sudden-onset rhythm disturbance: a paroxysm of atrial fibrillation (AF) at 27 (56%), atrial flutter – 9 (19%), ventricular tachycardia 4 (8%), supraventricular tachycardia 8 (17%). Male were 29, female – 19. The average age was 64.2±3.7 years old.

**Results:** In analyzing the results of neuropsychological testing in patients during sudden arrhythmias detected cognitive deficits manifested by a decrease in oral-aural short-term, long-term memory and productivity memorizing 27.1% (p=0.00), 39.6% (p=0.00), respectively, as well as visual short-term and long-term memory to 29.2% (p=0.00) and 25% (p=0.00), respectively, compared to the control group. Furthermore, it was revealed slowing of psychomotor speed (tables Schulte) to 45.8% (p=0.00) and reducing structurally – spatial gnosis (sample Yerkes) to 8.3% (p=0.00) compared to control group. As for their own assessments of memory and patients' attention, they, on the contrary, were higher in patients with rhythm disturbance. After the restoration of sinus rhythm occurred improvement in cognitive function. Thus, when performing the sample proofreading decreased the number of errors at 50% (p=0,01), which indicates the improvement of attention, psychomotor speed increased at 21% (p=0,02) (table Schulte) also observed increasing in performance audioverbal short-term, long-term memory and memorization productivity, compared with the initial results. Psycho-emotional status of patients during and after restoration of sinus rhythm was characterized by a high frequency of anxiety and depressive disorders.

**Conclusions:** The majority (83.3%) of patients with sudden arrhythmia observed cognitive dysfunction, which decreases after restoration of sinus rhythm. Adequate and timely identification of intellectual – mental and anxiety and depressive disorders and their correction can improve the results of treatment.

### Morbidity with temporary disability to work in employees of poultry farms in the Republic of Mordovia

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**Objectives:** Heals maintenance of the employed population has always been an issue of concern in present-day medicine. Incidence of morbidity with temporary disability to work (MWTd) is both an indication of the working conditions and the efficacy of therapeutic-preventive work. Our aim was to study MWTd among the employees of poultry farms in the Republic of Mordovia (RM) and find out correlation between occurring diseases and working conditions.

**Methods:** Analysis of the workplace charts was made to evaluate the working conditions of the employees of «Oktyabrskaya» and «Atemarskaya» poultry farms in RM; analysis of medical report forms 16-BH was made to evaluate annual incidence and duration of sickness per 100 of the employees (MWTd structure). The statistical data processing was performed on the basis of IBM SPSS Statistics 19 soft-ware.

**Results:** In the MWTd structure the respiratory diseases top the list in the employees of the poultry farms (54.1%). This is accounted for by the presence of ammonia, hydrogen sulphide and carbon dioxide produced both in the process of birds' vital activity and the decay process of the fodder nest bedding, fluff and feathers. Concentration of organic and inorganic dust amounts to 58.2 mg/m<sup>3</sup>. Bacterial contamination in the poultry yard is from 7000 to 1 mln. and more per 1 m<sup>3</sup>; the total level of microorganisms, in the air of the production area averages 3400±300 colony-producing units/m<sup>3</sup>, of which saprophytes and conventional pathogenic flora are predominant. The second in the list are osteo-muscular diseases (24%). The labor at the farms includes physical exertion and unfavorable microclimatic conditions of work: in incubators and some workshop the air t° is elevated to 28.0-35.5°C both in cold seasons, with 78-90% humidity.

**Conclusions:** In the general MWTd structure of the studied poultry farms the respiratory diseases are predominant. Unhealthy working of conditions (the air contaminated with fragments of dried milk, considerable workloads, the general microbial dissemination) result in the workshops. Prevalence of the respiratory diseases in the employees of the poultry farms over the corresponding indices of the year 2014 among the adult population of RM is authentic (p<0.01).

### Modified Early Warning Score and resource consumption

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**Objectives:** Modified Early Warning Score (MEWS) may serve as decision rule for the admission of medical patients. MEWS

≥4 is associated to a worse prognosis. RAY score allows the evaluation of nursing care complexity. We investigated the impact of MEWS and RAY score on resources consumption in acute medical wards.

**Material and methods:** From 1/1 to 12/31/14 2680 patients (mean age 78 years; 53% F) were admitted to our ward. MEWS on admission was full-filled in 2280, RAY score in 2008 patients. 463 patients (20%; mean age 80.3 years, 54.4% F) had MEWS ≥4, 783 patients (39%; mean age 83.5 years, 62% F) had RAY score ≥23. 250 patients (9.3%; mean age 85.8 years, 61% F) have MEWS ≥4 and RAY score ≥23. We collected the number of laboratory, radiological, US heart scans, nuclear medicine tests, hemotransfusions, and detections of BP, HR and SpO<sub>2</sub> and in-hospital mortality in patients with MEWS ≥4 and RAY score ≥23 and in overall patients.

**Results:** Tests performed in patients with MEWS ≥4 and RAY score ≥23 accounted for 41.7% of all lab tests requested in our ward, 31.3% of all radiological tests, 37.2% of all nuclear medicine tests, 30.3% of all US heart scans, 40% of all hemotransfusions. BP, HR and SpO<sub>2</sub> were detected much more frequent in patients with MEWS ≥4 and RAY score ≥23: 52%, 56%, 57% of all detections were done in that group. In-hospital mortality was also much higher (50% vs 7.7%,  $p=0.0001$ ).

**Conclusion:** Our data show that patients with MEWS ≥4 and RAY score ≥23 (10% of all admissions) absorb over 50% of nurses' work and over 30% of diagnostic services work and have significantly higher in-hospital mortality.

## Electronic medical records enhances clinical audits and research

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**Background:** Information technology is increasingly recognized as an important tool for health services. Of all the health information technology (IT) in use, the electronic medical record (EMR) has the most wide-ranging capabilities and thus the greatest potential for improving quality. Research has demonstrated the quality benefits of electronic documentation and viewing, prescription and test ordering, care management reminders and messaging.

**Objective:** To evaluate the impact of electronic medical records on clinical audits and research.

**Methods:** We measured the time required to complete a clinical audit on VTE prophylaxis in 2013 and 2014, with paper medical record (PMR) and EMR, respectively.

**Results:** In 2013, two independent physicians manually reviewed 2480 PMRs and filled the database for a total of 570 hours plus additional 10 hours for data analysis and discussion. In 2014, two independent physicians identified the queries and one electronic engineer extracted the data from 2681 EMRs in only 12 hours, plus additional 10 hours for data analysis and discussion. New queries could be added midway and VTE prophylaxis performance for single physician could be extracted.

**Conclusions:** EMR with associated statistical software really save time and improve quality of clinical audits. Clinical research

can share the same benefits. Focusing data extraction on single physicians allows to measure single performances and plan individual educational interventions.

## Padua prediction score and improve bleeding risk score as predictors of in-hospital mortality

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**Objectives:** Padua prediction (PPS) and Improve bleeding scores (IBS) are suggested by ACCP 2012 guidelines as useful tools to stratify hospitalized acute medical patients requiring VTE prophylaxis. The items listed in the 2 scores include conditions known to increase in-hospital mortality, such as advanced age, infections, myocardial infarction, active cancer, moderate to severe renal failure, INR>1.5, admission to intensive care unit, etc. The aim of the study was to evaluate if one or both the scores are able to predict in-hospital mortality.

**Material and methods:** Clinical outcomes (in-hospital death or alive at discharge) of all the patients admitted to our ward from 1 Jan 2013 to 31 Dec 2013 and stratified by PPS and IBS were collected.

**Results:** During study period 2676 patients were admitted to our ward. 1957 (73%) had PPS and IBS electronically fulfilled. Among them, 250 (12.7%) died. In-hospital all-cause mortality was higher in patients with PPS ≥4 (ranging from 7% for PPS=4 to 38% for PPS=11), than in patients with PPS <4 ( $p<0.0001$ ) and in patients with IBS ≥7 rather than IBS <7 ( $p=0.0005$ ).

**Conclusions:** According to our findings, Padua prediction score and Improve bleeding score seem to work as good predictors of in-hospital mortality in acute medical patients. Further and multicentric studies are needed to confirm our results on larger scale.

## Is bioethics moving away from patient and clinical practice?

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**Objectives:** During clinical activity the doctors are confronted with life and death decisions that involve clinical and ethical issues. In a patient-doctor relationship, the patient is the protagonist. Bioethics has emerged as a science to protect the patient's rights and autonomy. But patient's autonomy is perceived as if he should be responsible for the clinical decisions. As doctors, the authors believe that autonomy is information, and the clinical decision should rest on physicians' hands. Which is the bioethics role in the patient-doctor relationship? Does it reflect the patient's resolve and correspond to clinical practice? This study intends to analyze the opinions of different groups: physicians, patients and their families and bioethicists; realize the differences amongst them and understand if bioethics always defends the patient's best interests. To achieve this,

the authors apply a questionnaire to the different groups previously mentioned with four real clinical situations. The variables studied, in addition to the group which they belong to and their answers were individual traits (age, academy course and physicians' speciality).

**Methods:** The authors applied 600 questionnaires: 230 physicians (clinical doctors, surgeons, anesthetists and none differentiated physicians), 150 patients, 150 family patients and 70 bioethicists.

**Results:** All patients and families want extended life measures to always be instituted; otherwise, almost all of them believe that decision should remain in the doctor's hands. The same wasn't verified in bioethicists' opinions. Almost all the patients and families answered that intensive care units should be available for everyone, despite age, clinical condition or prognosis. In the majority of the situations the patients, families and doctors share the same ideas. There was a hole, particularly clear, between physicians and bioethicists, normally involving religious beliefs, in which bioethicists respect the patients' beliefs and wills, despite expected adverse outcome for them. Other conflicted issue was the understanding that the intensive care, while scarce and an expensive resource should be restricted. Patients, families, bioethicists and some younger and less experience doctors didn't agree with it.

**Conclusion:** In this small interview, it was clear that bioethics could have an important role in bonding health, society and social sciences, but if it stays away from the medical progress and patient's best interest they will miss their point of intervention.

## Physiological changes of brain death potential organ donors

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**Objectives:** Brain death potential organ donors experiment several physiological changes, which lead to multiple organ dysfunction influencing the quantity and quality of the organ to be transplanted. Our aim to describe the physiological changes in potential organ donors admitted in a referenced center during three years.

**Methods:** A retrospective study was made with 13 patients admitted in the intensive care unit (ICU) between January 1, 2012 and December 31, 2014, which evolved to organ donors. We evaluated sex, age, cause that led to brain death, physiological changes (arterial hypotension needing vasoactive support, diabetes insipidus, sodium and potassium disorders, temperature, glucose, lactate and pO<sub>2</sub> ratio / FiO<sub>2</sub>) and organs harvested for each donor.

**Results:** In the 13 cases analyzed, 30.8% were male with a mean age of 47.2 years. The causes of death were medical in 61.5%. 38.5% were due to severe traumatic brain injury, 30.8% spontaneous intracerebral hemorrhage, 15.4% to cerebral infarction, 7.7% subarachnoid hemorrhage and 7.7% post-cardiorespiratory arrest status. In 84.6% of cases there was need for vasoactive support, 23.1% had diabetes insipidus and 84.6% electrolyte disturbances. The hypernatremia was present in 84.6% of organ donors, with an average of 157.1 mmol/l (151-66 mmol/l); 61.5% with an average of hypokalemia 2.9

mmol/l (2.3-3.3 mmol/l). Hypothermia was present in 25% of the donors, hyperglycemia in 84.6% with an average of 289.5 mg/dL (153-500 mg/dL) and hyperlactacidemia in 84.6% with a mean value 4.5 mmol/l (2.3-13 mmol/l). In 84.6% there was deterioration in pO<sub>2</sub>/FiO<sub>2</sub> ratio, with a mean variation of 52.5 (6-195). The harvested organs for transplantation were: 38.5%, only kidneys; 7.7% only liver, 15.4% kidney and liver, 7.7% kidney, liver and heart, and 7.7% kidney, liver, heart and pancreas. The donor was lost in 7.7% of cases and in 15.4% is unknown whether there was organ loss before harvest.

**Conclusions:** Physiological changes resulting from brain death may compromise the viability of the donor and the organs to be taken, limiting the number of transplants. Is fundamental early detection of these changes and early treatment to ensure access to a greater number and quality of transplantable organs.

## A do not attempt resuscitation form does not mean do not treat

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**Introduction:** The care of patients with end stage carcinoma may be unintentionally adversely affected by their diagnosis. We present the case of a 57 years old female with a terminal diagnosis of bronchial carcinoma. The patient had a do not attempt resuscitation (DNAR) order in place. She presented to the emergency department (ED) with sudden onset shortness of breath (SOB). It was decided that no further intervention was deemed appropriate given her diagnosis. However, the patient was acutely distressed and a cause of the SOB was sought with a good outcome.

**Case report:** A 57 years old female presenting with sudden onset shortness of breath, wheeze and productive cough. She had a background of end-stage right upper lobe non-small cell bronchial carcinoma and had a right bronchial stent inserted one month prior to this presentation. Examination revealed tachycardia, tachypnea and oxygen saturations of 60% on air. There was reduced air entry throughout the right lung. Initial arterial blood gas (ABG) revealed a pO<sub>2</sub> of 7.6 kPa and pCO<sub>2</sub> of 6.6 kPa with an FiO<sub>2</sub> of 80%. Chest x-ray (CXR) was inconclusive and the stent was visible. Given her history it was presumed she had a pulmonary embolism (PE) and the patient was thrombolysed. The patient deteriorated and repeat ABG showed a pO<sub>2</sub> of 6.98 kPa and pCO<sub>2</sub> of 14.5 kPa. Urgent computerized tomography revealed no PE or stent migration. Bronchoscopy was performed in the ED that showed the stent was obstructing the right bronchus and acting as a one-way valve, preventing effective ventilation. CXR showed complete white out of the lung. The patient was intubated, but ventilation remained difficult. A reinforced endotracheal tube was placed in the left main bronchus. The ABG's improved and the patient was transferred to a tertiary centre for removal of the stent. The patient made a complete recovery from this episode and went on to live a fulfilled life for many months.

**Discussion:** DNAR does not mean do not treat. The patient had an acute cause for the SOB, and therefore as doctors we should not be prejudiced against acute care of patients with a terminal diagnosis and a DNAR form. Regardless of terminal diagnosis we should consider quality of life prior to the acute

presentation, likelihood of survival of the acute problem and prognosis of the disease. The case also showed that single lung ventilation and performing bronchoscopy in the emergency department is possible and can be life saving.

### Serious adverse events due to interactions with dietary and herbal supplements among inpatients

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**Objective:** Dietary and Herbal Supplements (DHS) consumption is common in hospitalized patients, albeit rarely documented in patients' medical files. DHS may cause interactions leading to serious adverse events. Until now, very few studies have assessed DHS-drug-DHS interactions that may have led to hospitalization or to adverse events during hospitalization. The aim of the study was to check for such interactions and delineate patients at risk.

**Methods:** Of the 1020 approached patients hospitalized in 11 departments of a public medical center in Israel, 927 agreed to complete a questionnaire regarding DHS consumption. In the 458 DHS users, we checked for DHS-drug-DHS interactions through Natural Medicine Database. The search included DHS and medications consumed just before and during hospitalization. We then reviewed patients' medical files for consequences of such interactions. In addition, statistical analysis was carried out to identify characteristics of patients at risk.

**Results:** In 17 of the 458 DHS users (3.7%), the hospitalization or a serious event occurring during hospitalization might have been attributed to DHS-drug-DHS interactions (25 interactions). The most encountered events were bleeding (12 interactions) and hypotension (5 interactions). The most serious adverse event was respiratory failure due to salvia/methadone interaction. Serious adverse events occurred more frequently in older ( $72 \pm 18.2$  years old vs  $60.9 \pm 19.4$  years old,  $p=0.025$ ), Jewish patients (15 (4.6%) vs 1 (0.8%) non-Jewish patients,  $p=0.05$ ), and in patients with ophthalmologic (3 (18.8%) vs 18 (4.1%),  $p=0.032$ ) or gastrointestinal (5 (31.3%) vs 34 (7.7%),  $p=0.008$ ) comorbidities.

**Conclusions:** DHS consumption might be dangerous due to various DHS-drug-DHS interactions that may cause hospitalization or worsen existing medical conditions. On average, one in every 55 hospitalizations may be associated with a serious adverse event due to such interactions. More studies should be done to confirm the causal relationship between such interactions and the described serious adverse events.

### Roux-en-Y gastric bypass is superior to sleeve gastrectomy in improving postprandial glycemia and lipid profile

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**Objectives:** Bariatric surgery is the most effective method for long term treatment of morbid obesity. Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are the most commonly used modalities, considered to be of almost equal effectiveness in terms of weight loss for the first postoperative year. Data regarding their comparative effectiveness in postprandial glycemia and lipid profile are scarce. The aim of the present study was to compare the two procedures regarding their effect on postprandial glucose (GLU) and triglycerides (TG), as well as overall lipid profile.

**Methods:** 71 patients were consecutively recruited. 28 underwent RYGB [mean $\pm$ SD age  $37.5 \pm 9.3$  years, body mass index (BMI)  $46.9 \pm 5.3$  kg/m<sup>2</sup>] and 43 underwent SG (age  $37.7 \pm 9.3$  years, BMI  $50.2 \pm 7.2$  kg/m<sup>2</sup>, both  $p=NS$  vs RYGB). They were evaluated preoperatively and one week, one, 3, 6, and 12 months (mo) postoperatively. In each time point they consumed a semi-liquid mixed test meal, before which blood samples for the assessment of fasting serum GLU, total cholesterol (TC), TG, HDL-C, and LDL-C were taken. Further blood samples were taken at 30, 60, 90, 120, 150, and 180 min post-prandially, and the overall GLU and TG responses were calculated as area under the curve (AUC).

**Results:** All baseline parameters did not differ between groups. Both RYGB and SG groups experienced gradual and significant weight loss. Their BMI was not different at any postoperative time point (RYGB vs SG: BMI 1 mo:  $42.2 \pm 4.7$  vs  $45.4 \pm 6.7$ , BMI 3 mo:  $38.7 \pm 4.6$  vs  $41.9 \pm 6.8$ , BMI 6 mo:  $34.7 \pm 4.2$  vs  $37.4 \pm 5.7$ , BMI 12 mo:  $30.9 \pm 4.5$  vs  $33.6 \pm 6.4$  kg/m<sup>2</sup>,  $p=NS$ ). TC was lower for the RYGB vs the SG group at 6 mo ( $168.9 \pm 26.6$  vs  $199.5 \pm 35.6$  mg/dl,  $p=0.004$ ) and 12 mo ( $166.9 \pm 23$  vs  $190 \pm 37.1$  mg/dl,  $p=0.037$ ), and LDL-C lower at 6 mo ( $108.3 \pm 24.9$  vs  $135.5 \pm 34$  mg/dl,  $p=0.007$ ). There were no differences in HDL-C. GLU AUC was lower for the RYGB vs the SG group at 3 mo ( $16794 \pm 2028.1$  vs  $19212.9 \pm 3347.7$  mg\*min/dl,  $p=0.008$ ), and 6 mo ( $15785.4 \pm 1884$  vs  $17535 \pm 1833.3$  mg\*min/dl,  $p=0.016$ ), while TG AUC was lower at 3 ( $18881 \pm 4785.3$  vs  $26730 \pm 6314.6$  mg\*min/dl,  $p=0.0002$ ), 6 ( $15535.7 \pm 4230.7$  vs  $24198.8 \pm 7480.1$  mg\*min/dl,  $p=0.001$ ), and 12 mo postoperatively ( $15863.1 \pm 4032.5$  vs  $22409 \pm 9225.2$  mg\*min/dl,  $p=0.043$ ).

**Conclusions:** Although RYGB and SG lead to comparable weight loss within the first postoperative year, the former is clearly superior in terms of its effects on postprandial glycemia and lipid profile. The postoperative incretin response and malabsorptive nature of RYGB are most probably the main reasons for this difference.

### Serum homocysteine levels in patients with retinal vein occlusion

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**Objectives:** Retinal vein occlusion (RVO) has usually been considered as a consequence of classical vascular risk factors. However, in last years, hyperhomocysteinemia has been suggested to have an etiological role in this disease. Our aim was to analyze serum homocysteine levels in a prospective cohort

of patients with RVO and controls from general population and to evaluate if hyperhomocysteinemia is a RVO risk factor.

**Methods:** We conducted a prospective case-control study, from July 2012 to January 2015, of all patients diagnosed with RVO at a tertiary-care hospital. We analyzed a similar number of subjects from a control group taking part in a population-based prospective cohort in the same geographic area. We constructed a general linear model to test differences in serum homocysteine levels between both groups and we used a multivariate model to evaluate if those differences were due to the presence of confounding factors.

**Results:** 85 patients and 82 controls were included. Anthropometric measurement, age, alcohol intake or tobacco use, previous cardiovascular disease and treatment as antiplatelet or anticoagulant therapy were similar in both groups. However, patients showed a more prevalent statistically significant presence of hypertension ( $p=0.002$ ), diabetes ( $p=0.008$ ), and dyslipidemia ( $p=0.04$ ) than control group. Median of serum homocysteine levels was higher in the group with RVO (15.1 vs. 11.2  $\mu\text{mol/l}$ ;  $p<0.0001$ ) than in control group. After adjusting by sex, age, BMI, glomerular filtration rate, hypertension, dyslipidemia or diabetes mellitus and alcohol intake or tobacco use, multivariable analysis evidenced statistical differences between homocysteine levels. Unadjusted OR for hyperhomocysteinemia was 3.4 (IC 95%, 1.7-6.6;  $p<0.0001$ ) and after adjustment for confounders was 4.9 (2.13-11.5;  $p<0.0001$ ).

**Conclusions:** Patients with RVO show higher serum homocysteine levels than same age and sex population controls. Hyperhomocysteinemia is an important risk factor for RVO, regardless age, BMI and classical vascular risk factors.

## Living Will: a conflict between ethics and law

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**Objectives:** If there must exist dignity in life, there must also exist dignity in death as death is a part of life. The authors try to show his fellows colleagues the emerging conflicts of the Living Will, between ethics and law. Also they intent to help clarifying some doubts about the use by medical doctors of the patients' Living Will.

**Methods:** With extended reading on the matter, the authors present the evolutionary aspects of Advance Directives, also called Directives to Physicians, which include the Living Will, but do not stop there. The authors will show the evolution through time and their use around the globe. Since the 1964 Oviedo Convention, which legally binds the majority of member states, the European Convention on Human Rights, on its Article 8, stipulate that there is a right to privacy but that there cannot be any intervention affecting a person without his or her consent. From here and other extended documents elaborated in many countries, we can conclude on the principles of personal autonomy and the principle of consent. These principles hold that a capable adult patient must not be manipulated to undergo medical treatment against his or her will. These documents

and Resolutions comprise the protection of human rights and dignity of the human being with regard to the application of biology and medicine principles. They cover the situation in which a patient is no longer able to express his or her own will, by stipulating that the previously expressed wishes relating to a medical intervention by a patient who is not, at the time of the intervention, able to express his or her wishes "shall" be taken in to account.

**Conclusions:** The author will make an attempt to resume in a diagram the construction and the appearance of this kind of Advance Directives, to clarify some doubts and to promote the discussion with their fellow colleagues around the world. Who knows if, with this small presentation, the authors can help legislators and bioethics to clarify some aspects that still need some legal and ethics adjustments, which represent barriers between these two aspects of the human life and the respect for it: ethics and law; boundaries between patients private life and physical integrity.

## Bronchospasm again?

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**Introduction:** Gastroesophageal reflux disease (GERD) potentiates extraesophageal manifestations including bronchospasm, laryngitis, chronic cough and recurrent pneumonitis. Complications from GERD can arise even in patients who lack typical esophageal symptoms.

**Case report:** An 82 years old woman was presented to the emergency room (ER) with progressive dysphagia (initially to solids, subsequently to liquids) and dysphonia for several months. She mentioned dyspnea and wheezing in the previous 2 weeks. She had a medical history of light chain K multiple myeloma, treated with chemotherapy, presumed restrictive syndrome, hemorrhagic erosive gastropathy, anemia and atrial fibrillation (AF). Physical examination revealed oropharyngeal candidiasis and pulmonary auscultation was normal. Gasimetric study revealed acute respiratory failure type 1 and chest radiography had no significant alterations. During ER observation, an episode of bronchospasm and rapid ventricular response to AF occurred, requiring noninvasive ventilation. Amoxicillin/clavulanic acid and fluconazole were initiated, nevertheless no PCR elevation or leukocytosis were documented, based on aspiration pneumonitis hypothesis. Even though, similar bronchospasm episodes followed. On ORL evaluation laryngeal reflux was revealed and pantoprazole 40 mg bid was prescribed. After that, patient remained asymptomatic, and no more bronchospasm or dysphagia were registered. Even so, residual dysphonia remained present.

**Discussion:** The most common GERD symptoms are heartburn (pyrosis), regurgitation, and dysphagia. Other symptoms may be present; mischieving and delaying the correct diagnosis, making this case a perfect example of that. So, bronchospasm and laryngitis are potential extraesophageal manifestations, and must not be forgotten, and not always bronchospasm is synonymous with pulmonary dysfunction.

## Pain assessment and adequate prescription inquiry in an internal medicine ward

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**Objectives:** Adequate pain management improves patients' recovery and reduces morbidity, with pain assessment being proposed as the fifth vital sign. Proper analgesic management, patient tailored, is the key to successful control. The authors aim to characterize pain prevalence and adequate management in an internal medicine unit.

**Methods:** Transversal, observational and descriptive study, including all patients currently hospitalized in an internal medicine ward. The numeric pain scales and the pain assessment in advanced dementia scales, were used accordingly to patients ability or not to communicate. Data, such as dependency status, existence of fractures, pressure ulcers (PU) or foreign medical devices, were included. Previous use of pain medication and current prescription of analgesic were also questioned. Furthermore we used the Pain Management Index (PMI) to assess proper pharmacological control with instituted therapy.

**Results:** We inquired a total of 50 patients, with a median age of 77,6 years (33-94 years old), 31 of them were women. 38 patients (76 %) admitted pain of some kind, 9 referring mild complaints (1-3), 22 moderate pain (4-7) and 7 severe pain (8-10). Acute pain was mentioned in 16 cases and chronic pain was registered in 24 patients. From the group of patient with complaints, only 5 had an admission cause, related to the source of pain such as fracture or infected PU. In 10 cases PU were identified and 15 individuals had complaints related to external medical devices (feeding tube, non invasive ventilation masks, etc) or recent procedures (biopsies, pacemaker implantation, tooth extraction, etc). Back pain was the most frequently mentioned in patients referring chronic pain. When analyzing current prescription, in the group of patients with pain, 37 of them had pain prescription with the majority -26 only with SOS prescription. 9 cases had calendarized analgesia. PMI was applied, revealing 10 patients with adequate pain control and 28 patients with insufficient analgesic prescription. NSAID were the principal class prescribed, present in 74,2%, with 15,8 % of opioid, from which only one third corresponded to high potency opioids.

**Conclusions:** This inquiry confirms us once again as 'opioid phobic' physicians. Our ability to control patients' pain complaints at the time is far from ideal, and a long way is still to be travelled.

## Two years adenopathies experience study in an internal medicine high resolution out-patient clinic

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**Objectives:** The appearance of a lymph node or group of them generates great alarm to patients and their environment. In

order to diagnose the cause of it, many expensive tests could be practiced which can range from a simple phlebotomy to aggressive open biopsies. The aim of our study is to describe all cases of lymphadenopathies attended in our department over a period of 2 years, evaluating several epidemiological, clinical and diagnostic procedures and results.

**Methods:** During 2 years all patient data and characteristics seen in clinic were collected. A survey was filled after the first patient clinic appointment and the final diagnose. In total there were about 91 patients evaluated during that period. Data were collected and coded and analyzed statistically using SPSS statistical program.

**Results:** The average age of patients was 41 years, with 42% male and 58% female. Approximately 33% were smokers and 22% drank alcohol regularly with an average of 21g/day. Most of our patients were referred from the GP (51%), emergency (16.7%) and general surgery (15.6). Most frequent location was cervical (37%) followed by inguinal (28%). According to the examination characteristics lymph nodes were less than 1 cm (46%), with soft consistency (66%), not painful (71%) and mobile (72%). During the diagnostic process ultrasounds were performed in 80% of cases, 37% required CT and a PET scan was requested 5 times. 13.3% required needle aspiration and in 25% of the cases a lymph node biopsy was performed. The most common diagnose was reactive lymphadenopathy (26.7%) and nonspecific lymphadenopathy (33%); although a total of 7 hematologic cancers were diagnosed. We also observed 8 adenopathies caused by infectious processes and 2 inflammatory conditions. Patients were diagnosed at a median time of 38 days and were referred mostly to the primary care (64%), hematology and infectious.

**Conclusions:** We may conclude that most of the patients have no risk factors; remitted because of the appearance of lymphadenopathy >1 cm cervical/inguinal location and with a final diagnosis of benign pathology. They required at least one analytical and one imaging test and the process usually ends in about 1 month. Long-term studies, in which more patients and monitoring are included, could help improve and understand this disease and its early diagnosis from high resolution consultations and avoid unnecessary admissions.

## Descriptive study of elderly patients above 80 years attended in out-patient clinic in an internal medicine tertiary hospital

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**Objectives:** In recent years there has been a significant aging of the population accompanied by a clear improvement in the quality of life for the patients who are attended in outpatient clinics of internal medicine. Consequently the profile of patients seen it has changed increasing the comorbidities and the complexity of the patients. Through this study, the data collected in a general internal medicine outpatient clinic in the last year, in order to describe what kind of patients over 80 years are studied.



**Methods:** They have been collected the data of 52 patients older than 80 years who have come to the general outpatient Internal Medicine, University Hospital Cruces in the past year. The data were collected in the first visit clinic and a survey was filled in at the end of the diagnosis proceeds. Data were collected and coded, and analyzed statistically using SPSS statistical program.

**Results:** From 52 patients 61% were women. 60% went derived from MAP. 85% of the patients had minimal test normal. 98% were independent to perform basic daily and only 29% needed a caregiver activities. The 54% of patients had a Charlson Index above 4-6. 68% had received the flu vaccine and only 10% for pneumococcus. Among personal history 73% of patients had hypertension in drug treatment, 29% and 39% diabetes and dyslipidemia. We found only 4 patients stratified as complex pluripathologies patients. The most frequent reason for consultation was anemia with a share of 23% followed by general syndrome to study. Regarding tests, analytical found altered in 74% being the ferric profile parameter the most frequent abnormal data. In 8 cases tissue biopsy was performed, of which 6 were pathological. By the end of the study, 21 patients (40%) were referred to their primary care physician for follow-up.

**Conclusions:** Through our study it is observed that patients over 80 years attended in our out-patient general clinic have a good quality of life with higher functions preserved in most cases. We suggest that the age is not always the best to evaluate the prognosis of the patients and other markers as Charlson test, Minimal test are more related with the quality and the necessity of invasive test involved in the diagnostic process.

## How to improve the quality of drug prescription for elderly patients in medical wards? A randomized controlled study to evaluate the effects of an e-learning educational program

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**Objectives:** Polypharmacy is associated with increased occurrence of adverse drug reactions (ADRs) and negative clinical outcomes, namely in elderly people. Many ADRs are unpredictable, but others can be foreseen and prevented, such as those due to well-established drug-drug interactions (DDIs). Aim of this study, promoted by 4 Italian scientific societies (FADOI, SIMI, SIGG and SIGOs) and the "Mario Negri" Research Institute, was to evaluate whether a web-based teaching was able to improve the quality of drug prescription in elderly patients hospitalized in Internal Medicine (IM) and Geriatric (G) wards.

**Methods:** 20 IM and G Units were randomized to intervention (e-learning educational program) or control (basic geriatric pharmacology notions). The effect of the intervention on the use of potentially inappropriate medication (PIM, primary outcome) at hospital discharge, and according to Beers criteria, was assessed by means of logistic regression analysis. Secondary outcomes were the prevalence of at least one potential DDI, and potentially severe DDI at discharge. Mortality rate and incidence

of re-hospitalizations were assessed at 12-month follow-up.

**Results:** A total of 697 patients (347 in the intervention and 350 in the control group) aged  $\geq 75$  were enrolled, being 7 the median number of drugs at baseline in both arms. No statistically significant difference in the prevalence of PIM at discharge was found comparing intervention and control arms (OR 1.29, 95% CI 0.87-1.91) as well as no significant decrease in the prevalence of DDI (OR 0.67, 95% CI 0.34-1.28) and potentially severe DDI (OR 0.86, 95% CI 0.63-1.15 – Intention-to-treat analysis). No differences between groups were observed at 12-month follow-up for mortality and re-hospitalization (21.4% vs 20.4%, and 40.2% vs 36.7%, respectively).

**Conclusions:** In this study, an e-learning educational program had no clear effect on the quality of drug prescription and clinical outcomes in hospitalized elderly patients, possibly due to its low level of interactivity. Given the high prevalence of PIMs (42%) and potentially severe DDIs (56%) recorded in our study, more aggressive educational programs or other approaches should be evaluated in order to improve clinicians' prescriptions in hospitalized elderly people.

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## A case report of acute febrile neutophilic dermatosis

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**Introduction:** Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is a rare skin condition characterized by the abrupt appearance of painful, edematous, and erythematous papules, plaques, or nodules on the skin. Fever and leukocytosis frequently accompany the cutaneous lesions. In addition, involvement of the eyes, musculoskeletal system, and internal organs may occur. Sweet's syndrome can be classified based upon the clinical setting in which it occurs: classical or idiopathic Sweet's syndrome, malignancy associated Sweet's syndrome, and drug-induced Sweet's syndrome. First line treatment is systemic glucocorticoid therapy.

**Case report:** A 65 years old man was presented to the emergency department with non-pruriginous and painful cutaneous lesions. Reported also fever with 3-day history. Three days earlier was diagnosed with upper respiratory tract infection and treated with oral antibiotics (amoxicillin/clavulanate). On examination, he had multiple edematous and erythematous papules with 2 cm that coalesced and formed pseudo-vesiculations, distributed around the face, neck, upper chest, back and extremities. The remainder of the physical examination was normal. Laboratory studies revealed leukocytosis (14.3908 /mm<sup>3</sup>), with neutrophilia (90%), elevation of erythrocyte sedimentation rate (80 mm/h) and C-reactive protein (25,5 mg/dL). Other laboratory tests, included urinalysis, renal function and ionogram were normal. Proteinogram was also normal. A skin biopsy revealed epidermal and subepidermal (reticular dermis) dense infiltration of acute inflammatory cells (neutrophils), compatible with diagnosis

of acute febrile neutophilic dermatosis/Sweet's syndrome. Treatment with oral prednisolone (20 mg) was initiated, with clinical improvement within 72 h.

**Discussion:** This is a well-documented clinical and histological case report of Sweet's syndrome, with classical manifestations. However, the differential diagnosis of cutaneous lesions is broad and sometimes misleading. A thorough clinical evaluation, a detailed patient history and identification of classic symptoms should be made in order to diagnose a disease with excellent prognosis with early treatment.

## Increased mortality in patients with enlarged red cell distribution width hospitalized in an internal medicine service

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**Objectives:** To analyze the prognostic value of red cell distribution width (RDW) and to determine which factors are associated with increased RDW.

**Methods:** We include 310 patients hospitalized in an internal medicine department. We determined comorbidity (Charlson index), organ dysfunction (SOFA), hemoglobin and red cell indices, B12 and iron metabolism, and nutritional status.

**Results:** During the follow-up from admission 125 patients died with a survival median of 615 days. Long-term mortality was related to an increased RDW. The following factors were related to increased RDW (>14%) and mortality: serum creatinine >1.2 mg/dl, albumin <2.8 g/dl, cholesterol <100 mg/dl, Charlson index >2, velocity <1.2 m/s in the 6-minute walking test (6MWT), alkaline phosphatase >100 UI/l, SOFA >2, hypotension ( $\leq 90$  mmHg) and tachypnea. The presence of anemia and low red cell indices MHC and MCHC, were all closely related to increased RDW and mortality. By multivariate analysis (Cox regression) a RDW >14%, malignancy, CRP >90 mg/l, creatinine >1.2 mg/dl, severe malnutrition, handgrip <33th percentile, inability to perform the 6MWT, a Charlson index > 2 and hypotension showed independent predictive value for long-term mortality.

**Conclusions:** The relationship between increased RDW and mortality is related to a network of factors such as disease, malnutrition, organ failure and comorbidity. However, even after controlling for all these conditions, increased RDW showed an independent predictive capacity for mortality.

## Oxygen consumption determination administering benzturone

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**Objectives:** Research of new isothiourea derivatives has reached significant proportions in recent years. Generally, they are known as effective vasoconstrictor substances possibly to be used in arterial hypotension. The last studies of these compounds undermined a substance with hypotensive effect chloride-S-benzilzotiorone (benzturone). The aim: benzturone influence experimental elucidation of oxygen consumption in laboratory animals.

**Material and methods:** Oxygen consumption was determined within 3 min using S.V. Miropolski system at the time intervals: 1-3 min; 5-8 min; 15-18 min; 30-33 min; 60-63 min; 120-123 min. The experience included 2 groups of rats of the Wistar line, 10 in each, weighing 208-320 g. The rats from the control group were administered 2 ml of saline solution intraperitoneally, those in the test group, benzturone in the dose of 2 mg/kg. Statistical study according to t-Student criterion.

**Results:** In the time intervals 1-3 min; 5-8 min; 15-18 min; 30-33 min significant statistical differences of the mean value of oxygen consumption between the test group and control group were not determined. Conversely a difference in the mean value of the control group was observed:  $19.61 \pm 0.95$  in 60-63 min;  $17.54 \pm 0.43$  min in 120-123 and test group:  $14.36 \pm 1.33$  in 60-63 min;  $11.22 \pm 1.55$  in 120-123 min, where  $p=0.004$  for 60-63 min; and for 120-123 min  $p=0.001$ .

**Conclusions:** As a result of experiments a decrease in oxygen consumption was observed due to benzturone administration comparing with the control group. The decrease was significant starting with the minute 60.

## How to develop a new comprehensive predictive model to evaluate the complexity of patients hospitalized in internal medicine? The COMPLIMED study by the Italian scientific society FADOI

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**Objectives:** Measuring patients' complexity has important implications for clinical decision-making, organization of care and resources allocation. Despite the availability of several tools (e.g. MPI, PROFUND index), there is a stringent need for a simple, user-friendly but comprehensive method for patient's prognostic stratification. Aim of this study is to develop and validate a new predictive model to measure complexity of patients in internal medicine (IM): the COMPLIMED score.

**Methods:** Consecutive patients admitted to IM units for any cause were eligible, with a planned one-year follow-up. Demographic information was collected at admission to IM. 13 questionnaires were selected and they were administered to evaluate domains representing the complexity of patients: comorbidity (Charlson, CIRS), clinical stability (MEWS), social frailty (Flugelman), cognitive dysfunction (SPSMQ), depression (5-item GDS), functional dependence (ADL, IADL, Barthel), risk

of sore threats (Exton-Smith scale), nutrition (MNA), pain (NRS), adherence to therapy (Morisky scale). Principal Component Analysis (PCA) was used to isolate domains and variables with the highest influence on complexity and to be considered for the COMPLIMED score.

**Results:** 576 patients from 29 IM Units were enrolled, with the following main characteristics: mean age  $78.2 \pm 9.8$  y.o.,  $\geq 5$  diseases in 60.1% of cases, a mean of  $6.4 \pm 3.7$  concomitant treatments. One patient out of 3 was bedridden and more than 70% of subjects needed a caregiver for home assistance. One-third of patients had a cognitive dysfunction and 50% of the subjects declared to be unhappy of their quality of life. PCA has revealed that complexity of patients is a 2-dimensional phenomenon, accounting for about 70% of all the information collected in the study. Namely, results coming from only 3 questionnaires (Barthel, Exton-Smith and CIRS) could be used to obtain approximated scores of the 2 "faces of medallion", i.e. dependency and comorbidity. From these items we are going to build up the COMPLIMED scores by developing a specific algorithm.

**Conclusions:** Our analysis should ultimately allow us to select the minimum number of items that comprehensively describe the phenomenon of complexity. The value of the COMPLIMED score, based on 1-year mortality, will be compared with an already validated tool (MPI score). Follow-up is ongoing and expected to be completed in September 2015.

## Digital ulcers: the similarities between Buerger's disease and systemic sclerosis – case report

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**Introduction:** Buerger's disease, also called thromboangiitis obliterans (TAO), is a non-atherosclerotic inflammatory vasculitis, which typically affects distal arteries, leading to distal extremity ischemia, ischemic digit ulcers and digit gangrene. It is associated with Raynaud's phenomenon (RP) in 40% of patients. Systemic sclerosis (SSc) is a systemic disease with multi-organic involvement, characterized by fibrosis and vasculopathy. Raynaud's phenomenon and digital ulcers (DU) are common manifestations and are observed in approximately 90 and 50% of patients, respectively.

**Case report:** 48 years old man, shoemaker, smoker, with history of bilateral, symmetrical and three-phase hand RP since childhood. He was sent to an autoimmune diseases appointment by multiple and painful digital ulcers in hands, having the first one appeared about three years ago. He denied gastrointestinal, respiratory, cardiovascular or general symptoms. On physical examination he had malar telangiectasias and multiple digital ulcers in both hands in different stages of healing. No skin thickening was present. Cardiac auscultation was normal and pulmonary auscultation revealed some scattered wheezing. Jugular venous pressure was normal. The laboratory investigations showed negative immunity. Thus, the patient was referred to the vascular surgery appointment, where he was diagnosed with Buerger's

disease and started intravenous iloprost, maintaining clinical follow-up currently.

**Discussion:** Buerger's disease and systemic sclerosis are both rare clinical entities. The RP is associated with these diseases in a high percentage of patients, representing DU more advanced and debilitating stage of this phenomenon. The therapeutic approach to active DU is similar. However, the differential diagnosis is critical because the systemic approach in these diseases is different. In this case, the absence of other specific clinical manifestations, no laboratory evidence of other entities that cause occlusive vascular disease (such as diabetes, the vasculitides and thrombophilias) and the strong association with smoking were crucial data on suspected TAO, fulfilling the criteria for diagnosis of this entity. The awareness of the possible presence of these entities should lead to an earlier diagnosis, avoiding the functional disability and risk of amputation. The main features of the DU associated with TAO and SSc was reviewed in this clinical case.

## Combined evaluation of rehabilitation potential of patients after acute ischemic stroke in the background comorbid disease

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**Objective:** To evaluate the effect of comorbid pathology in the rehabilitation potential and the prognosis of patients after acute cerebrovascular accident (ACVA).

**Methods:** Retrospective study was performed in 65 patients after suffering ACVA who were treated at the Medical Rehabilitation Department of Municipal Clinical Hospital №2 of Stavropol (Russia). To measure comorbidity used Charlson comorbidity index and the system CIRS (Cumulative Illness Rating Scale). Statistical analysis of the results was performed using "AtteStat". Parametric and nonparametric tests (F-Fisher test, t-Student test and Mann-Whitney U-test) were used to determine the statistical significance of the continuous variables.

**Results:** The first group consisted of 47 (72.3%) survived, the second – 18 (27.7%) died patients. Among the patients were women – 68.1% (n=45), mean age –  $75.6 \pm 2.4$  years. Ischemic strokes occur in 83.1% (n=54) cases, hemorrhagic stroke – in 16.9% (n=11). In the structure of comorbid pathology respondents marked mainly cardiovascular disease (CVD): arterial hypertension – 87.7% (n=57), angina – 47.6% (n=31), myocardial infarction – 20% (n=13), atrial fibrillation – 9.2% (n=6), a history of stroke – 7.6% (n=5), and various combinations. The average value of the Charlson comorbidity index in patients of the first group was  $2.87 \pm 0.32$ , and in patients of the second group –  $2.64 \pm 0.27$ . Index CIRS allowed assessing not only the presence of comorbidities, but also its severity. On average, CIRS comorbidity index among the first group of patients was  $13.6 \pm 5.1$  points, and the second –  $17.5 \pm 4.8$  points. The level of rehabilitation potential was estimated using the scale as high, medium, low and lack thereof. Graduations of the rehabilitation potential were ranked from 1 to 4. The average level in the group of surviving patients was  $1.7 \pm 0.6$ , in the group died –  $2.8 \pm 0.3$ .

**Conclusions:** It's necessary to use 2 or more indexes for the assessment of comorbidity, which allows estimating the overall status of the patient in different positions. The presence of vascular comorbidity significantly reduces the level of rehabilitation potential and deteriorates the prognosis of patients with cerebral and cardiac history.

## Malnutrition and nutrition risk in elderly hospitalized patients, an internal unit experience

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**Objectives:** The aim of the study is to screen patients nutritional status by using Mini Nutrition Assessment (MNA), Nutritional Risk Screening 2002 (NRS2002), anthropometric measurements, laboratory tests and to examine the relationship between them.

**Methods:** Elderly patients (>65) hospitalized in our Internal Medicine Ward during the period of 01.03.2014-01.03.2015 were evaluated. The patients who have malignancy and/or discharged from an intensive care unit were excluded. All patients were screened for nutrition status by using NRS-2002 and MNA forms; height, body weight, Body Mass Index (BMI), waist circumference (WC), calf circumference (CC), mid upper arm circumference (MUAC), upper arm length, triceps skin fold (TSF) measurements were measured; total protein, albumin, calcium, phosphorus, magnesium, parathormon, complete blood count, fasting glucose, creatinine, alanine aminotransferase, aspartate aminotransferase, uric acid, serum iron, HbA<sub>1c</sub>, TSH, free T3, free T4, C-reactive protein (CRP) levels were studied. Obtained data were analyzed using SPSS for Windows 16.00 version.

**Results:** A total of 192 patients (mean age 80±7.2 years) were enrolled. A number of 106 (55,2%) patients who had NRS-2002 score of ≥3 were at malnutrition risk. By using MNA 24% of patients had normal nutritional status, 31,8% had nutrition risk, 44,3% had malnutrition. When the patients divided into two groups in terms of having NRS2002 score ≥3 or <3; age, CRP, leukocyte number, magnesium levels were significantly higher; weight, BMI, WC, CC, MUAC, TSF, total protein, albumin, creatinine, free T3, free T4, HbA<sub>1c</sub>, phosphorus, serum iron levels were significantly lower in nutritional risk group (p<0.05). On multiple logistic regression analysis age, free T3, free T4 were found to be independently associated with malnutrition risk. When correlation of nutritional status with antropometric measurements were evaluated, the calf circumference was found to be independently associated with the risk of malnutrition.

**Conclusions:** Regarding to the NRS2002 the prevalence of malnutrition risk in our hospitalized elderly patients was very high (55.2%). In addition to various screening methods serum phosphorus, magnesium, free T3, free T4 levels should be considered to evaluate malnutrition. While assessing nutritional status calf circumference should not be ignored due from it's not only a validated but also an easy method to use.

## Atrial fibrillation and infrequent thromboembolic sites: two case reports

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**Introduction:** Atrial fibrillation (AF) is the most common cardiac arrhythmia and the most severe complication of this is thromboembolism. Examples of such complications are renal and splenic infarction, both are difficult to diagnose because for their unspecific clinical presentation. This work aims to present two cases of renal and splenic infarctions occurring in AF.

**Case reports:** The first case is a 72 year old fit and independent male, with no significant past medical history. He was admitted to the emergency department (ED) with a 2 week history of progressively worsening abdominal pain localized to the left hypocondrium. The ED diagnosed AF with a rapid ventricular response, multiple splenic infarctions, thrombosis of the left renal artery and subsequent renal infarction. The second case is a 50 years old male with a past medical history significant for a mechanical mitral valve replacement, stroke and AF on warfarin treatment. He presented to the ED with severe abdominal pain localized to the hypogastric region, left iliac region and left flank. On admission his international normalized ratio (INR) was found to be sub-therapeutic. The patient was subsequently diagnosed with left splenic and renal infarction and right-lower quadrantanopia compatible with stroke of the left posterior cerebral artery.

**Discussion:** Several mechanisms lead to a high risk of thrombus formation, embolism and stroke. AF is associated with a hypercoagulable state and other factors, such as dilation of the right atrium and arterial hypertension, may lead to an increased risk of stroke.

**Conclusions:** In patients with AF it is essential to prevent thromboembolic complications with an effective anticoagulant treatment and close monitoring of INR levels. In the inaugural cases, it's important to note the occurrence of these complications.

## Risk factors for venous thromboembolism

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**Objectives:** Venous thromboembolism (VTE) is a major health problem. It combines two related conditions- pulmonary embolism (PE) and deep vein thrombosis (DVT). Until recent decades VTE was viewed primarily as a complication of hospitalization for major surgery or associated with the late stage of terminal illness. However, recent trials in patients with a wide variety of medical illnesses have demonstrated a risk of VTE in medical patients comparable with that seen after major general surgery. Independent risk factors for VTE include increasing patient age, surgery, trauma, active cancer with or without specific cancer therapy, hospital confinement, and prior vein thrombosis among others. The aim of this study was to

identify those risk factors that contribute to development of VTE in patients hospitalized either with PE or DVT.

**Methods:** A retrospective study was performed. The data of all DVT and PE patients were obtained from two main hospitals of Riga – East University Hospital and Pauls Stradins Clinical University Hospital during the period from 1 of January until 31 of December 2014. Risk factors such as age, gender, previous thrombotic events, ischemic heart disease, previous myocardial infarction, arterial hypertension, atrial fibrillation, cardiomyopathies, congestive heart failure, chronic obstructive pulmonary disease, asthma, pulmonary hypertension, chronic kidney disease, tumors, recent operations, hip replacement surgery, and traumas were identified. Chronic DVT and PE were excluded out of the study.

**Results:** In total we identified 362 confirmed cases of VTE (mean age of  $69.4 \pm 14.8$  years). 89.5% (n=324) had PE and 43.4% (n=157) had DVT. Among those 41.2% (n=149) were men and 58.8% (n=213) were women. Mean hospitalization time was 12.5 days. Among all cases 7.2% (n=26) were hospital-acquired VTE and 15.2% (n=55) were in-hospital deaths. Positive statistically significant correlation was observed between PE and DVT ( $\chi^2=5.94$ ;  $p=0.001$ ). Men showed to have almost 2 fold higher risk acquiring DVT than women [OR 1.95, CI 95% 1.27- 2.99,  $p=0.02$ ]. Previous thrombotic events also have 2-fold higher risk for DVT [OR 1.93, CI 95% 1.14- 3.28,  $p=0.014$ ]. Among other risk factors only arterial hypertension showed statistically significant correlation with PE ( $\chi^2=8.99$ ;  $p=0.011$ ). DVT accounts for higher incidence rates with increasing age in both genders, peaking at age 65-80.

**Conclusions:** Pulmonary embolism is strongly correlated with deep vein thrombosis. Men have higher risk for developing deep vein thrombosis. DVT accounts for higher incidence rates with increasing age in both genders. Previous thrombotic events have higher risk for DVT to occur. Arterial hypertension contributes to development of pulmonary embolism.

## Sexual dysfunction in men with psychoemotional disorders is associated with androgenic deficiency

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**Objective:** The aim of this study was to investigate androgenic deficiency and sexual dysfunctions in patients with psychoemotional disorders.

**Methods:** 110 men (mean age was  $48.7 \pm 7.2$ ) with sexual dysfunctions and anxiety and depressive disorders were studied. Erectile function was assessed according to International Index of Erectile Function – 5 (IIEF-5), questionnaire Men's Sexual formula (MSF), and plasma total testosterone was detected. Depression and anxiety severity were measured by Hospital Anxiety and Depression Scale (HADS).

**Results:** Duration of sexual disorders averaged  $4.9 \pm 2.3$  years. The main part of tested patients had a history of significant

clinical psychopathological and physical stresses, including adjustment disorders (56% of patients), mixed anxiety-depressive disorder (20%), anxiety-phobic disorder (14%) which were identified through clinical psychopathological examination. All patients who took part in the investigation had sexual dysfunctions in form of decrease of libido with lessening of sexual fantasies, sexual incentives, thoughts about sexual side of life, difficulties in beginning and maintaining of erection sufficient for satisfactory coitus. Analysis of erectile dysfunction according to the scale IIEF-5 showed that in 20% patients the values were within normal range, 53% patients had mild erectile dysfunction, and 27% patients had medium erectile dysfunction. It was found that 81 (74%) men had low level of testosterone ( $<13.5$  nM/L). These patients showed more severe indicators of anxiety compared to the group of patients where testosterone level was normal ( $14.6 \pm 0.7$  vs  $10.8 \pm 0.8$  points, respectively,  $p=0.032$ ) and depression ( $13.9 \pm 0.7$  vs  $9.8 \pm 0.9$  points, respectively,  $p=0.03$ ). Androgenic deficiency patients more often had vegetative-vascular symptoms such as sudden hyperemia of face, excessive sweating, short of breath, fluctuations of blood pressure; psychoemotional – irritability, "fall of vital forces", decreased concentration of memory and attention. MSF showed a decrease of the structural indicators in both groups, but more in the group with low level of testosterone ( $17.8 \pm 2.5$  vs  $13.7 \pm 1.9$  points,  $p=0.032$ ).

**Conclusions:** Sexual dysfunction in patients with anxiety and depressive disorders is associated with low level of testosterone. The influence of correction of androgenic deficiency on clinical manifestation mental disorders needs to study.

## The ability of patients to define oral lesions and to find out oral lesion rates

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**Objectives:** Oral aphts are the most common form of oral lesions. Although the prevalence is reported between 5-50% in different studies, 20% of general population have oral aphts and ulcers. Behcet's disease is a systemic vasculitis which can cause repetitive oral and genital ulcers, uveitis and variable skin lesions. First clinical finding is especially repetitive oral aphts and/or ulcers.

**Findings:** In the cross-sectional study that we made between 1000 patients applied to Meram Medicine Faculty Internal Medicine clinic for outpatients, the prevalence of oral aphts and ulcers were 8 and 7,7% respectively. Verbal questioning can cause 17% underestimation of real aphts and cause of non-aphtous lesions to be perceived as aphtous ulcers compared to questioning with pictures. Verbal apht questioning cause 32,4% overlook to real aphts and cause 40,9% of non aphtous lesions to be perceived as aphtous lesions. The consistence with kappa factor between verbal questioning and questioning with pictures was very low (kappa 0,04) between patients who were not diagnosed as Behcet disease.

The consistence of 2 methods was medium between patients who had Behcet's disease ( $\kappa$  0,56). Between the answer of patient with Behcet's disease and without the diagnosis of Behcet's disease which they gave to verbal questioning and questioning with pictures there was significant difference. When questioning with pictures is accepted as main diagnostic tool all of the 62 patients with Behcet's disease diagnose described oral lesions. At 30,6% of this patients there was ulcers without aphts. In physical examination of 32% of patients who were diagnosed as Behcet's disease there was oral lesions and 59% of them were oral aphts.

**Conclusions:** In our study questioning the oral lesions with pictures was significantly superior and was beneficial to establish the lesions the lesions which can be overlooked or misdiagnosed by only verbal questioning. This study showed us especially the knowledge about aphts can be insufficient between patients without Behcet's disease so visual questioning is more favorable.

## Pharmacomechanical thrombolysis in the treatment of ilio-femoral deep vein thrombosis

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**Introduction:** Ilio-femoral deep vein thrombosis is associated with a high morbidity in the form of the post-thrombotic syndrome. Pharmacomechanical thrombolysis uses local fibrinolysis and thrombectomy as an alternative to anticoagulation alone.

**Case reports:** We present 2 cases of ilio-femoral deep vein thrombosis treated with pharmacomechanical thrombolysis at our unit. Case 1 is a 38 years old woman with extensive deep vein thrombosis from ilio-femoral to popliteal veins, associated with hormonal contraception. She was treated with local pharmacomechanical thrombolysis using the Trellis device in superficial femoral, common femoral, external iliac and left common iliac veins. 72 hours later, she had experienced significant clinical improvement. She was discharged with rivaroxaban. 3 months later the patient remained asymptomatic. Case 2 is a 27 years old woman with history of high risk thrombophilia (double heterozygosity for factor V Leiden and prothrombin mutation) and 6 episodes of deep vein thrombosis in different locations, in spite of many anticoagulant treatments (enoxaparine, warfarin, rivaroxaban). She was diagnosed with a new episode of deep vein thrombosis, affecting inferior cava vein to both iliac veins. She was treated with pharmacomechanical thrombolysis 2 times. The patient had a good evolution and was discharged with dabigatran. In patients with acute DVT, ilio-femoral thrombosis has a worst prognosis with more frequent and severe forms of post-thrombotic syndrome.

**Discussion:** Thus, early removal of thrombus could reduce morbidity in these patients. When iliac vein is affected, oral anticoagulation alone seems not enough to prevent post-thrombotic syndrome. Pharmacomechanical thrombolysis uses a catheter which allows direct administration of fibrinolytic agents with mechanical fragmentation of the thrombus. The Trellis catheter, which was used in our patients, has a double mechanism: 1)

administration of a thrombolytic agent with 2 occlusive balloons, which are located in the extreme of the thrombus, allowing local administration of the drug 2) mechanical fragmentation of the thrombus through a rotating wire. This technique avoids systemic fibrinolysis. Pharmacomechanical thrombolysis with catheter in patients with ilio-femoral thrombosis is a technique that allows complete removal of thrombus, recovering the vein function and potentially preventing the post-thrombotic syndrome. Although the results are promising in terms of efficacy and safety, more studies are needed supporting this technique.

## Follow up patients in palliative unit

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**Objectives:** Palliative medicine consists on the symptomatic treatment of patients who have an illness, which is not a subsidiary of curative treatments; or those who are about to died. Physician practitioner should adapt to changes in the patient's symptoms, measures to ensure comfort and avoid suffering. It aims to analyze the epidemiological characteristics of patients referred to the unit, and the reason for derivation.

**Methods:** Patients were followed for the unit from January 2014 to June 2015. They were derivated from primary care and other hospital services, except oncology; as all the derivation are oncologic patient. 230 patients were followed, who were made regular home visits until their death.

**Results:** 46.3% were women with a median age of  $80 \pm 0.8$  years. The mean Karnofsky index (IK) and Charlson (IC) was 53.2 and 5.03, respectively. Median patient follow-up days since they were included in the program until the death was 25.5 days. The derivations came from primary care (41.9%), internal medicine (12.8%), other medical services (21.1%), and surgical services (8.7%). The main reason for referral was oncological pathology (86.8%). Most of the tumors were of gastrointestinal origin (36.6%). Analyzing the non-oncology referrals, the most frequent cause was heart failure (4.8%), followed by respiratory failure (3.1%). Most of the patients died at home (76.2%) and 59.9% underwent palliative sedation. Notice that, 48.5% of patient analyzed were aware of the diagnosis of the disease and only 26% knew the outcome or progress of the same. If we analyze only patients derive the internal medicine (32 patients), 51.7% were women, with a median age of 81 years, the mean IK and IC was 52 and 6.03, respectively. The main reason for referral remained oncological pathology (82.8%). Of the 5 patients who were followed for a medical condition, the main pathology was heart failure.

**Conclusions:** Palliative medicine in our hospital is a widespread practice. It is not only dedicated to the management of patients who are about to died, as the median days of follow approximates to a month. The object of this unit is symptomatic control of the diseases. Although most cases are referred by neoplastic disease, we think that patients suffering from very advanced medical; can benefit from a home-based management of their symptoms, which would reduce the need for hospital admissions. The main reason for referrals from internal medicine is still being oncology pathology, although most of the patients in our service are elderly people with comorbidity, in a state of advanced disease.

## Intensive insulin therapy and a discharge strategy in hospitalized patients with type 2 diabetes can improve and maintaining glycemic control during several years

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**Objectives:** Current guidelines recommend the use of a basal-bolus insulin regimen in hospitalized patients with hyperglycemia or type 2 DM, because these protocols to manage hyperglycemia are feasible and enable improved glycemic control without increasing hypoglycemia episodes. In addition, these studies also demonstrated that a simple strategy facilitating the reconciliation of medication on discharge can improve glycemic control post-discharge. With our study we want to test whether this better glycemic control is maintained over time (metabolic memory).

**Methods:** Our study is a prospective and observational study during routine clinical practice. It has been held in the Department of Internal Medicine during hospitalization, with follow-up visit at 3 months after discharge and followed up for 3 years. Study patients (48) were treated with a regimen of basal-bolus insulin during hospitalization and an adjustment of their antidiabetic treatment at discharge. As a control group we included patients (30) hospitalized with similar characteristics, treated with other regimen of insulin or oral antidiabetic agents and to which either no treatment adjustment is recommended at discharge. A follow-up to all patients at 3 months after discharge and again after 3 years (during which time the patients were treated according to standard clinical practice).

**Results:** Comparing the study group with the control group there found no differences in baseline HbA<sub>1c</sub> (8.55 vs. 8.61), age (67,7 vs 67,8), sex (53,3% male vs. 57% male) and BMI (30.3 kg/m<sup>2</sup> vs 30.5 kg/m<sup>2</sup>). Compared with baseline, the HbA<sub>1c</sub> at 3 months after discharge is lower (8,55 vs 7,49) and 3 years after discharge also remains lower (8,55 vs 7,8). Compared with control subjects, patients included in study have lower HbA<sub>1c</sub> at 3 months after discharge (7,49 vs 8,71) and lower HbA<sub>1c</sub> at 3 years after discharge (7,8 vs 8,91).

**Conclusion:** This study confirm that protocols to manage hyperglycemia with basal-bolus insulin regimens are also feasible and effective in routine clinical practice, and demonstrate that a simple strategy facilitating the reconciliation of medication on discharge can improve glycemic control post-discharge, that remains after 3 years of follow up.

## A rare case of hypertension

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**Introduction:** Malignant catatonia is an unusual neuropsychiatric condition which can present with clinical and biochemical

manifestations similar to those of pheochromocytoma.

**Case report:** 57 years old man, admitted with vomiting, abdominal pain, accompanied with polydipsia, polyuria and weight loss. On examination he was dehydrated, BP 200/114 mmHg with epigastric and right hypochondrial pain on abdominal palpation. Blood tests: glucose 417 mg/dL and creatinine 1.4 mg/dL. ECG: sinus tachycardia and left ventricular hypertrophy. Normal abdominal and renal ultrasound and X-ray. Decided hospitalization with hypertensive crisis, diabetes type 2 and acute kidney injury. Glycemic control was achieved after hydration and insulin, but poor control of blood pressure with Ca channel and  $\beta$ -blockers and loop diuretic in maximal doses, accompanied by vomiting, fluctuation of blood pressure, sudoresis and palpitation. After excluding other target lesion, started investigation of secondary hypertension. Blood tests: increase of noradrenaline and slight elevation of adrenaline, dopamine and vanillyl mandelic acid. Abdominal and adrenal CT with no changes and MiBG without ectopic hyperfixation. Clonidine suppression test: catecholamines suppression after 3h. Head-CT: normal. The patient remained with vomiting with symptomatic therapy, paroxysmic hypertension, sudoresis and palpitation. Started investigation of digestive causes with upper gastrointestinal endoscopy and rectosigmoidoscopy with no changes. Looking for motility alterations it was preformed gastrointestinal motility test, autoimmunity, immunofixation and capillaroscopy without changes. Negative result for abdominal wall fat pad biopsy. Normal EMG and head MRI. The patient maintained the symptoms, accompanied by asthenia, depressive humor (medicated by psychiatrist) and food refusal which required PEG. Repeated abdominal CT and an exploratory laparoscopy were performed without any abnormal changes. With exclusion of organic causes and with no improvement of the patient, it was made a new request for psychiatric support. After observation form psychiatrist it was made the diagnosis of melancholic state of major depression associated with catatonic state. He was transferred to the psychiatric service with clear improvement after therapy.

**Discussion:** Malignant catatonia should be considered in the differential diagnosis of the hypercatecholamine state, particularly in a patient who exhibits concurrent catatonic features.

## Therapeutic goals of blood pressure in the Valencian pharmacies. FARMAPRES project

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**Objective:** Knowing the reality of taking blood pressure (BP) in pharmacies of Valencia and self-perception of the importance of pharmacology in the control and monitoring of hypertensive patients.

**Methods:** Survey sent to holders of the pharmacies of Valencia, through professional associations of the 3 provinces.

**Results:** The number of received polls was 381, which represents 16.7% of the whole. Being distribution by provinces as follows:

Alicante 230 (60.4%), Castellón 70 (18.4%) and Valencia 81 (21.3%). Almost half of respondents (46.5%) considered a normal BP figures between 120-129/80-84 mmHg and the 25% considered normal figures of BP between 130-139/85-89 mmHg. However, 56.2% considered poor BP control figures between 140-159/90-99 mmHg and even 15.5% rises up those numbers to 160-180/100-110 mmHg. When a pharmacist detects figures of BP which he considers high, only the 66.4% of them repeat taking. As for referral to medical emergencies, 31.5% do so if it detects BP of 160-179/100-109 mmHg figures, while 58.5% do so only to figures blood pressure >180/110 mmHg and among these, only 16.5% directed referral to the emergency room. Highlighting the pharmacist that detects high BP, almost half (49.6%) encourages patients changes in their lifestyle and even 35.4% of the pharmaceutical verify completion of drug treatment prescribed by their doctor.

**Conclusions:** Despite the high degree of knowledge of the figures considered as a normal or high-normal, the perception of poor control figures is undervalued, however more than 15% of the pharmacists considered 160-180/100-110 mmHg as poor control figures. Moreover, referral to medical emergencies figures of poor control of blood pressure is high; especially when you consider that more than one third only makes one take of BP.

### Case of a massive abdominal swelling: mesenteric pseudocyst

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**Introduction:** Mesenteric pseudocysts are rare intra-abdominal masses, mostly benign, without identifiable organ origin.

**Case report:** We describe a case of a 55 years old man, with self-limited febrile respiratory condition in 2009, associated to polyserositis (bilateral pleural effusion with exudate characteristics, pericardial effusion and small perihepatic and peri-splenic effusion), with inconclusive investigation. The patient remained clinical and ultrasonographic stable between 2010 and 2012, and since then, with occasional complaints of discomfort on the right abdominal quadrants, when sitting. One year later, the physical examination revealed an asymmetric abdominal inspection, with a palpable and painless right abdominal mass, with very little mobility. Analytical studies were normal. Abdominal ultrasound (ULS) suggesting collected peritoneal fluid. Abdominal-pelvic computer tomography (CT) showed a lesion with a liquid content, thin-walled, extending from the right infr diaphragmatic level, over the right edge of the liver, till the umbilical level. Eccinococcus serology and amebiasis microbiology were negative. Abdominal magnetic resonance imaging (MRI) suggested a large cystic lesion, compressing the inferior vena cava and pushing abdominal aorta to the left. The patient was oriented to surgery. An excision attempt by laparoscopy was changed to laparotomy due to the extension and organ adhesion of the cystic mass. The histopathology showed a mesenteric pseudocyst.

**Discussion:** Mesenteric pseudocysts do not cause specific symptoms. Although most are asymptomatic, the symptoms could be associated with size, location, and complications

(infection, rupture, hemorrhage and intestinal obstruction) of the cysts. ULS, CT and MRI scanning have been used for pre operative diagnosis. However exact differentiation is only made post operatively by histopathology.

### Medication management improvement: double check by certified pharmacist or electronic medical system – what is better to avoid medication errors?

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**Objectives:** Medication errors are a threat for patient safety in a hospital. Double check for medication prescription is required by international JCI standards. In "Medicina" clinic prescription control is done by privileged pharmacist.

**Results:** 4,2% of medication errors were discovered and corrected by pharmacist. Among them 33,6% were time errors, 31,6% – administration errors, 36,8% – interaction between different medications, 6% – dose errors and 2,4% – prescription of two drugs with the same international name. The main reasons for these errors were human factor and doctors' lack of knowledge. Use of electronic systems for medication prescription control can improve patient safety in a hospital. Special soft ware for medication prescription was implemented in "Medicina" clinic.

**Conclusion:** The main results of electronic system implementation is decrease of drug interaction errors and critical errors (dose errors, use of inappropriate drugs in patients with allergy, pregnancy, lactation, kidney and liver insufficiency) and improve of laboratory and clinical control of medication treatment in multiprofile hospital.

### Cooperative management of hip fracture. Results along one year after the implementation of orthogeriatric program

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**Objective:** To analyze the characteristics of patients with hip fracture (HF) and compare the results of their care after a cooperative management program was implemented in the Hospital of Cabueñes.

**Methods:** A retrospective descriptive study of patients older than 65 years admitted by HF between May and December of 2014 was done. Results of healthcare were compared with the same period in 2013. Data was collected from medical records and DRG provided by the Clinical Information Department. Statistical analysis using SPSS 20.0 was done.

**Results:** Between May and December 2014, 233 patients were admitted due to HF, 80% were women average age of 84.1



years. These figures were quite similar in 2013. Barthel index was  $76.6 \pm 28.4$ . 88.8% of were required surgical procedures and 41.5 % suffered various complications. On the discharge, (47.3%) were transferred to chronic care hospital, (27.2%) to a geriatric residence and (17.4%) to their own home. Comparing with 2013, we achieved a reduction of the length of stay (LOS) of 3 days (15.7 vs 12.7), mainly in the postoperative (11.1 vs 8.3). The hospital mortality was 12 patients in both groups.

**Conclusions:** Falls are a big problem in elderly population, not only by its high frequency, but also due to its high morbidity and mortality. These patients are usually pluripathologic, and in recent years, cooperative management is being established between Internal Medicine and Trauma services. After the implementation of the program, we achieved an important improvement in the quality of care. A reduction of 3 days in LOS supposing that 700 stays were saved along 8 months means a significant enhance of opportunity cost; also the mean number of diagnoses raised from 4.9 to 7.7 (attributed to the identification and reporting of comorbidities and complications in Internal Medicine discharge report). Main complications were heart failure and urinary tract infection. More than 1 out of 10 patients were transferred definitely to another hospital for rehabilitation therapy and chronic care due to loss of autonomy and functionality.

## Main differences between training programs. An international survey

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**Objectives:** To describe the differences between countries throughout the training program of new specialists. Given the broad spectrum of them, it was our aim to address specific features of the residency, as well as theoretical and practical skills.

**Methods:** Descriptive cross-sectional study based on a structured questionnaire with closed questions. A 69 items questionnaire was performed and given to trainees from 20 different countries at ESIM (European School of Internal Medicine) the last day of the course. 38 questionnaires were received and statistically analyzed.

**Results:** Average working hours (h) are 8.4 per day and 5.2 shifts per month, with 16 h length and a remarkable variability from 9 h to 32 h in Cyprus. Vast majority of residents do the ward taking care an average of 12.7 patients daily, whereas just 52% of them run outpatients clinics attending 20 patients per week. There is also a wide variation on the level of acquisition of practical skills such as placement of central venous lines, orotracheal intubation and US scanning, being all of them extremely infrequent. 50% of the trainees have competence-defined programs and 65.8% identify a tutor role. More than two thirds rotate on accident and emergency, intensive care unit and cardiology, but a few rotate on dermatology, radiology or primary care. Just 39.5% of them are allowed to ask for optional additional attachments. Level

tests are mandatory in all countries except in Canada and Spain. 47% of residents will accomplish another subspecialty. Average training length is 5.2 years although in countries like the United Kingdom can be prolonged. 28% and 57.9% of respondents perform during their program a PhD or a Master respectively. More than half (68%) do not have specific time dedicated to research and 4.6 hours per week on average are dedicated to it. 52% of trainees remark the necessity of psychological support but just 34% of them have access to it. Quality of life perception was 6.6/10 and global satisfaction 6.7/10. 83% of them would like to keep working on their own countries and 63% of residents are confident about that.

**Conclusions:** It seems clear then that a huge range of approaches to the training program exist. Furthermore, living in a globalized world leads people to high mobility and migration as a normal fact. Taking into account that residents from different origins can spread around countries, it is reasonable a new insight in order to reach new agreements and consensual frameworks.

## Venous congenital malformations – a rare pathology

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**Introduction:** The global incidence of vascular malformations among the general population is perhaps under 1.5%. About 2/3 of them have predominant venous birth defects. Abnormalities of the deep venous system have been seen in association with superficial compensatory varices, most commonly they are unique, localized in a particular anatomical segment, but can appear in multiple areas, especially in cases with familial aggregation. Distribution is equal in both sexes, but there are variations depending on geographic area. Vascular malformations may be associated with systemic disease. Sometimes venous thromboses appear at malformations; these are low-flow lesions.

**Case reports:** We present two cases of venous congenital malformation diagnosed by venous Doppler ultrasound and angio-CT. The first case is a female patient, 65 years old, with known superficial varicose veins, but asymptomatic until 6 months ago, when there occurred a persistent pain in her left thigh. Doppler ultrasound of the lower limbs diagnosed left common femoral vein thrombosis and patient began treatment with oral anticoagulants. Due to persistent symptoms, we decided to conduct an angio CT, which showed the existence of vein birth defects – left common iliac vein aplasia, and multiple anastomosis situated in the lower lumbar and hypogastric region, which connects the left superficial femoral vein distally. As a result, oral anticoagulant treatment was discontinued and we have continued investigations to elucidate the cause of pain in her left thigh. The second case is a woman aged 41, which presents a right popliteal fossa pain, accompanied by functional impotence. Doppler ultrasound examination highlights a tubular venous malformation, partially thrombosed, in the posterior muscles of the thigh and in the popliteal fossa, which probably communicate with the deep venous trunks. Angio CT confirmed the diagnosis, and because of cranial communication with an extended network of superficial veins and distal with the

tibioperoneal venous trunk, surgery could not be performed and we opted for medical treatment with oral anticoagulants.

**Discussion:** Venous malformations are rare in current medical practice; we met two cases in four years. They require a complex evaluation and appropriate treatment for each case.

## Pneumoperitoneum, a rare diagnosis – 2 case reports

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**Introduction:** In this case we want to enhance pneumoperitoneum as a rare but fatal condition if not promptly treated, sometimes difficult to diagnose due to the lack of symptoms and the difficulty to interpret certain images by an unexperienced eye.

**Case report:** Two cases of pneumoperitoneum caused by the perforation of a hollow viscus that were initially observed by Internal Medicine after being admitted at the Emergency Room. Two different situations were observed – an ischemic bowel/bowel dysmotility and a bowel obstruction as a rare consequence of the local growth of a prostate cancer. The first presented with diffuse abdominal pain, without tenderness, and constipation, and the second mostly with respiratory symptoms but also with constipation and abdominal pain, also without tenderness. Although both presented with elevated inflammatory parameters, the diagnosis was not immediate as X-ray images were merely suggestive hence needing confirmation with an abdominal CT-scan. After establishing the diagnosis, surgery was promptly initiated in both patients but was only successful in the second one.

**Discussion:** Pneumoperitoneum is a condition defined by the finding of air within the peritoneal cavity. It is mostly caused by the perforation of the abdominal viscus, most frequently as a consequence of medical procedures, although not every perforation results in a pneumoperitoneum. When a hollow viscus is perforated it may cause peritonitis which may rapidly evolve to septic shock, multiple organ failure and mortality in a rate of 35-45%, therefore being classified as a surgical emergency. Clinical findings may be poor and CT-scan is the gold-standard for its diagnosis' confirmation as it is more sensitive than a plain abdominal radiography. Undoubtedly, it is the brevity of the diagnosis that may avoid a fatal ending.

## Compliance of venous thromboembolism prophylaxis in internal medicine ward, a prospective study

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**Objective:** To analyze the appropriateness of thromboprophylaxis applied to inpatients of internal medicine ward from a tertiary health center, according to local protocol (adjusted from the

Portuguese Internal Medicine Society national guidelines related to venous thromboembolism (VTE), published in 2010).

**Methods:** Prospective study, enrolling all patients admitted in the internal medicine ward during 24h per month (first Friday of the month), in a period of five years (since 1/3/2010 to 31/12/2014). Exclusion criteria were: admission inferior to 4 days or previous hypocoagulated patients. Data collected included VTE written risk assessment, adequate method prescription and errors at day one (D1) and day four (D4).

**Results:** In the study 243 patients were included, mean age 73.9 years, 50.2% females. At D1, 13 of 243 had no written VTE risk assessment data; 12 had no indication for prophylaxis. Of the 231 eligible adequate VTE prophylaxis was given to 88.8% (low molecular weight heparin was the most common anticoagulant used). At D4, 86.6% of the patients maintained adequate VTE prophylaxis. Decrease in written risk assessment data and consequent errors were noted. During this five year study, the global adequate VTE prophylaxis rate in the eligible patients was 87.8%.

**Conclusions:** Considerable efforts have been made to implement prophylaxis in patients at risk, resulting in high thromboprophylaxis compliance. Local adjusted protocols and the systematic assessment of its applicability represented a major step for the achievement of best practices and outcomes.

## DRESS syndrome due to carbamazepine

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**Introduction:** DRESS syndrome (drug reaction with eosinophilia and systemic symptom) is a secondary effect induced by medication, with an incidence of 1:1000-1:10000. It has great variability and can be presented by fever, exanthema and organ involvement. It usually occurs 2-6 weeks after starting medication and can be life-threatening. We intend to present a clinical case on DRESS syndrome after starting carbamazepine and discuss the treatment options.

**Case report:** A 46 years old female patient, with bipolar disorder who went to the emergency department with fever and pruriginous maculo-papular cutaneous rash for a week. We made a complete clinical history and found that she had initiated carbamazepine 2 weeks ago. All medications, including carbamazepine were stopped and we done further a complete laboratory evaluation. On laboratory evaluation, we found eosinophilia and mild elevation of the liver enzymes. Besides, the patient was gradually getting better after stopping medication. We reinitiate one by one the other medication, except carbamazepine, with no other secondary effects. The patient was discharged on corticosteroid therapy, with clinical and laboratory improvement and was followed-up on Internal Medicine Outpatient Clinic.

**Discussion:** With this report, we want to show the importance of a detailed clinical history, namely with focus on medication, even those that were started several weeks before. DRESS syndrome can be due to genetic enzyme deficiencies, genetic associations with HLA and possible drug-virus interactions,

namely HHV-6. It can be life-threatening with 10% mortality. The main responsible medications are allopurinol and phenytoine, but there are already described cases with carbamazepine. There are also 2 sets of diagnostic criteria that can be used to predict the possibility of DRESS syndrome. The prompt diagnosis is essential, because the earlier the medication was stopped, the better the prognosis. The treatment is based on corticosteroids, but other immunosuppressants can be used.

## Sarcoidosis – the strange facets of a disease full of unknowns

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**Introduction:** Sarcoidosis remains one of the most challenging diseases in medicine. It is a granulomatous disease of unknown etiology, in which genetic, immunological, environmental and infectious factors seem to participate. Any organ or system can be affected with a wide range of clinical manifestations.

**Case report:** Disclosing the case of a 37 years woman without relevant medical history or usual medication that was admitted at the hospital for limiting pain in the lower back, night excessive sweating, weight loss, fever, headache and vomiting for 2 weeks. During the first days there was a progressive worsening of symptoms, namely severe headache and profound fatigue. A large analytical study was performed. Of relevance, there was no anemia and inflammatory markers were not very significant. Microbiological exams including blood cultures for Brucella and Mycobacteria were negative. Autoimmune markers were also within normal range. A lumbar puncture was performed but without relevant findings. Chest radiography, abdominal and renal ultrasound, and brain and spine tomography were also normal. The patient was assessed by ophthalmologist and neurologist, without identifying any pathology. Finally, the chest tomography revealed no changes in the lung parenchyma but found mediastinal lymphadenopathy, compatible with the hypothesis of sarcoidosis. Bronchoscopy revealed adenopathic subcarinal conglomerate and bronchial lavage was collected; cytological examination was negative for malignant cells, as well as to Ziehl-Neelsen test. At this point, and having excluded other causes, it was decided to start prednisolone at a dose 1mg/kg/day and there was a marked improvement of symptoms. The patient was discharged asymptomatic and oriented to pulmonologist consultation.

**Discussion:** In medicine, as in many areas of human occupation, the occult tends to enchant. Perhaps this explains the great interest in sarcoidosis, a disease full of unknowns. The most common symptoms are dyspnea, cough and chest pain, commonly presents with bilateral hilar adenopathy, pulmonary infiltrates in radiography and skin or eyes lesions. This case report shows that despite the absence of suggestive symptoms, sarcoidosis should be considered in the differential diagnosis of systemic diseases. The diagnosis is based on the clinical presentation and evolution over time, and its crucial to exclude infectious or neoplastic conditions.

## Allopurinol associated DRESS

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**Introduction:** Iatrogenic effects represent a burden problem in polymedicated patients with multiple comorbidities.

**Case report:** We describe a case of a 66 years old Caucasian woman that was admitted to our hospital with a one-week history of facial edema and pruriginous erythematous rash, initially localized in both hands, with progression to arms and lower limbs. She also complained of diarrhea and oliguria. There was no history of fever, arthralgia, or contact with animals. The physical examination revealed a wound on the right hallux with purulent exudate, and dehydration. Her past medical history included diabetes mellitus, hypertension, obesity, diabetes-associated stage 3 chronic kidney disease and arterial peripheral vascular disease. She started taking allopurinol about 3 weeks before. In the complementary exams, there was leukocytosis, elevation of hepatic enzymes, worsening of serum creatinine level, C reactive protein, and rhabdomyolysis markers levels. She started a cephalosporin directed to a scenario of sepsis with hallux wound starting point and prerenal azotemia. During hospitalization, rash evolved into scaly lesions, and there was a worsening of liver enzymes, coagulations tests, and onset of eosinophilia. In the face of a suspected DRESS (drug reaction with eosinophilia and systemic symptoms) syndrome associated with allopurinol intake, the patient started high dose corticosteroid therapy. There was a gradual lowering of serum creatinine and hepatic tests, accompanied with regression of the scaly rash. The patient was discharged from the hospital, with slow weaning corticosteroids.

**Discussion:** With an estimated incidence of 1 in 1000 to 1 in 10,000 drug exposures, DRESS represents a severe idiosyncratic drug reaction with a long latency period, being allopurinol one of the most frequent reported causes. The clinical suspicion can be substantiated by a history of exposure to high risk medication, mucocutaneous rash, fever, facial edema and adenomegalies. Eosinophilia >700/microL, abnormal liver function tests and renal impairment constitute other diagnostic criteria. The main treatment is withdrawal of the offending drug and corticosteroids according to the symptoms and renal or pulmonary involvement. Pharmacogenetic studies have found an association between HLA haplotypes and susceptibility to DRESS, namely HLA-B\*5801, reported in Portuguese patients with allopurinol-induced DRESS. Clinicians should be aware of this potential adverse reaction as well as other DRESS inducer drugs.

## Assessing the nutritional risk of hospitalized patients in an internal medicine ward

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**Background:** A significant part of all hospitalized patients is at risk of malnutrition because they often have multiple pathologies,

risk factors and poor social support. Despite that, the nutritional status of the patients is often overlooked, resulting in higher risks, increased mortality and longer hospital stays.

**Objective:** Analyze and characterize the patients hospitalized with risk of malnutrition and how it was dealt with.

**Methods:** The data was gathered in a single day, through direct observation and consultation of the clinical processes of all the patients hospitalized in an Internal medicine ward. The analyzed data included age, gender, chronic bed riddance, comorbidities like stroke, diabetes mellitus, chronic kidney failure, chronic pulmonary obstructive disease and others, body mass index (BMI), type of feeding and prescribed diet. The risk of malnutrition was calculated according to the NRS 2002 Scale, and a score equal or greater than 3 was considered as nutritionally at risk.

**Results:** Of the 30 included patients, 15 (50%) were at risk of malnutrition, 12 (80%) of which were men, and with a mean age of 81 years. The mean NRS was 4, 7 (47%) of the patients were underweight, 1 (7%) overweight and 1 (7%) obese. The most common comorbidity associated with a nutritional risk was diabetes mellitus, chronic pulmonary obstructive disease and chronic kidney failure. Of all the patients at risk, 5 (33%) were fed by nasogastric tube, 100% had diets in the medical prescription, but only 9 (60%) were doing what was prescribed. Just 1 patient at risk was receiving additional nutritional care by a nutritionist.

**Conclusions:** The risk of malnutrition in our population is high and associated with multiple comorbidities. The nutritional status is seldom assessed in the daily practice and can be improved. The NRS 2002 is a simple and useful tool that provides valuable information and can be applied easily in the clinical practice.

### **Concomitant renal and splenic infarction: uncommon complication of atrial fibrillation and hyperhomocysteinemia**

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**Introduction:** Atrial fibrillation (AF) and hypercoagulable states are known risk factors for thromboembolic events. Cardiac arrhythmia is responsible for cerebral ischemic events in elderly population but systemic embolization can also occur. The aim of this report is to present the case of a rare presentation of systemic embolization with renal and splenic infarction as a complication of atrial fibrillation and hyperhomocysteinemia. The authors report the case of a patient with concomitant renal and splenic infarction as a complication of AF and hyperhomocysteinemia.

**Case report:** A 70 years old man is admitted to the emergency department with left upper quadrant and flank abdominal pain with 12 hour evolution. Afebrile and hemodynamically stable, the physical examination revealed tender abdomen in the left upper quadrant and flank, with no peritoneal reaction. Laboratory analysis showed elevated LDH 430 UI/mL and serum creatinine (SCr) 1.4 mg/dL, with no elevation of inflammation parameters. Abdominal ultrasound showed no relevant aspects but the patient had persistent and worsening pain complaint. Enhanced contrast abdominal computer tomography showed peripheral spleen infarction and bilateral kidney ischemia, with no

visible thrombus and with preserved aorta, iliac and mesenteric arteries, suggesting an embolic cause. The patient started on hydration and pain treatment, as well as anticoagulation with enoxaparin. Investigation revealed permanent atrial fibrillation on 24 hour Holter with frequent periods of tachyarrhythmia. Transesophageal echocardiogram showed no intracavitary thrombus or valve vegetation. No neoplastic cause was found, and autoimmune study was normal. Hyperhomocysteinemia (41.3  $\mu\text{mol/L}$ ) was found. The patient evolved with clinical stability and is anticoagulated with warfarin and supplementing folic acid, with no recurrent thromboembolic event since.

**Conclusions:** Renal and splenic infarctions are uncommon conditions that can occur from systemic embolization. Most cases are due to AF but other conditions must be excluded, such as cancer, infectious endocarditis, autoimmune and hypercoagulable conditions. The diagnosis must be considered in patients that present with and left quadrants abdominal pain, elevated LDH and SCr. The authors alert to this condition because it is rare, it has an increased morbidity and mortality rates and is often associated with a large range of primary causes that can determine the long term outcome.

### **Bone Paget's disease: when other comorbidities hide the diagnosis**

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**Case report:** 78 years old woman, with hypertension, dyslipidemia, type II diabetes mellitus and chronic renal disease, was admitted to an internal medicine ward for 7 days, diagnosed with acute heart failure caused by pulmonary infection. She was treated with amoxicillin clavulanate for 8 days. During hospitalization, patient complained about bone pain. Due to blood analysis changes (alanine aminotransferase 15, aspartate aminotransferase 41, alkaline phosphatase 324) she was submitted to an abdominal ultrasound which showed a semi enlarged gallbladder, with normal wall, 3 nodular formations (8 mm maximum), medium echogenicity, compatible with cholesterol polyps. Patient was then discharged. New blood analyses in outpatient consultation showed persistent cholestasis. Magnetic resonance cholangiopancreatography was conducted for clinical enlightenment, but nothing was found. Despite all clinical research, cholestasis had no clinical improvement and patient complaints were a very important source of impairment. Following a further assessment new blood analyses showed: calcium 9.3, phosphorus 3.8, alkaline phosphatase 430 (increased since last control); urinary hydroxyproline 60.7/24h. Treatment with alendronic acid was rapidly implemented. Full body scintigraphy showed: clinical evidence compatible with Paget disease, with involvement of several dorsal and lumbar vertebrae, first right costal arch, left scapula, pelvis and right femur.

**Discussion:** The relevance of the case relates to the need to alert clinicians to the importance of integrated symptomatology in changes detected in the diagnostic tests. Only then it is possible to direct the investigation to obtain precise etiological diagnosis. Particularizing the conduct to this clinical case, only through

research carried out was possible to identify the elevation of the FA presented, as well as to verify that osteoarticular complaints were not due to degenerative bone disease but due to Paget's bone disease, allowing adaptation of therapeutic approach and consequent improvement of patient's quality of life.

## Carotid involvement in patients with atherosclerotic lower extremity artery disease

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**Background:** The carotid arteries are one of the most important target vessels for atherosclerotic involvement. Among the most serious complications are stroke (produced by embolization of fragments from the atherosclerotic plaque), cardiac ischemia, cranial nerves involvement, arterial hypo- or hypertension and hematomas.

**Objective:** To identify carotid changes in patients diagnosed with atherosclerotic lower extremity artery disease.

**Material and methods:** 52 patients (26 male, 26 female), mean age 68,2 years, asymptomatic from carotid standpoint (no stroke or transient ischemic attack in the last 6 months), diagnosed with atherosclerotic lower extremity artery disease, whose carotid arteries were evaluated by ultrasonography. They were divided in three groups according to the La Fontaine classification: stage II: 27 patients, stage III: 7 patients and stage IV: 18 patients.

**Results:** The majority of the patients (57,7%) had non-significant carotid stenosis, 21,2% had incipient changes, 15,4% had significant stenosis and only 5,8% had no changes. This pattern was observed in both sexes, as well as in all La Fontaine stages (57,7% non-significant stenosis in both sexes, 48,1% non-significant stenosis in stage II, 85,7% in stage III and 61,1% in stage IV).

**Conclusions:** Patients with atherosclerotic lower extremity artery disease are likely to have carotid involvement, especially non-significant stenosis. This can be observed in both sexes and in all stages. One particular aspect is that we couldn't establish a correlation between the severity of the lower extremity involvement and the carotid one (we had a patient in stage IV La Fontaine with no carotid changes and 6 patients in stage II with significant stenosis). However we believe patients with lower extremity artery disease should be screened for carotid involvement before they suffer a debilitating or fatal stroke.

## Diagnostic and therapeutic challenge of asymmetric lower extremity edema

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**Introduction:** Differential diagnosis of asymmetric lower extremity edema is not always straightforward. The most likely cause of leg edema is venous insufficiency and idiopathic edema (woman under age 50) but deep vein thrombosis because of its risk of pulmonary embolism has to be ruled out first.

**Case report:** A 51 years old male was admitted for high intensity right thigh pain with subsequent lower extremity edema and melanic stools for 10 days. Past medical history is significant of an episode of right DVT (in the previous year) on anticoagulation with acenocoumarol 4 mg/day at admission. Physical examination reveals important right lower extremity edema, erythema, tenderness and numerous ecchymosis. The laboratory data indicates: highly increased INR (21.86) and APTT (239 s), accelerated VSH, severe microcytic anemia, hyposideremia and high ferritin in context of chronic inflammation, increased LDH (1102 U/L) and GGT (188 U/L), negative viral markers (HBV, HCV), normal AFP but increased CEA (4 times normal range). The possibility of bleeding from acenocoumarol toxicity and a calf hematoma rather than a deep vein thrombosis is taken to account. The Doppler venous ultrasound ruled out the diagnosis of DVT. The abdominal ultrasound reveals a hyperechoic, poorly delimited mass that occupies 2/3 of right hepatic lobe later confirmed on a MRI as hepatocellular carcinoma. A month later the patient presented the same signs and symptoms (left lower extremity edema, pain and tenderness) and the Doppler venous ultrasound confirmed the diagnosis of left popliteal and femoral DVT. After carefully consideration of benefits versus risks the anticoagulation treatment was started with apixaban.

**Discussion:** The small correlation of cancer diagnosis in a 30 month follow-up period after an unprovoked DVT (3.2%) raises many questions; a perspective is the extensive screening investigations with high doses of radiation, increased days of hospitalization and costs; on the other side is the clinical and ethical issue of early cancer detection with the possibility of lowering cancer related mortality.

## Arterial hypertension in women with early rheumatoid arthritis

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**Objective:** To detect the characteristics of arterial hypertension (AH) and its association with the risk factors (RF) for cardiovascular diseases (CVD) and the disease activity in women depending on the duration of rheumatoid arthritis (RA).

**Methods:** 204 women with RA were examined, 64 (33%) had early RA with the duration less than 1 year. RA was diagnosed by ACR/EULAR (2010) criteria. The groups were comparable according to the age: the patients with early RA were 19 (54.9) 76 in other cases of RA they were 32 (55.3) 77 years. The average duration of early RA was 4 (6.6) 10 months, in other cases of RA the duration of the disease was 2 (11.2) 31 years. The activity of early RA according to DAS 28 was high (>5.1) 60 (94%), that of RA was 106 (76%), the average activity – (3.2-5.1) 6% and that of RA was 24%, low activity was not revealed. Statistical data were obtained with «Statistica» v 6.1 software.

**Results:** In the patients with early RA arterial hypertension was revealed in 74% and in other cases of RA – in 70%, primary AH was diagnosed in 17 and 16% respectively at the same time with RA. Blood pressure in patients with early RA was SBP 100 (141) 179 / DBP 60 (80) 120, in patients with RA – SBP 100

(140) 212 / DBP – 60 (81) 112, ( $p < 0.05$ ). Blood pressure was increased two times frequently in patients with early RA than in patients with RA after they were diagnosed with RA (60% and 31%, respectively), before being diagnosed (53% and 30%); although both groups regularly had antihypertensive therapy in 33% and 37% of cases ( $p < 0.05$ ). In patients with RA and AH the risk factors for CVD according to the incidence were decreased physical activity because of early RA – 86% (because of RA 88%), malnutrition – 91% (88%), abdominal obesity – 79% (81%), tachycardia – 71% (69%), the increased total blood cholesterol level – 79% (61%), family history of early CVD – 58% (63%), menopause under 45 years – 44% (45%), stress / depression – 68% (45%), anxiety – 86% (61%), sleep disturbance – 69% (30%), hyperglycemia – 12% (13%), smoking – 6% (4%), alcohol consumption – 0% (1%). The most common markers of chronic immune-inflammatory process in RA and AH were ESR and C-reactive protein (CRP). ESR in case of early RA was 1.3 times more common (100, 80%), CRP – in 10% more often (70, 60%) ( $p < 0.05$ ).

**Conclusions:** Thus, AH in early RA has the following characteristics: the increased blood pressure was recorded twice as often and 1.2 times more often after the diagnosis of RA ( $p < 0.05$ ). RA is supposed to influence on the development of AH (before being diagnosed with RA – 51%, after – 62%) ( $p < 0.05$ ). In addition, AH is associated with the risk factors for CVD ( $p < 0.05$ ). The influence of chronic immuno-inflammatory process on the development of AH is observed more frequently in case of early RA ( $p < 0.05$ ).

### Evolution of the relationship between glycemic status at type 2 diabetic and carotid intima media thickness and the rate of neutrophil/lymphocytes

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**Objectives:** There is a significant relationship between atherosclerosis and inflammation. The studies conducted in recent years, as a marker of a new, simple and cheap inflammation the ratio of neutrophil/lymphocytes (NLR) is emphasized. In our study we purpose to evaluate the relationship between macrovascular complications in diabetic patients and carotid intima-media thickness (CIMT) and NLR.

**Material and methods:** There are 63 type 2 diabetic patients and as a control group 37 healthy volunteers on study. The patients who have acute and chronic infection, systemic disorders (cardiac, renal, hepatic insufficiency, hematologic and autoimmune diseases), blood transfusion history, drug uses that could affect the bone marrow have not included into the study. The tests of the patient's kidney and liver functions, electrolytes, thyroid hormones, fasting blood glucose and A1c levels, lipid parameters, CRP, erythrocytes sedimentation rates (ESR), hemogram levels have measured. After measuring anthropometric measurements of all patients

ultrasound CIMT was calculated by the same radiologist.

**Results:** There were not any differences between the groups in terms of age, sex, BMI, hemoglobin and platelet counts. There were significant differences in terms of lipid profile, glucose, ESR, CRP values between case and control groups. NLR averages of patients type 2 diabetes was  $2.8 \pm 2.2$  and healthy control group average was  $1.78 \pm 0.56$ . Between the two groups there was a statistically difference ( $p = 0.01$ ). Patients diagnosed with type 2 diabetes have a positive correlation between A1c- NLR ( $r = 0.204$ ,  $p = 0.046$ ) and CIMT-mean ( $r = 0.274$ ,  $p = 0.008$ ). There was a correlation between blood glucose values and NLR ( $r = 0.192$ ), but this correlation was not statistically significant ( $p = 0.055$ ).

**Conclusions:** Our study shows that NLR may be an important marker to predict macrovascular complications in diabetic patients. We think it is needed more comprehensive studies in this issue with more patients are required.

### Self-perception in the taking blood pressure in the pharmacies of Valencia. FARMAPRES project

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**Objective:** Knowing the reality of taking blood pressure (BP) in pharmacies of Valencia and self-perception of the importance of pharmacy in the control and monitoring of hypertensive patients.

**Methods:** Survey sent to holders of the pharmacies of Valencia, through professional associations of the 3 provinces.

**Results:** The number of received polls was 381, which represents 16.7% of the whole. Being distribution by provinces as follows: Alicante 230 (60.4%), Castellón 70 (18.4%) and Valencia 81 (21.3%). 62.7% of pharmacists believe that pharmacies fulfill their role in taking blood pressure. 33.6% considered having an important role. The strengths highlighted by the pharmacists themselves to vindicate their importance in the control and monitoring of hypertensive patients are: client proximity (91.6%), scheduling flexibility (82.7%), direct health education in the patient (65%), decreasing the white coat effect (52.8%), the least cost to the patient (37.8%) and the possibility of detecting asymptomatic arterial uncontrolled hypertension (13%).

**Conclusions:** Although, up to 62.7% of pharmacists believe that pharmacies fulfill their role in making blood pressure, only 33.6% considered to have an important role. Pharmacists base their relevance in the control and monitoring of hypertensive patients, in their proximity to the patient. This proximity confers the ability to detect asymptomatic uncontrolled hypertension and perform more direct health education on the patient. All this would result in a reduction of the costs of control and monitoring.

## Lung function of Latvian patients with a newly diagnosed sarcoidosis

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**Objectives:** Sarcoidosis is a multisystem granulomatous disease with unknown etiology that in 90% of cases affects the lungs. Clinical manifestation and development severity of the disease varies in different countries and ethnic groups. Extensive research on sarcoidosis has not been made in Latvia. The aim of the study is to assess a correlation of the lung function tests with sarcoidosis radiological stage and demographic indicators.

**Material and methods:** Almost all patients with primary diagnosed sarcoidosis have been investigated at Riga Eastern Clinical University Hospital "Tuberculosis and Lung Diseases Centre". In the study retrospectively were analyzed medical records of all the patients who had been hospitalized during time period from January 1st 2013 till December 31st 2014. Further analysis includes only patients with histologically verified sarcoidosis functional indexes – VC, FVC, FEV1, FEV1/VC, the transition factor (DLCO) and conversion rate (KCO). Medical data has been analyzed in relation to patients' age, gender, radiological stage of disease manifestation (acute or chronic), and smoking.

**Results:** 208 of 275 patients have histologically proven sarcoidosis (109 men and 99 women). Patients' average age at the time of diagnosis was  $37 \pm 12$  years. There are 19.7% of smoking patients, 68.9% of non-smoking patients and 11.7% of ex-smokers. Reduced function tests <80% from predicted FEV1, VC, FVC, are 4.8%, 2.9%, 7.2% of patients respectively. For 38.5% of the diagnosed patients' diffusion factors were less than 80%. Statistically significant correlation between lung function tests and age, gender, or smoking has not been found. Dividing the patients by stages of sarcoidosis, pulmonary function tests decreased depending on the stage. On IV stage FEV1/VC averages decreased to 88% (predicted form), that indicate on lung obstruction. There is a statistically significant correlation between the radiological stages of sarcoidosis and lung function VC, FVC, FEV1 results ( $p < 0.01$ ). It was found that lung diffusion factor decrease depend on the stage (DLCO decreased from 89.6 to 79.1%), which was statistically significant ( $p < 0.05$ ).

**Conclusions:** From this work we can conclude that in Latvia sarcoidosis affects mostly young and middle-aged people. Smoking or patient age does not significantly affect the development of sarcoidosis. Lung function and FEV1, VC, FVC, FEV1 / VC, DLCO tend to decrease.

## Rehabilitation in intensive care unit: a protocol for auditing current practice (RE-BREATH: REaBilitation of REspiratory failure Audit in Hospital)

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**Objectives:** The amount of rehabilitation performed in intensive care unit (ICU) is often inadequate and there is a need to standardize pathways for clinical decision-making and education. A clinical audit of current rehabilitative practices in the ICU of Ospedali Riuniti of Ancona (RE-BREATH: REaBilitation of REspiratory failure Audit in Hospital) is therefore being conducted in order to evaluate the impact of an expert-driven vs event-driven rehabilitative management of patients with respiratory failure hospitalized in intensive care units on clinical and organizational outcomes and eventually export the model to other settings, using a systematic approach based on daily assessment of patients rehabilitative needs rather than an occasional approach consequent to the demand of the physician who has the patient in care.

**Methods:** After a proper literature research, a multidisciplinary team made by internal medicine methodologists, physiotherapists, physiatrists and anesthesiologists gathered up in order to select best evidence about expert-driven rehabilitative management of patients hospitalized in intensive care units and to agree upon criteria to build indicators.

**Results:** The criteria were derived from the NICE guideline "Rehabilitation after critical illness", published in 2009. A consensus list of data items, including patient demographics, reason for admission, time to referral for rehabilitation management, successive physiotherapy item, hospital length of stay and ventilator-free days were included as part of the audit. Health professionals involved in data collection were specifically identified and trained before the audit started. A pilot audit have been also conducted to test the feasibility of the audit protocol and to undertake the subsequent protocol refinements. The comprehensive prospective audit process has been estimated to last about three months, until the recruitment of at least 130 patients. Data will be collected with a dedicated data entry paper table and encoded to be analyzed using MS Excel®, then reported as means and percentages as appropriate.

**Conclusions:** This ambitious project aims to identify possible strengths and weaknesses of usual clinical practice in an area of interest (rehabilitation) lacking strong high quality evidence. Our results will constitute an important platform for implementation of evidence-based management in rehabilitative and critical care settings focused to achieve best patient and health outcomes.

## A rare cause of rhabdomyolysis

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**Introduction:** Rhabdomyolysis is a clinical entity triggered by a number of factors, including trauma, hyperthermia, infections or other health disorders. It can result in myoglobinuria, acute renal failure, electrolyte abnormalities, acidosis, clotting disorders and hypovolemia. Physical symptoms include muscular weakness, pain, cramping and darkened urine. Non-traumatic causes include drug use such as statins and strenuous exercise. Several food-related causes of rhabdomyolysis have been recognized, including quail (coturnism). We report an interesting

case of a patient diagnosed with rhabdomyolysis after quail ingestion.

**Case report:** A 78 years old Caucasian woman with no previous history of illness was referred to our clinic during September 2014 for left pleuritic discomfort and myalgias. Her symptoms began about 3 hours after eating a meal of roasted quails; before eating, she experienced muscular exertion completing household activities. Her physical examination revealed diffuse muscle weakness with no neurological signs and no muscular stiffness. The laboratory test results were indicative of rhabdomyolysis, showing mildly increased levels of aminotransferases and lactate dehydrogenase and highly elevated CK levels of 6652 U/L (normal range 45-171 U/L). CK-MB and troponin levels were normal. Urinalysis revealed myoglobinuria. Results of ECG, echocardiography and chest CT were unremarkable. None of her family members, who also consumed quails, reported any symptoms. The patient was hospitalized; she received adequate fluid replacement and then discharged.

**Discussion:** Rhabdomyolysis after quail ingestion is a rare entity. It is caused by coniine, an alkaloid that has a curare-like action and nicotine effects on autonomic ganglia and which is contained in seeds eaten by the quail, especially from hemlock (*Conium maculatum*). However, coniine triggers clinical manifestations only in sensitive people, while muscular exertion before or after the meal is believed to aggravate and accelerate the manifestations. It should always be considered in the differential diagnosis of rhabdomyolysis especially in endemic regions like Greece and during the quail migration period in autumn.

## Hypomagnesemia due to long-term use of proton pump inhibitors

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**Introduction:** Hypomagnesemia is an electrolyte disturbance with variable clinical presentation. Low levels of magnesium can be caused by decreased intake, redistribution of magnesium from extracellular to intracellular space, gastrointestinal and renal loss and drugs such as proton pump inhibitors (PPIs). We report an interesting case of a patient diagnosed with hypomagnesemia due to long-term use of omeprazole.

**Case report:** A 73 years old Caucasian man, with a history of coronary heart disease, diabetes mellitus type 2 and chronic use of omeprazole due to gastroesophageal reflux disease, was admitted to our clinic due to weight loss (>10 kg), worsening anorexia, vertigo and vomiting over the last month. The patient remained bedbound for the last 2 months and developed symptoms of depression, with poor response to already prescribed antidepressant therapy. He presented with a plethora of neurological signs (muscle twitching, rest tremor, apathy). Computed tomography of the brain was unremarkable. Gastroscopy revealed hypertrophic gastric mucosa; histology findings were consistent with the patient's chronic use of PPIs. Serum magnesium levels were extremely

low (0.2 mg/dL). The patient was treated with IV magnesium replacement and esomeprazole was discontinued. 24-hour urinary magnesium, stool magnesium and fat measurements showed no abnormal urine or gastrointestinal magnesium loss respectively. The patient showed immediate clinical response after magnesium replacement, with impressive reversal of his neurological symptoms and was discharged after 5 days with oral magnesium supplementation (121.5 mg/day). He had no clinical or laboratory relapses on follow-up.

**Discussion:** Patients with neurological symptoms and long-term treatment with PPIs should always be checked for hypomagnesemia, since it can present with misleading symptoms. All other causes of hypomagnesemia should be meticulously excluded.

## Palliative needs in an internal medicine ward

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**Introduction:** Palliative care (PC) is fundamental when considering the National Health System. As global population «grows old» and chronic diseases increase their prevalence, the need for health assistance and dependence of care gives increase. Consequently we have seen an increase in the need of human resources and in the costs of care. Identifying correctly and earlier the patients which need PC is a critical step to better organize and distribute these precious resources.

**Objectives:** To evaluate the prevalence of patients in need for PC admitted to an internal medicine ward in an acute care hospital and further study these patients concerning demographic data. Evaluate the burden of oncology patients in this population.

**Methods:** The patient population studied concerned the patients admitted to our ward between January and March of 2015. The study was observational and prospective. An internal survey adapted from the "Supportive and Palliative Care Indicators Tool (SPICT)" was applied to identify the need for PC to every patient admitted. Once identified the need for PC the patients were further investigated in terms of clinical and demographic data. Coding of patients, clinical and demographic data registration and statistical analysis were performed using the Epi Info™ 7 program.

**Results:** 95 patients in 204 (total admitted to our ward), that is 47%, were found to fulfill the criteria for PC. We did not observe any difference in this respect between the genders. Only 18% of those patients had an oncological disease. The average age of patients with PC need was 78 years. Infectious diseases were the most frequent reason for hospital admission, either amongst the patients with oncological disease and the ones without. Amongst the oncologic patients the digestive tumors were the most frequent determining the need for PC and dementia was the most frequent determinant for PC need amongst the other group of patients.

**Conclusion:** This study showed that the population of patients PC need is significant in an acute care hospital particularly in an internal medicine ward. It reveals the need for active specialization in the care for these patients.



## Severe deficit of vitamin D and plaque psoriasis, a casual relationship?

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**Introduction:** The vitamin D deficiency is associated with multiple autoimmune diseases, including type 1 diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease. It is also known association of low levels of vitamin D with psoriasis, even without extensive skin lesions that could justify a decrease in absorption. It is also unaware of the pathogenic mechanisms that explain this relationship. It is known that the active vitamin D metabolite functions as immunomodulator, and inhibits activation of the immune system acquired. Apart from autoimmune diseases there is still a wide range of diseases and causal mechanisms of vitamin D deficit, including stress, decreased intake, reduced skin synthesis, advanced age, diminished sunlight, hospitalized patients, chronic kidney disease, people undergoing gastric bypass, vitamin resistance D.

**Case report:** A woman of 67 years old with a history of hypertension, dyslipidemia, hearing loss, and extensive plaque psoriasis with infiltrative and widespread lesions, reaching the scalp and nails was admitted to the medical service by opening seizures associated with hypocalcemia. In the etiologic study of hypocalcemia diagnosed severe deficit of vitamin D with normal parathyroid hormone. The supplementation with calcium and vitamin D noticeably improved the clinical condition of the patient.

**Discussion:** The authors acknowledge the importance of knowing identify risk groups that may make vitamin D deficit, including among them integrated ill in institutions, hospitalized obese patients with intestinal malabsorption (celiac disease, inflammatory bowel disease) autoimmune diseases, or individuals with limited sun exposure (black skin, skin changes, abuse of sunscreens).

## The main reasons of fatal outcome in cases of internal diseases comorbidity

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**Objective:** To determine the main reasons for fatal cases in comorbid somatic patients.

**Methods:** 2751 fatal cases in the Municipal Clinical Hospital of internal medicine were studied, the final diagnosis consisting of 2 and more nosological units. Among the deceased there were 1035 (37,6%) males, 1716 (62,4%) females at the age of  $69,4 \pm 11,5$  and  $76,0 \pm 9,8$  ( $p < 0,001$ ), accordingly. The average age came to  $73,5 \pm 10$  years old.

**Results:** The main reasons for fatal cases, both in the male and female populations are the following: brain infarction – 822 cases (30%); decompensation of the chronic forms of IHD – 632

(23%), myocardial infarction – 532 (19%), chronic cerebrovascular diseases – 403 (14,7%). Malignant neoplasms (9,2%), intracerebral hemorrhage (7,8%), the digestive system diseases (5,9%), the urinary system diseases (4,8%), COPD (3,3%) were found in the heading of the paragnosis “final diagnosis” somewhat more rarely. The immediate causes of death were the following: decompensated congestive heart failure (32,2%), pulmonary artery thromboembolism (14,2%), secondary pneumonia (19,5%), acute gastric erosions with gastrointestinal hemorrhage (8,6%), chronic renal disease (5,4%).

**Conclusions:** The main reasons for fatal cases in the great majority of comorbid patients are cardiovascular and cerebrovascular diseases. Concurrently, the share of their acute forms comes to 19% and 30%, accordingly. The main fatal complications were: decompensated congestive heart failure which occurred in every third patient, secondary pneumonia – in every fifth patient and pulmonary artery thromboembolism in 14,2% of the cases.

## Health indicators in palliative care unit

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**Objective:** Describe the organization of palliative care unit and measurement of health indicators from 2012-2014 in the area of Aljarafe.

**Material and methods:** In our hospital, the Palliative share plan is established as a model of collaboration between primary care and internal medicine, which is distributed by health-care districts with a reference internist which can be contacted from the health center by telephone, email or digital interconsultation. A direct entry to the hospitalization floor can be managed if the patient requires it or make appointments on day hospital/outpatient care to solve treatments that can not be conducted at home, avoiding emergency services for these patients. These patients are identified in consultation, during hospitalization or through primary care. When they are discharged at the hospital, an alert is sent automatically to their physician and nurse of the health center, to be reviewed by them at 48 hours of discharge. There is also a support team to support primary care integrated by a physician and a nurse. Some health indicators are established and we measured and compared them during 2012, 2013 and 2014: Patients with Advance Health Care Directives document made, direct admission to recovery ward, specific plan of care, conducted ICCAES, social evaluation of the palliative patient, contact with the Spanish association against cancer, coordination with social services, coordination with nursing department, patients who died at home, assessment in primary care within 48 hours of discharge.

**Results:** Measurement of health indicators from 2012-2014:

- Patients with Advance Health Care Directives document knowledge made: 2012 – 0%, 2013 – 29%, 2014 – 51%;
- Direct income floor admission to recovery ward: 2012 – 21%, 2013 – 15%, 2014 – 23%;
- Specific plan of care: 2012 – 38%, 2013 – 30%, 2014 – 42%;
- Conducted ICCAES (nursing care plan): 2012 – 69%, 2013 – 54%, 2014 – 74%;

- Social evaluation of the palliative patient: 2012 – 14%, 2013 – 15%, 2014 – 23%;
- Contact with Spanish association against cancer: 2012 – 21%, 2013 – 25%, 2014 – 13%;
- Coordination with social services: 2012 – 10%, 2013 – 33%, 2014 – 38%;
- Coordination with nursing of the area: 2012 – 31%, 2013 – 52%, 2014 – 45%;
- Patients who died at home: 2012 – 52%, 2013 – 49%, 2014 – 58%;
- Assessment in primary care within 48 hours of discharge: 2012 – 60%, 2013 – 62, 2014 – 65%.

**Conclusions:** 1) The palliative "Share" model allows 25% readmissions at hospital are done directly on the floor, avoiding long waits at emergency services. 2) A high percentage of patients die at home. 3) It has improved the social work and nursing evaluation. 4) It has provided the resources required for discharge and handling at home. 5) Most of the patients are evaluated at 72 hours discharge at home.

## The impact of sarcopenia and associated factors in pluripathological patients

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**Objectives:** The aim of this study is to know the prevalence of sarcopenia in a sample of pluripathological patients (PP) in a hospital scope; as well as to establish the clinical-epidemiological characteristics and the factors associated with it.

**Methods:** We conducted a cross-sectional multicenter study that included PP from outpatient services and hospitalization floor of 2 Internal Medicine Services, through weekly prevalence studies. We included the PP who was identified in the studies and that had signed their consent, excluding those who were carrier of metallic devices, had an amputation or were in the agony stage in the moment of hospitalization. Demographic, clinical, analytical and comprehensive assessment variables were surveyed and we determined whether each one of them met the sarcopenia criteria according to the 2010 European Consensus. We carried out a descriptive study of the clinical-demographic characteristics of patients with sarcopenia, as well as an inferential bivariate analysis in order to know the main risk factors associated with the presence of sarcopenia. To do that, SPSS statistics 20.0 was used.

**Results:** A number of 208 PP were included (58.3% male, average age 77.3 years old) belonging to the Hospital Universitario Virgen del Rocío and the Hospital San Juan de Dios (Bormujos), from which 43.3% (90 patients) met sarcopenia criteria in the moment of hospitalization. Among the patients with sarcopenia, the average age was 77 years old (SD±7.8), most of them males (80% of the patients). The most frequent category of PP was the category A: cardiovascular (83.1%). Inside this category, A1 stands out: heart failure (51.7%); the average of pluripathology categories was 2.66 (SD±0.79) and the one of co-morbidities was 5.7 (SD ±2.1) for each one of the patients with sarcopenia. The number of chronicle prescription medicines was 9.61 (SD±3.72). Regarding

the functional characteristics: 38.8% of patients needed a carer (Barhel >60 and/or Pfeiffer >5 errors); the average Barthel was 70 (SD±30) and the PROFUND index was 7.02 (SD ±3.1). The factors associated with sarcopenia were: male (80% vs 42.4%; p=0.000), low weight (76.1±15.8 vs 82.3±19.2; p=0.013), BMI (27.9±5,8 vs 32.2±6.9; p=0,000), overweight (24.4% vs 50.4%; p=0.000), cachexia (5.6% vs 0.9%; p=0.048), anemia: Hb <10 g/dl (36% vs 22.5%; p=0.036), cerebrovascular disease (32.6% vs 19.1%; p=0.028), presence of delirium in the last hospitalization (27.8% vs 15.3%; p=0.027) and very close to the statistic signification the PROFUND index (7.02±4.78 vs 5.73±4.27; p=0.054).

**Conclusions:** We notice high sarcopenia prevalence in our sample of pluripathological patients included in the study, up to 43%. The values associated with it were the low weight and undernourishment, cerebrovascular disease, the PROFUND index, the delirium in the last hospitalization and anemia.

## Role of adhesion molecules to heart remodeling progression in patients with inherited connective tissue disorder

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**Objective:** The aim of the study to assess the adhesion molecules associated with progression to heart remodeling in patients with inherited connective tissue disorder (CTD).

**Methods:** We examined 21 patients with CTD. Mitral valve prolapse syndrome was revealed in 19 patients and increased dysplastic stigmatization – in 3. We divided patients into 2 groups: group 1 (n=11; 10 men and 1 woman, aged 21.4±4.7 years) – patients with heart remodeling progression, group 2 (n=10; 9 men and 1 woman, aged 22.0±4.3 years) – patients without echocardiographic features of heart remodeling progression. Control group comprised 10 age- and sex-matched healthy subjects without CTD and with normal echocardiographic parameters. Heart remodeling progression was defined as increase in aorta route diameter, left atrium size, posterior wall thickness, intraventricular septal thickness, degrees of mitral prolapse and regurgitation, left ventricular volumes. The follow-up period was 3 years. Circulating levels of plasma L-, E-, P-selectines, cell adhesion molecules 1 type – intercellular (ICAM-1), platelet/endothelial (PECAM-1) and vascular (VCAM-1) were measured by using ELISA kits commercially available (Bender MedSystems GmbH, Austria). The data received were processed statistically with the help Kruskal-Wallis and Dunn tests, ROC-analysis, odds ratio (OR) and its 95 % confidence interval (CI).

**Results:** We found no evidence of association between L-, P-selectines, PECAM-1, VCAM-1 levels and heart remodeling progression. Plasma level of E-selectine were significantly higher in group 1 (42.3 [37.6–53.3] ng/ml) than in group 2 (34.5 [28.8–42.1] ng/ml) and control (36.8 [25.7–37.9] ng/ml). The incidence of ICAM-1 increased level was also significantly higher in group 1 (683.2 [597.9–841.8] ng/ml) than in group 2 (676.2 [591.7–720.0] ng/ml) and control (572.9 [570.0–605.9] ng/ml). ROC-analysis showed heart remodeling progression exacerbation in patients with E-selectine levels ≥42 ng/ml and ICAM-1 ≥957.4 ng/ml. Nevertheless OR demonstrated only E-selectine as independent heart remodeling progression predictor (OR 10.5; 95% CI 1.4–81.1).

**Conclusion:** Revealed association between heart remodeling progression and E-selectine plasma level for possible contribution of the latter in development of progression to heart remodeling in patients with CTD.

## Drugs interactions with dietary and herbal supplements in hospitalized patients

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**Objectives:** Dietary and herbal supplement (DHS) consumption increased in recent years, especially in hospitalized patients. Their use is under-reported to medical teams, although they may lead to potentially dangerous interactions between DHS and prescribed medications. In this study we evaluated DHS-drugs interactions during hospitalization and characterized DHS users at risk for interactions.

**Methods:** Of 1020 patients hospitalized in 11 departments of a public medical center in Israel between 2009 and 2014, 927 agreed to complete a questionnaire regarding DHS consumption. In the 458 DHS users, we checked through Natural Medicine Database for interactions between DHS and medications consumed during hospitalization. Multivariate logistic regression analysis was carried out to assess potential risk factors for those interactions.

**Results:** 215 of the 458 DHS consumers (46.9%) had at least one potential interaction during hospitalization (759 interactions of 174 types). 573 interactions (75.5%) had pharmacokinetic mechanism. 52 interactions were classified as having high severity. The most common potential severe interaction was bleeding in 37 interactions (52%). In multivariate logistic regression analysis, it was found that older age (OR 1.029, 95% CI 1.018-1.041,  $p < 0.0001$ ), male sex (OR 1.79, 95% CI 1.189-2.706,  $p = 0.005$ ) and rural residence (OR 1.599, 95% CI 1.00-2.5,  $p = 0.05$ ) were associated with interactions in DHS users.

**Conclusions:** DHS-drugs interaction is a common phenomenon in inpatients. They are most commonly encountered in older men of rural residence. Physicians should be alert of those interactions since they may be severe and lead to adverse events that might be dangerous in hospitalized patients with various comorbidities. More studies should check for the occurrence of serious adverse events as a consequence of DHS-drugs interactions in inpatients.

## Influence of combination therapy with amlodipine and ramipril on diastolic function of left ventricle in patients with arterial hypertension

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**Objective:** To evaluate the effect of combination therapy of calcium antagonist – amlodipine (A) with angiotensin converting

enzyme inhibitor – ramipril (R) on the diastolic function of the left ventricular (DF LV) in patients with arterial hypertension (AH).

**Material and methods:** Investigated 130 hypertensive patients were divided into 2 groups depending on the labor of their work schedule: group 1 (n=67) – persons working only day shift; group 2 (n=63) – working in shifts. Therapy was appointed from the start A/R. The final daily doses of A/R as follows: 1st group –  $8,3 \pm 1,3/16,5 \pm 2,9$  mg/day, in the 2nd –  $9,5 \pm 1,5/26,8 \pm 1,5$  mg/day. Doppler-echocardiography was performed at baseline, after 12 weeks, and after 6 months of therapy.

**Results:** In 1 group in the treatment of A/R noted positive dynamics of diastolic filling, which was expressed by the 12-th week, a significant increase in the maximum rate of early diastolic filling LV (Vm E) (8,3%), decrease in the maximum rate of late diastolic filling LV (Vm A) (3,8%) and, as a consequence, an increase of 10,4% in the ratio of the maximum velocity (E/A). By the end of the study there was a significant reduction Vm A, isovolumic relaxation time LV (IVRT), and deceleration time Vm E (DT) (5,7%, 13,4% and 11,8%, respectively); increasing Vm E and E/A (16,7% and 18,9%, respectively). Revealed reduction in size of the left atrium (PL) 2,7% (after 12 weeks) and 4,4% (after 6 months). DD in group 1 was initially detected in 68,6% of patients with AH (I stage – 54,3%, II stage – 14,3%). By the end of the study DD determined in 38% of individuals (I stage – 34%, II stage – 4%). In the 2-nd group therapy with A/R DF significant improvement occurred towards the end of the study: showed a reduction IVRT (15,1%) and DT (12,2%); increasing Vm E (20%) and E/A (22%). Dimensions PL decreased by 3% (after 12 weeks) and 4,7% (after 6 months). DD in the 2-nd group initially was detected in 91,7% of patients with AH (I stage – 61,4%, II stage – 24,5%, III stage – 5,8%). By the end of the study it was determined by DD in 49% of patients with AH (I stage – 40%, II stage – 9%).

**Conclusions:** Combination therapy A/R had a significant positive trend diastolic filling in group 1 since the 12-th week of treatment, in the 2nd – until the end of the study. 6-month therapy with A/R contributed to halving the number of patients with DD in both groups.

## Febrile syndrome... that ceases to be undetermined!

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**Introduction:** The definition of fever of unknown origin (FUO) was established in 1961 and consists of 3 assumptions: illness lasting 3 weeks of more, temperatures above  $38,3^{\circ}\text{C}$  on several occasions and the absence of a diagnosis after 3 outpatient consultations or 3 days of hospital investigation. There are numerous causes for this that include infection, cancer, rheumatic diseases, or even immunological among others.

**Case report:** The authors present a case report of a patient without any relevant history that came to the emergency room for fever, weakness (asthenia) and diarrhea lasting 3 weeks. Upon admission he had a fever ( $38^{\circ}\text{C}$ ), he was pale, icteric and dehydrated without any other signs upon physical examination. Analytically: red blood cells  $3,95 \times 10^{12}/\text{L}$ , Hb  $10,6$  g/dL, white blood cells  $5,0 \times 10^9/\text{L}$ , platelets  $114 \times 10^9/\text{L}$ ,

total bilirubin 1,5 mg/dL, conjugated bilirubin 0,53 mg/dL, AST 210 U/L, ALT 120 U/L, ALP 51 U/L, GGT 159 U/L, LDH 850 U/L, urea 82 mg/dL, creatinine 1,85 mg/dL, CRP 9,97 mg/dL, Widal Typhi H 1:320, ferritin 50585 ng/mL. Full-body CT scan did not reveal any anomalies. Colonoscopy of the right colon revealing lympho-plasmocytic infiltrate of the corion with the formation of intramucosal lymphoid aggregates. The bone marrow examination was compatible with anemia from chronic illness. Despite the initial clinical and analytical improvement, a high persistent fever reoccurred. Negative cultures and serologies along with a series of CT's and transesophageal echocardiogram excluded endocarditis while the liver biopsy showed granulomatous hepatitis. After 3 weeks of investigation a right cervical tumefaction appeared with the full body CT showing diffuse infiltration of the right parotid gland, lungs, abdomen, hepatosplenomegaly and intra-abdominal lymph nodes with the final diagnosis of anaplastic T cell lymphoma.

**Discussion:** Despite infection being the most common cause of FUO, the neoplastic and rheumatic diseases are perhaps the most challenging and least predictable in their outcome.

## Characterization of medical care in a tertiary Greek hospital

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**Objectives:** In our department we hospitalize patients admitted from the Emergency Department and patients under treatment in

one of the independent subspecialty departments (oncological, hematological, rheumatological). The aim of the study is to analyze the characteristics of the patients hospitalized during 2014.

**Methods:** We studied all patients admitted to our department between January 1st, 2014 and December 31th, 2014. For those patients diagnosis on admission, demographics, length of stay (LoS) and outcomes were recorded. The diagnosis on admission was classified in 28 categories, which included clinical findings, syndromes or disease entities.

**Results:** During the study, 1769 patients were hospitalized. Their age ranged between 14-101 years old (median value 72 years, IQR=54-81 years). The total mortality in the department was 11,2%. The diagnosis on admission bearing the greatest mortality rates were shock (mortality 60%), respiratory distress (28%), neoplastic disease (22%), nephrologic syndromes (21%) and electrolyte disturbances (19%). Most common diagnosis on admission were neoplastic disease (15% of admissions), acute fever (9,5%), hemoglobinemias (7%), anemia (6,5%) and abdominal pain/intra-abdominal infections (6.1%). Mean bed occupancy rate was 98% and total mean length of stay was 5 days. The diagnostic categories with the longest LoS were lymphadenopathy, fever of unknown origin, pulmonary disorders and soft tissue infections, all with a median LoS of 7 days. Patients suffering neoplastic or hematologic diseases account for 36,8% of total patient-days.

**Conclusions:** Our department hospitalizes a large number of patients suffering neoplastic or hematologic disease which account for approximately one third of patient-days. One third of our patients are people >81 years old. These data need to be taken under consideration in planning health care policy and suitable education for medical and nursing staff.

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