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**BOOK OF ABSTRACTS**

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## ORAL PRESENTATIONS

### METABOLIC SYNDROME AND EPIDEMIOLOGY

#### Prospective study of Slovak forty-year old population – cardiovascular mortality and morbidity after ten years of follow-up

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In 2003 and 2006, we performed a population study aimed to screen risk factors (RF) of cardiovascular disease (CVD) in subjects at the age of forty at the year of the examination. This age was chosen with respect to low cardiovascular risk in that category and thus effective possibility to diagnose treat and prevent future cardiovascular event. 4736 subjects were examined in eight cities covering major part of Slovakia in cooperation with MEDPED lipid clinics and general practitioners. In 2016, we examined cardiovascular mortality and morbidity among this population. The information was extracted from the database of National Centre of Health Information. There were 84 deaths mainly due to cancer, CVD and injuries (28, 22, and 15, respectively) and 280 subjects were hospitalized for cardiovascular reason.

For evaluation of differences in CVD RF, the subjects were divided into three groups: group 1 [subjects who lived without hospitalisation, 1740 men and 2500 women], group 2 [subjects hospitalized from dg of CVD, analysis was done in 136 men and 131 women], group 3 [subjects who died from CVD, 15 men and 7 women]. The proportion of men was continuously increasing from group 1 to group 3 with  $p < 0,001$ .

When compared the groups 1, 2 and 3, at the age of forty, there was increasing prevalence of arterial hypertension [9,5%, 18,7%, 50%  $p < 0,001$ , respectively] and smoking [27,3%, 31,5%, 54,5%;  $p < 0,007$ , respectively]. Patients from group 3 had also the highest cholesterol [ $p < 0,014$ ] and triglyceride [ $p < 0,001$ ] levels and men from group 3 had significantly lower HDL-cholesterol levels when compared with group 2 and 1 [1,01; 1,24; 1,25 mol/l,  $p < 0,03$ , respectively]. Among women, the highest waist circumference had group 3 and the lowest one was found in the group 1.

**Conclusion:** at the time of our follow-up, the prospective evaluation of Slovak population of men and women showed incidence of total mortality of 1,77% [84 : 4736] and CVD mortality of 0,46% [22:4736]. The hospitalisation from CVD was high – 5,6% [280:4736] and both CVD mortality and morbidity were strongly related with RF found at the age forty.

**Keywords:** Cardiovascular mortality and morbidity, prospective study, Slovak population

## YOUNG INTERNISTS

### Potential Use of Circulating microRNAs in the Clinical Practice

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Differential diagnostics of internal diseases and the choice of the proper therapeutic approach is still challenging even in the era of modern medicine. Leading symptoms of various diseases are very similar and even though the laboratory and paraclinical biomarkers are very helpful, there is still need to seek for more sensitive and specific biomarkers that would provide more precise information about the patient diagnosis and prognosis.

Novel group of biomarkers is represented by circulating microRNAs. microRNAs are tiny molecules belonging to the group of small non-coding RNAs. Intracellularly they regulate gene expression and are involved in the pathophysiology of nearly all thinkable diseases by affecting various signaling pathways. In 2008, their presence in the extracellular fluid was described, including blood [and its derivatives, such as plasma or serum] and urine, which opened a new field of research focusing on unveiling circulating microRNAs diagnostic and prognostic potential. Levels of circulating microRNAs in plasma/urine are stable, can be reproducibly measured and reflect the changes occurring within the organism – either organ damage [as some of them are organ/tissue-specific and damage to these organs leads to their release into circulation] or the changes in the intercellular communication that occurs during specific diseases.

Biomarkers discovery is a multi-step process and in the field of microRNAs usually begins with the microRNA profiling, i.e. determination of more than 700 microRNAs in a few patients' samples aiming to identify those microRNAs that are the most dysregulated. These studies show that individual diseases do present with specific microRNA profiles [i.e. different microRNAs are upregulated/downregulated in individual diseases], however, due to the prices and time demands of microRNA profiling, this approach is not suitable for everyday clinical practice. It is thus necessary to identify the smaller sets of several microRNAs that are then validated on the independent and larger patients' cohorts to determine their specificity and sensitivity. Current use in the clinical practice is still limited mostly by the non-standardized methods used for RNA isolation and microRNAs levels measurements in different laboratories, by the longer processing times compared to currently used biomarkers and by the lack of the large enough validation cohort studies.

Within the lecture, the general introduction focusing on the circulating microRNAs will be provided followed by the review of their potential use in the differential diagnostics of dyspnea. Current perspectives for the future use of microRNAs in the clinical practice will be summarized.

**Keywords:** microRNA, biomarkers, dyspnoea

## GENERAL INTERNAL MEDICINE

### Thrombotic Thrombocytopenic Purpura and Hodgkin's Lymphoma – an unlikely connection

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Thrombotic Thrombocytopenic Purpura (TTP) is a pathology characterized by thrombocytopenia due to the incorporation of platelets in microvasculature thrombi, and microangiopathic haemolytic anemia due to the destruction of erythrocytes in the microcirculation. TTP can have a congenital or acquired etiology. Among the acquired etiology the idiopathic type is the most common meaning that the diagnosis is not easy.

A 53-year-old male presented to the emergency department after 1 week of left hand and homolateral hemiface paresthesia, temporary dysarthria and dark stools. The patient had no pathological antecedents, regular medication or drug abuse history. Except for skin pallor the physical and neurological examination were unremarkable. Blood analysis showed macrocytic anemia (Hb: 6.3g/dL), 17'000 platelets per microliter [mcL], increased haptoglobin and reticulocytes, mild kidney injury, increased total bilirubin, LDH and troponin-I. A thoraco-abdominal-pelvic CT scan showed generalized axillary, hilar and retroperitoneal lymphadenopathy, and mild heterogeneous splenomegaly. The patient was admitted to the medical wards where he received erythrocyte concentrate transfusions and plasmapheresis. During 8 days with continuous sessions platelets recovered to 108'000 per mcL, kidney function improved and there were no further thrombotic events. Mielogram showed erythroid hyperplasia with unaltered medullar immunophenotyping. Bone biopsy showed marked hypercellularity and collagenous fibrosis. Autoimmune investigation presented hypocomplementemia and JAK2 negative cells. Three days after the suspension of plasmapheresis a new drop in blood values and the reappearance of schizocytes led to the reintroduction of plasmapheresis together with corticoid therapy. The patient had a good initial response but latter there was a worsening of the thrombocytopenia with controlled microangiopathy meaning that TTP was to be blamed for the fall in platelets. Despite the high surgical risk, the patient was splenectomized for diagnostic purposes. Meanwhile a septic screening for bacterial and viral infection was negative. The measurement of ADAMTS13 was normal and there were antibodies anti ADAMTS13 and the splenic histology showed its involvement by a lymphoproliferative process characteristic of mix-cellularity type classical Hodgkin Lymphoma. The patient was started on chemotherapy with LVPP regimen because of the serious thrombocytopenia and the recent surgery. Latter, because of the worsening of thrombocytopenia and development of a febrile neutropenia this scheme was suspended and the patient was started on ABVD scheme with full remission of the disease.

Microangiopathic haemolytic anemia related to malignant pathology is a very rare entity with an estimated incidence of about 0.25–0.45 patients per million. Usually it's associated with metastasized solid tumours and it behaves more as intravascular disseminated coagulation than TTP. The lack of experience on this pathology made its diagnosis and management much more difficult. This problem was overthrown through a multidisciplinary approach. The physiopathology of this condition is still not clear, but this case supports the notion that both the cytokine production by the malignant disease and the unclear role of the activity of ADAMTS13.

**Keywords:** ADAMTS13, Hodgkin's lymphoma, Splenectomy, Thrombocytopenia

## FREE COMMUNICATIONS

### VARIA

#### Digestive tract pathology of patients with gout

**Milana N. Petrova** [North-Eastern Federal University, Yakutsk, Russian Federation]

**Introduction:** Gout is now considered an important all-medical problem that is connected with data obtained on the influence of hyperuricemia's progression of atherosclerotic defeat of vessels. Gout is a metabolic disease, and is hyperuricemia — one of the most important components of a metabolic syndrome. Close interrelation between disorders of a purine exchange and a hypertriglyceridemia is found. Communication between a hyperuricemiya and insulin resistance is proved. Hyperuricemia is an independent risk factor of cardiovascular diseases. Therefore diagnostics and treatment of gout, hyperuricemia, and also complications of the disease, are an actual problem of therapy. In some cases, special difficulty is represented by a choice of adequate analgesic therapy, especially in patients with the accompanying stomach pathology.

**Research objective:** To study the modern trend of gout and the pathology of the digestive tract of these patients in the Republic of Sakha [Yakutia].

**Results:** 44 patients were registered, including 42 men and 2 women in the years 2006–2011. Median age of patients is 56 years [35; 76]. Secondary forms of gout and relapses of the disease are common. Forms of arthritis: acute in 3 patients, prolonged in 8 patients, chronic in 2 patients.

The accompanying gastrointestinal tract pathology: in 1 patient – a reflux-esophagitis, chronic pancreatitis, stomach ulcer; chronic erosive gastritis and reflux-esophagitis in 1 woman; in 1 man – chronic gastritis, in 1 patient – chronic calculus cholecystitis, chronic pancreatitis.

Gastroprotektors and selective COX-2 inhibitors were given to patients with revealed accompanying pathology of their gastrointestinal tract.

**Conclusion:** Thus, we observed patients with the accompanying digestive tract pathology. Maintaining such patients requires an individual approach to therapy. Results will be used for specifying the features of a course of gout in the Republic of Sakha [Yakutia], creating recommendations of diagnostics and treatment of gout, for ensuring the modern, adequate, hi-tech assistance for such patients.

**Keywords:** gout, digestive tract, stomach, complications of anti-inflammatory therapy

## INTENSIVE CARE

### Score in gout patients in Yakutsk

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**Introduction:** Gout is considered a metabolic disease and ranked among the diseases connected with obesity, such as an arterial hypertension [AH], coronary artery disease [CAD], stroke, and type 2 diabetes mellitus [WHO, 2000]. A research project has been initiated to determine the incidence and characteristics of gout in Yakutia in 2007–2012. Patients hospitalized in the department of rheumatology of Yakut City Hospital with gout arthritis were studied.

**Methods:** Patients are being studied by means of a questionnaire developed by the Institute of Rheumatology [Moscow]. Additional data being collected include: laboratory measures, radiographic assessment of feet and wrists; ultrasound of kidneys.

**Results:** 42 patients were registered between 2006–2012, including 37 men and 5 women. Median age of the subjects is 56 years [35–76]. Average SCORE is 2, 8 [0, 12–6, 87]; SCORE >5% in 4 men. Accompanying pathology includes: AH in 22 patients, CAD in 7 patients, type 2 DM in 4 patients, glucose intolerance + obesity in 1 patient, metabolic syndrome + obesity in 1 patient, uncomplicated obesity in 1 patient, metabolic syndrome without obesity in 1 patient, chronic renal insufficiency in 1 patient and cardiovascular incidents in 3 patients. Average TC is 4,3 mmol/l [2,4;6,3]; average systolic BP is 133 mmHg [110;180]; 5 smokers.

**Conclusion:** Results will be used for characterization of the incidence and diagnostic features of gout in the Republic of Sakha [Yakutia] with the goal of standardizing guidelines for diagnosis and prevention of gout and comorbidity.

**Keywords:** gout, score, Yakutia

## RHEUMATOLOGY AND CVD

### Frequency of Inflammatory Back Pain and Structural Changes of Axial Skeleton in Inflammatory Bowel Disease

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**The aim of the study** is to find out the frequency of inflammatory back pain (IBP) and to identify the signs of a lesion of the axial skeleton according to X-ray and magnetic resonance imaging (MRI) of the lumbar spine and sacroiliac joints in patients with Inflammatory Bowel disease (IBD).

**Material and methods:** 70 patients with verified diagnosis of ulcerative colitis (UC) – 45 patients (64.3%), and Crohn's disease (CD) – 25 (35.7%) were included into prospective study. The average age of the patients –  $44 \pm 3.34$  years. Availability and characteristics of inflammatory back pain were evaluated by ASAS criteria (2009). Patients were performed imaging of the lumbar spine and sacroiliac joints by X-ray [44 patients] and MRI in T1 mode and STIR [25 patients].

**Results:** Low back pain was observed in 60 patients with IBD (85.7% of respondents), 36 (51.4%) patients suffered from back pain for more than 3 months. At the time of evaluation 31 patients (44.3%) were present in back pain. Back pain started before the age of 40 years in 45 patients (64.3%); onset of back pain was gradual in 44 (62.9%) patients. 37 (52.9%) patients mentioned the improvement of pain after physical activity – (52.9%); increased pain at rest – 25 (35.7%); back pain at night time – 35 (50%) patients. Eligible criteria for ASAS inflammatory back pain [criterion 4 of 5] corresponded to 25 patients (35.7%)

X-ray was performed to 44 patients, 21 patients followed the criteria of the IBP. Radiographic changes were observed in 11 patients: unilateral sacroiliitis II stage – 5 patients, bilateral sacroiliitis stage II – 4 patients, bilateral sacroiliitis stage IV – 2 patients. 5 patients corresponded to the requirements of the New York classification criteria for ankylosing spondylitis.

MRI was performed to 25 patients, 19 of them met the criteria for inflammatory back pain. Of these changes on MRI were detected in 16 people, in 3 data for the inflammation has not been revealed.

**Conclusion:** IBP for ASAS criteria was detected in 35.7% of patients with IBD. In this group there is a high rate of changes according to the X-ray and MRI.

**Keywords:** Inflammatory Bowel Disease, Low back pain, Sacroiliitis, Ulcerative Colitis, Crohn's Disease

## Clinical Predictors of Outcomes in Calcific Aortic Valve Disease

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Calcific aortic valve disease is a slowly progressing disease, which remains asymptomatic for a long time. At the initial stage there is a formation of solitary calcinates and thickening of aortic leaflets, later deformation and narrowing of lumen of aortic valve – formation of aortic stenosis. After the onset of clinical symptoms the natural five-year survival rate is below 20%, which stresses the urgency for identification of the predictors of disease progression.

The aim was to study the predictive value of a number of clinical and demographic parameters in calcific aortic valve disease.

The objects were 108 patients with calcification of the tricuspid aortic valve [aged over 65]. CAVD was verified through multislice computed tomography and transthoracic echoCG. Study population profile: the mean age of those with calcified aortic valve disease was 72 years. 32% of the patients showed no signs of aortic stenosis; 44% had mild stenosis; 7% had it moderate, the share of those with severe aortic stenosis was 17%. The three-year dynamic observation was carried out. Every six months the clinical and instrumental examination of the patients without indications for surgery at the start of the study [90 subjects] was performed. The primary end-points were cardiovascular death, myocardial infarction, stroke, myocardial revascularization, pulmonary embolism, aortic valves surgery. The occurrence and/or progression of the aortic valve stenosis, measured in cm/year, were the surrogate endpoints.

During the observation period five patients died from cardiovascular causes, myocardial infarction occurred in four patients, stroke – in six, pulmonary embolism – in five, myocardial revascularization – in two, aortic surgery – in four patients. Survival rate [without endpoints] was 72%. Multifactor regression analysis has identified age >70 years [OR 1,4 [1,1; 2,4],  $p < 0,05$ ], congestive heart failure [OR 1,3 [1,2; 2,1],  $p < 0,05$ ], history of myocardial infarction [OR 1,7 [1,2; 2,7],  $p < 0,01$ ] as independent risk factors for adverse outcomes. Aortic stenosis occurred or progressed in the majority of patients. The rate of aortic valve narrowing was  $0,16 \pm 0,12$  cm/year, the velocity of transaortic bloodflow increased for  $27 \pm 20$  cm/sec/year. The disease progressed more rapidly in men [ $n = 42$ ,  $0,25 \pm 0,11$  vs.  $0,08 \pm 0,04$  cm / year,  $p < 0,05$ ] and overweighted patients [ $n = 51$ ,  $0,32 \pm 0,12$  vs.  $0,07 \pm 0,03$ ,  $p < 0,05$ ].

Therefore, age >70 years, congestive heart failure and history of myocardial infarction increase the risk of adverse clinical outcomes in calcific aortic valve disease. Aortic stenosis progresses more rapidly in men and overweight patients.

**Keywords:** Calcific Aortic Valve Disease, Outcome, Predictors, Prognosis, Clinical factors

## GENERAL INTERNAL MEDICINE

### Adverse effects of spironolactone during long-term treatment of resistant arterial hypertension

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**Introduction:** Spironolactone had relatively few adverse effects in short term clinical trials, but data about their occurrence during long-term treatment of resistant hypertension are scarce.

**Methods:** We retrospectively analysed medical records of patients with resistant arterial hypertension, who originally participated in the ASPIRANT-EXT trial and received open label spironolactone after finishing the trial. We assessed the length of spironolactone use, dosage, side effects, blood pressure (BP) and biochemical findings at the last clinical visit at our department.

**Results:** We analysed a total of 91 patients, 31 women and 60 men, who used spironolactone for a mean time of 41 months. The mean dose of spironolactone was 28.4 mg/day (79 patients used 25 mg/day, 9 patients 50 mg/day, 1 patient 100 mg/day and 2 patients 12.5 mg/day). Hypertension was controlled at the last visit in 62% patients (BP  $\leq$ 140/90 mmHg), the mean office BP was 136.0/79.5 ( $\pm$ 16.4/9.9) mmHg and mean serum potassium 4.63 $\pm$ 0.47 mmol/l. Adverse effect occurred in 25 patients (27.5 %) and in all but one patient lead to discontinuation of spironolactone (24 patients, 26.4 %). The most common adverse effects were symptomatic hypotension (9 patients), hyperkalemia (7 patients), gynecomastia (5 patients), mastodynia (2 patients) and impotence (2 patients).

**Conclusions:** During long-term treatment of resistant hypertension by spironolactone, adverse effects occur in more than a fourth of patients and usually necessitate discontinuation of this treatment.

**Keywords:** hypertension, resistant hypertension, spironolactone, adverse effects

## Sensitivity and specificity of fecal NGAL in the management of Crohn's disease patients

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**Background.** Today evaluation and clinical application of new non-invasive markers are important in Crohn's disease [CD]. Neutrophil gelatinase associated lipocalin [NGAL] is proposed as the new biomarker of inflammation, which is produced by neutrophils and epithelial cells of the intestine in inflammation.

**Aim:** to access the diagnostic value of fecal NGAL as a surrogate marker of inflammation in CD.

**Methods.** We prospectively included 35 patients with CD [29 patients with active CD, 6 patients in remission] and 15 healthy controls. The levels of NGAL was determined by enzyme immunoassay method. We used a set of Human Lipocalin-2 / NGAL ELISA, production BioVendor, Czech Republic. The average age of patients with CD was 36±2 years and controls – 31±2 years. Severity of CD was assessed by CDAI: mild CD was seen in 7 [24%], moderate 13 [45%], severe 9 [31%].

**Results:** The increase of fecal NGAL level was observed in active CD – 2688 [200; 5710] ng/ml comparing with in the control group – 181 [169; 720] [ $p<0,001$ ]. A tendency to a decrease in fecal NGAL was in disease remission [382 [116; 1788] ng/ml]

In patients with severe CD level of fecal NGAL was 5908 [2860; 12920] ng/ml, which was higher than in moderate CD – 2236 [172; 4236] ng/ml [ $p<0,05$ ] and mild – 896 [200; 3828] ng/ml [ $p<0,05$ ].

ROC-analysis has defined the threshold of fecal NGAL for determining an active phase of intestinal inflammation in CD – 1144 ng/ml [empirically determined sensitivity – 59%, specificity – 100%, and AUC – 0,77.

Distribution of patients according to location of the lesion showed that level of NGAL was the highest in lesions of the colon. So, when fecal NGAL in ileitis was – 1340 [195; 2860] ng/ml, ileocolitis – 1788 [192; 5512] ng/ml and colitis of CD – 2879,5 [361; 8168] ng/ml. The sensitivity in colitis of CD [58%] was increased then sensitivity in ileitis [50%].

An analysis of the diagnostic value of determination of fecal NGAL as a marker of active CD relative remission showed a different result. When threshold fecal NGAL 1784 ng/ml, the sensitivity was 55%, specificity – 67%, and AUC – 0,73.

**Conclusions:** Fecal NGAL is a novel non-invasive marker to distinguish active CD from healthy individuals with a high specificity. Diagnostic value to determine the stage of CD was lower. The sensitivity in colitis of CD was increased then sensitivity in ileitis.

**Keywords:** Crohn's disease, non-invasive markers, neutrophil gelatinase associated lipocalin, fecal NGAL

## Mitral valve prolapse – the results of 15 years observation

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**The purpose of the study:** the results of the prospective cohort long-term observations to develop the tactics of conducting and treatment of patients with mitral valve prolapse (MVP) based on a comprehensive assessment of their clinical, phenotypic, psychological characteristics and also the functional state of the cardiovascular system.

**Materials and methods:** the study involved 31 patients with PMK: 18 men [mean age  $39.4 \pm 0.9$ ] and 13 women [mean age  $38.9 \pm 1.1$ ], which was identified initially expressed phenotypic DST violations, including PMK and regularly taking magnesium for 15 years. Patients received magnesium orotate in a dose of 1500 mg per day [97,4 mg of elemental Mg] during the entire period of observation [15 years] 2 times per year [course duration is 3 months]. All patients underwent clinical examination, was estimated phenotypic features were assessed psychopathological status was conducted echocardiography (EchoCG), Holter monitoring, daily monitoring of blood pressure (BP), spectral analysis of heart rate variability. A morphological study of biopsy specimens of the skin were assessed for morphological signs of disease of the skin, reflecting the activity of the pathological process in the skin before and after treatment. We determined the Mg content in hair, the total level in serum, a study was conducted of the endogenous opioid system and the immune interferon system, psychological examination and evaluation of the quality of life by self-assessment of surveyed on the scale of VAS [Visual Analog Scale] and DISS [Disability Scale], as well as the effectiveness of pharmacotherapy.

**Results:** as a result of long reception of magnesium orotate positive dynamics, manifested in the improvement of the General condition and well-being, and to change the specific symptoms and syndromes. After therapy the number of patients with cardialgia decreased by more than 3 times, pain in the left side of the chest in all patients appeared at most once per month. It is established that the frequency of pain in the thoracic and lumbar spine with application of magnesium salts significantly decreased more than in 2 times. Also noted positive effect on disorders of the gastrointestinal tract, psychogenic dysuria, disturbance of thermoregulation. Significantly decreased after therapy the severity of vascular disorders, and hemorrhagic. Syncope was presented with syncope and neurogenic orthostatic mechanism, whereas the latter is diagnosed in 1.5 times less. After the examination, orthostatic, and neurogenic syncopes were detected with the same frequency as before the treatment. We observed a statistically significant decrease in the depth of the prolapse and degree of mitral regurgitation, a decrease in the maximum systolic and diastolic blood pressure, normalized heart rate variability in systolic and diastolic BP during the day. Also noted a significant increase of parasympathetic tone and reduced tone of the sympathetic division of the autonomic nervous system (ANS), the self-esteem of patients significantly improved marked improvement on all three scales DISS. Complete or almost complete disappearance of symptoms [a significant index of efficiency] identified in 51.6% of cases, partial [average performance index] in 35.5% and a slight improvement [minimum efficiency index] – 12.9%.

**Conclusions:** magnesium orotate, when the appointment, effective against most clinical manifestations in patients with MVP: the General condition of patients improved significantly, decreases the frequency and severity of all clinical signs and symptoms of the disease. The depth of the prolapse of the mitral valve, the degree of mitral regurgitation, the left atrium is reduced. Also reduced the average and maximum heart rate, the number of episodes of tachycardia, duration of the interval QTc, frequency of paroxysmal supraventricular tachycardia, supraventricular and ventricular arrhythmia, the QOL improved.

## Hydration Matters – A Quality Improvement Project for Improving Intravenous fluid prescribing practices and documentation in line with NICE CG174 guidance

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Intravenous (IV) fluid prescribing is a common occurrence in general medical wards and it has been repeatedly demonstrated that high levels of mortality and morbidity are associated with inappropriate IV fluid prescribing. IV fluid prescriptions are often completed by the most junior and inexperienced members of the clinical team. In recognition of the issues surrounding IV fluid prescription and in an effort to combat the issues surrounding current practice, the National Institute for Health and Care Excellence (NICE) in the United Kingdom published guidance in December 2013 – 'Intravenous fluid therapy in adults in hospital [CG174].

We took this up as a quality improvement project and when we conducted our baseline measurement we found that at our hospital the approach to IV fluid prescribing amongst junior doctors was highly variable with poor awareness of the NICE guidance. Our initial data showed that these components were infrequently documented, with prescriptions often having no indication for IV fluid, no 24-hour plan / review, no documentation of patient weight and no current or requested fluid balance charts.

As part of the first cycle we conducted education sessions emphasising the necessary components of prescription, which were delivered to all junior doctors. The attendance in these sessions were poor and repeat measurements showed no improvement.

For the second PDSA (Plan, Do, Study, Act) cycle we displayed posters in medical areas and near nursing stations showing performance graphs and essential components of a good prescription and repeat analysis showed improvement.

As part of our third cycle [ongoing] we are designing lanyard cards to be distributed to junior doctors detailing components of a good prescription, monitoring and assessment plan.

We believe that with repeated interventions we can ensure a unified approach and a sustained improvement in IV fluid prescribing, practices and documentation at our hospital.

**Keywords:** Intravenous fluids, quality improvement, prescribing

## Plasma lipidomic profiling in patients with cardiac arrhythmias

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**Background:** Genesis of cardiac arrhythmias is multifactorial. Routinely we assess arrhythmogenic substrate and triggers including influence of autonomic nervous system and internal milieu from point of view of mineral dysbalances, but more importance is desirable. Cardiac electrical activity and its disorders are closely associated with function of cardiomyocyte membrane. Lipids play crucial role in cell membrane composition, its properties and function. Lipidomic analysis is new approach to study of heart diseases as well as arrhythmias. Association between fatty acids metabolism, especially omega-3 polyunsaturated fatty acids, and cardiovascular disease development is studied for last decades. But their role in atherogenesis, arrhythmogenesis or cardioprototoxicity still remains not fully understood.

**Purpose:** Plasma fatty acids status assessment in persons suffering from cardiac arrhythmias.

**Methods:** Comprehensive analysis (gas chromatography) of plasma fatty acids, besides standard biochemical markers, in group A: 18 men (average age 50.9 years, hypertension 66%, lipid lowering therapy 16%, dilated cardiomyopathy (DCMP) 38%, left ventricle ejection fraction LVEF 45%) with history of arrhythmias (22% ventricular, 78% atrial) in comparison with group B: 36 men (average age 47.8 years, hypertension 25%, myocardial infarction 30%, lipid lowering therapy 36%, DCMP 5%, LVEF 60%) without history of arrhythmias. Research was conducted according to the principles of the Declaration of Helsinki of the World Medical Association.

**Results:** (group A versus group B, mean  $\pm$  SD):

Eicosadienoic acid (n-6):  $0.18 \pm 0.1$  vs  $0.09 \pm 0.09$ , p-value 0.005 Erucic acid (n-9):  $0.04 \pm 0.06$  vs  $0.01 \pm 0.03$ , p-value 0.039  
Oxobond acid (n-6):  $0.08 \pm 0.06$  vs  $0.04 \pm 0.06$ , p-value 0.005 Phosphatidylcholine:  $64.83 \pm 2.67$  vs  $61.53 \pm 3.55$ , p-value 0.001  
Sphingomyelin:  $16.24 \pm 1.91$  vs  $18.88 \pm 3.19$ , p-value

**Conclusion(s):** Omega-3 index revealed very low level of cardioprotection in the range of the highest risk of sudden death from cardiovascular causes in both study groups probably due to inappropriate food intake in inland country. There were significantly lower plasma levels of sphingomyelin and significantly higher levels of oxobond acid, erucic acid, eicosadienoic acid and phosphatidylcholine in the group with arrhythmias. Lipidomic analysis offers individual risk stratification as well as rationale for tailored therapy intervention with n-3 fatty acid supplementation in high risk patients.

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**Keywords:** arrhythmias, lipidomic analysis, fatty acids

## Determinant factors of the mortality for pneumonia in a service of Internal Medicine

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**Objective:** To analyse the factors associated with increased mortality in patients admitted for pneumonia in a service of internal medicine.

**Methods:** retrospective study that analyzes the demographic and clinical features, comorbidity, functional status, cognitive status and severity of patients admitted for pneumonia in a service of internal medicine. We compare the group of patients admitted who had died from pneumonia during 2013 with patients admitted and discharged with the diagnosis of pneumonia during the first half of this year. We used the Barthel's Index [BI] to assess the functional status and APACHE II Score [ASII] for the determination of the severity. Comorbidity was determined with the Charlson's Index [CI]. The data were analyzed with the statistical program SPSS22.0

**Results:** There were 1022 admitted into the service of internal medicine in 2013. 138 patients died, reaching a mortality rate of 13.5%. Deaths from pneumonia were 36.95% of total deaths. With respect to mortality from pneumonia: the middle age between the deceased patients was significantly higher: 85.82 vs 80.36 years [p:0.008]. There were no differences between genders. The average BI was lower among the deceaseds: 26.35 vs 59.59 [p<0.005]. Moderate-severe cognitive impairment was associated with increased mortality, OR 11 [p:0.001]. There were no differences in mortality among patients that live at home and who lives in a nursing home. The most common chronic pathologies no showed association with increased mortality [Hypertension, DM, COPD, CKD, heart failure, anemia]. However, there was association between the multimorbidity and increased mortality. CI between the patients who died was 3.65 versus 2.92 in whom they continued alive [p: 0.049]. At the time of admission, the severity was higher in patients who eventually died. ASII 21.37 vs 14.21 [p<0.001]. Finally, the mortality associated with higher number of admissions during the previous year 0.9 vs 0.5 [p:0.05] and more visits to the emergency during the previous year 1.94 vs. 0.97 [p<0.005].

**Discussion:** in recent years shown an increase in the rate of in-hospital mortality in Spanish internal medicine services. Despite medical advances, around 50% of deaths are due to infectious causes and pneumonia is the most important. Death by pneumonia is associated with older age, worse functional status and moderately-severe cognitive impairment. The most frequent chronic diseases do not associate with major mortality on having been analyzed individually. However, the condition of multimorbidity constitutes an important risk factor. Deceased patients had more hospital admissions and visits to the emergency services, during the previous year.

**Conclusions:** factors associated with major mortality by pneumonia are the age, worse functional status and moderate-severe cognitive impairment, severity presentations, condition of multimorbidity and major utilization of sanitary resources during the last year.

## HYPERTENSION

### Can the addition of statins to antihypertensive monotherapy replace combination treatment in some hypertensive patients?

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**Objective:** We tested the hypothesis that addition of statins, which are known for their BP lowering effect, to monotherapy in hypertensive patients with dyslipidemia, having moderate risk, would replace to some extent the combination antihypertensive therapy.

**Design and method:** 210 hypertensive males aged 40–55 with systolic BP within 140–179 mmHg and diastolic BP within 90–109 mmHg, low-density cholesterol more or equal to 3,5 mmol/l and one additional risk factor without signs of atherosclerotic disease not achieving BP goals (<140/90 mmHg) during one month of healthy life-style changes were included in the trial. All patients were placed on antihypertensive monotherapy. Following four weeks 88 pts [40%] achieved BP goals. The rest 122 patients [60%] were randomly divided in two groups by 61 persons in each. In the first group [main group] 10 mg of rozuvasstatin was added to antihypertensive therapy. In the second group [reference group] pts were switched to combination antihypertensive treatment [as it is recommended by ESH guidelines]. The duration of trial was 3 months.

**Results:** In the main group systolic BP decreased by 24,2mmHg [from 162,4 mmHg to 138,2 mmHg],  $p < 0,005$ . In the reference group systolic BP decreased by 24,1 mmHg [from 160,8 mmHg to 136,7 mmHg],  $p < 0,005$ . The decrease of diastolic BP in the main group was 13,8 mmHg [from 100,4 mmHg to 86,6 mmHg] and in the reference group – 13,3 mmHg [from 101,2 mmHg to 87,9 mmHg],  $p < 0,005$ . The difference between the decreases of both systolic and diastolic BP in two groups was non-significant,  $p > 0,05$ . As a result, the achievement of BP goals by the end of the study was similar in two groups – 77% [48 patients] in the main group and 75% [46 patients] in the reference group,  $p > 0,05$ .

**Conclusions:** Results show, that statins can provide additional BP-lowering effect. So, at least in hypertensive patients with dyslipidemia having moderate risk the addition of statins to antihypertensive monotherapy could provide the achievement of BP similar to that of combination antihypertensive treatment.

**Keywords:** hypertension, dyslipidemia, statins

## Gender features in risk of hypertension in population with depression in Russia/Siberia: WHO epidemiological program MONICA-psychosocial

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**Purpose:** To determine the gender differences in the effect of depression (D) on the risk of arterial hypertension in general population aged 25–64 years in Russia/Siberia.

**Methods:** Under the third screening of the WHO “MONICA-psychosocial” program (MOPSY) random representative sample of including both genders aged 25–64 years old was surveyed in Novosibirsk in 1994 (men: n = 657, Mean age 44,3 ± 0,4 years, response — 82,1 %; women:

n = 689, Mean age 45,4 ± 0,4 years, response — 72,5 %). Registration of socio-demographic data and assessment of depression was made at baseline. 229 cases of new-onset arterial hypertension (AH) in women and 46 cases in men were identified over 16-year of follow-up.

**Results:** In a general population of 25–64 years 54.5% of women and 29% of men had a D. 11.8% of women and 3.1% of men had a major D. The risk of hypertension in men with D was 6.7-fold higher over 5 years of follow-up, it was 4.2 and 2.15-fold higher compared to those without D for 10 and 16 years of follow-up respectively (p for all <0.05). Risk of AH in women with D was 1.6 and 1.74-fold higher than without D for 5 and 10 years of follow-up, respectively (p for all <0.05). AH risk was higher in men with elementary education, in those who was retired and in heavy physical workers, in divorced men.

**Conclusions:** Depression is more common in women than in men. The risk of developing hypertension in men with D is significantly higher than in women.

**Keywords:** epidemiology, depression, hypertension, population, risk

## Home BP telemonitoring system with data transmitted to a physician's office

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HBP values reported by a patient may not always be reliable. They may be unintentionally or intentionally altered while manually rewritten from home BP measuring device (BPMD) to a paper logbook. The presented telemedicine system for HBPM enables patients to transfer data from BPMD to a physician automatically, without any manual interaction.

The patient's set consists of the validated BPMD Fora P30+ [ForaCare, USA, available in the Czech Republic] that is wirelessly connected to a low cost mini PC – currently we are using Intel Compute Stick [Intel Corp., USA] – but any computer able to run Windows 7 or later with Bluetooth [BT] 2.0 and internet connection can be used. Since the mini PC does not have any display a special method for connecting to a Wi-Fi has been implemented. We have developed a separate software that can be downloaded from the internet [without installation, using ClickOnce technology] that generates an encrypted file with Wi-Fi credentials and saves it to a flash disk that is that used to transfer the file to the mini PC. For patients without internet connection a set with GSM modem can be used.

Mini PC contains a software that is awaiting BT connection from the BPMD and immediately save it to the local database and then tries to upload the measured values to the central server via secured web services. Both patients and physicians have access to the measured data via a web application.

Data are presented in form of the standardized ESH logbook transferred to Excel which enables an easy calculation of the average systolic and diastolic BP [total, morning and evening] from several monitoring days. We implemented the version presented in 2012 London European Meeting on Hypertension that introduced differently colored cells for extreme values.

Before printing patients are asked to fill in medication information. If a sequence of multiple daily measurements (e.g. each hour) is detected the report will also contain chart and table with daytime BP profile for easier detection of hypotension. The report can be viewed via the web application or can be generated as a pdf and sent to a physician by email or be printed and brought in the paper form. Currently we are providing patients preconfigured sets and patients only need to setup a Wi-Fi connection.

Advantages of the presented solution are:

- Measured values are transferred automatically – it eliminates the chance of patient's transcription errors or forgotten logbook when visiting the physician
- Data are stored permanently and can be used for a long term follow up
- Multiple deployments of the solution are possible – every physician or organization can have the data under their control

**Keywords:** telemedicine, web application, home monitoring, hypertension, logbook

## Influence of metabolic syndrome on course of arterial hypertension with the position of evaluation the central aortic pressure and arterial stiffness

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**The purpose of this study** was to assess the daily dynamics of the central aortic pressure (CAP) and arterial stiffness in patients with arterial hypertension (AH) associated with metabolic syndrome (MS).

**Material and methods:** Observed 82 patients divided into 2 groups: group 1 – patients with AH – 33 [40%], group 2 – patients with AH associated with MS [AH+MS] – 49 [60%]. Control group [CG] were 22 practically healthy subjects. All the subjects underwent examination ABPM with oscillometric sensor [BPLab Vasotens, Russia] with assessment CAP [systolic blood pressure,  $SBP_{ao}$ ; diastolic blood pressure  $DBP_{ao}$ ; pulse pressure  $PP_{ao}$ ; Augmentation index  $Alx_{ao}$ ; amplification of pulse pressure, PPA] and AS [pulse wave velocity, PWV<sub>ao</sub>].

**The results of the study:** Analysis of CAP parameters showed statistically significant differences of the levels of the daily average of  $SBP_{ao}$  [AH:  $119,61 \pm 11,62$  AH+MS:  $119,20 \pm 12,11$ ] and  $DBP_{ao}$  [AH:  $82,21 \pm 6,9$ ; AH+MS:  $81,94 \pm 8,55$ ] in the studied groups compared to CG [ $110,81 \pm 6,64/76,9 \pm 5,68$ ] [ $p < 0,01$ ;  $p < 0,03$ ]. Significant differences in the parameters of PP during the day, these groups are not mentioned, but the PP was higher in group of AH [ $37,39 \pm 8,22$ ], AH+MS [ $37,18 \pm 6,75$ ] compared with CG [ $33,95 \pm 5,13$ ]. In all the study groups revealed significantly high levels of the augmentation index to the aortic  $Alx$  [AH:  $-13,52 \pm 28,31$ ; AH+MS:  $-26,41 \pm 23,21$ ] compared with CG [ $-43,43 \pm 13,07$ ] [ $p < 0,00007$ ;  $p < 0,004$ ] as well as between the group of AH and AH+MS [ $p < 0,04$ ]. Amplification of pulse pressure was significantly lower in the AH group [ $125,12 \pm 8,12$ ] compared with the group of AH+MS [ $131,29 \pm 8,92$ ] and CG [ $133,24 \pm 4,46$ ] [ $p < 0,002$ ;  $p < 0,00007$ ], pulse wave velocity PWV<sub>ao</sub> significantly higher in the group of AH+MS [ $10,36 \pm 1,33$ ] compared with CG [ $9,02 \pm 0,96$ ] [ $p < 0,0001$ ] and a group of AH [ $9,02 \pm 1,43$ ] [ $p < 0,00006$ ]. Correlation analysis revealed a statistically significant correlation of pulse wave velocity PWV with triglyceride levels [ $r = 0,34$ ], HDL [ $r = -0,19$ ], blood glucose [ $r = 0,25$ ], body mass index [ $r = 0,36$ ] and left ventricular myocardial mass [ $r = 0,32$ ].

**Conclusion:** Our study results indicate a more pronounced changes in the central aortic pressure in AH group, while the worst parameters elastic properties of vessels observed in group of AH+MS. Evaluation of CAP and arterial stiffness in hypertensive patients with cardiometabolic disorders necessary to assess the cardiovascular risk.

**Keywords:** arterial hypertension, central aortic pressure, arterial stiffness, pulse wave velocity, metabolic syndrome

## Patient's noncompliance with the antihypertensive treatment – a frequent cause of resistant hypertension

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Arterial hypertension is the most frequent cardiovascular disease and when uncontrolled it increases significantly the cardiovascular risk. Treatment-resistant hypertension is relatively frequent [12–15% of hypertensive patients]. Before seeking for secondary hypertension, exclusion of pseudo-resistance is of a great importance. The most frequent causes are white coat effect, physician inertia and a poor adherence of the patient. Nowadays, the most reliable method for the assessment of non-compliance is the measurement of serum antihypertensive drug concentrations by means of Liquid Chromatography–Mass Spectrometry. Recent studies showed a very high prevalence [25–50%] of noncompliance among patients with resistant hypertension. In our clinical practice, it is of a great importance to identify a potentially noncompliant patient as it is shown in following two typical case reports.

First patient, 49-years old female with 15 years history of hypertension, was referred as out-patient by an internist to exclude secondary hypertension. The patient was treated by an overwhelming combination of 8 antihypertensive drugs including candesartan, hydrochlorothiazide, 250mg [!] of spironolactone, rilmenidine, moxonidine, doxazosine, bisoprolol and verapamil SR. Despite of this, the office BP was 148/109mmHg and resting HR 120/min. After the patient confirmed regular drug intake, a serum analysis was performed and showed the absence of the whole antihypertensive medication. The noncompliance of the patient lead the despaired physician to a repeated treatment fortification ending up with an inappropriate overcombination. Our recommendation was to educate the patient, and to prescribe a much reduced antihypertensive medication.

The second patient, 47-years old female, was send to a planned hospitalization to our hypertension unit by the GP for exclusion of secondary hypertension due to resistance to the treatment. At the time of admission the BP was 155/105mmHg and HR 75/min on treatment with a combination of betaxolol, hydrochlorothiazide, moxonidine, losartan and spironolactone. After the patient confirmed regular drug intake [emphasized beneficial effect of the beta-blocker on palpitations], a serum analysis was performed. During the hospitalization, the medication was given under the supervision of a nurse. On the third day the patient started to feel dizzy and the blood pressure dropped to 70/40mmHg, therefore it was decided to significantly reduce the medication. The results showed the absence of the whole antihypertensive medication with the exception of betaxolol at the time of admission. The patient was interviewed and admitted not taking the medication.

**Conclusion:** Both case reports showed a typical clinical picture of a non-compliant patient. The measurement of serum antihypertension drug levels was crucial for the diagnostic work-up. Importantly, it may save costs of unneeded secondary hypertension work-up. Non-compliant patients have an increased cardiovascular risk with high BP levels, on the other hand, at a risk of severe hypotension when suddenly taking whole, previously not taken drug combination. Beneath elevated BP levels, the absence of some typical clinical findings as bradycardia on beta-blockers or side effects as ankle oedemas on calcium channel blockers or dry mouth on centrally acting drugs may be also suspicious of noncompliance.

**Keywords:** resistant hypertension, compliance with treatment, antihypertensive treatment

## Descriptive study to evaluate patients with chest pain admitting to Preliminary Care Unit (PCU) D G H Ampara, Sri Lanka

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**Introduction:** The clinical manifestation of acute coronary syndrome (ACS) varies. Patients present frequently with symptoms other than typical chest pain. An accurate diagnosis and early treatment of patients with ACS is crucial to reduce morbidity and mortality.

**Objective:** To identify the socio-demographic characteristics and risk factors in patients presenting with chest pain to the PCU, to evaluate the patients with atypical chest pain and identify how many of them had ACS.

**Method:** Retrospective descriptive study was carried out in 250 patients admitted to PCU with chest pain from 01/05/2014 to 20/07/2014 using Bed Head Tickets (BHT) and Admission Register.

**Results:** Majority [51.2%] were females. Highest percentage [18.8%] among females were between the age of 40 and 46 years whilst among males [18%] were between the age of 54 and 60 years. 84.4% presented with atypical chest pain.

22% had symptoms for >3days. 66.4% presented within 12 hours from which 26.1% presented within 30 minutes. 58.8% had no ECG changes. 12.6% had ST Elevations. 38.5% out of them had atypical chest pain. ( $p>0.05$ ) 39.8% had other ECG changes suggestive of ACS. 19.4% had arrhythmias from which 10% patients had Gastritis symptoms.

From patients with ACS, 9.3% had no risk factors. The commonest risk factor was age. 53% had multiple risk factors. 0.8% was admitted to the ICU. 7.6% patients were discharged from the PCU and 1.2% expired. 46% patients were discharged within 2 days. 15.6% more than 4 days. 1.8% transferred for interventions.

**Conclusion:** Large number of patients having atypical chest pain had ACS though it is not statistically significant. Majority of chest pain patients presented within 12 hours and had multiple risk factors. Half of the patients were discharged within 2 days. Further studies are needed to elaborate on the findings.

**Keywords:** Atypical Chest pain, Preliminary care unit, Myocardial Infarction, Aute coranary syndrome, ST elevation

# METABOLIC SYNDROME

## The frequency of the main factors of risk for CHD in women in different age groups

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In the development of coronary heart disease [CHD] are important so-called risk factors [RF], which contribute to its rise and pose a threat to its further development. The contribution of various RF in the development of CHD in women is different from men of the same age. In the development of CHD in young and middle-aged among the important factors to the fore, in addition to traditional factors [arterial hypertension [AH], obesity, lipid disorders, diabetes, smoking], the so-called specific RF, such as abnormal menopause, hormone replacement therapy, use oral contraceptive and other. It is advisable to analyze their impact and to assess their role in the development of CHD in women of all ages.

**Objective:** To study the incidence of major RF of CHD in women in different age groups.

**Material and Methods:** 200 women were examined with CHD who were selected because of the epidemiological and clinical examination. Among the examinees in the reproductive age was 79 women and in menopause – 121. All patients performed ECG study, measured blood pressure, defined abdominal obesity [AO] and anthropometric data with the calculation of the index of Kettle, and conducted laboratory studies to examine the lipid profile – total cholesterol [TC], triglycerides [TG], and calculated atherogenic index [AI]. Registration of low degree of physical activity [LPA] was carried out by filling in a special questionnaire.

The resulting digital data is processed by the medical statistics methods using SAS application packages and Statistic for Windows v. 5.5.

**Results:** Our study showed that the overall rate of registration of all studied RF is almost at the same rate found in both age categories. The most common RF in both groups was AO, which reached almost 100% mark and reached 94.5% in the fertile and 93.2% in menopause age. Then followed the overweight [BMI], which is more prevalent in postmenopausal women, compared to women of fertile age to 93.5% and 91.7%, respectively. Of the lipid profile was more frequent hypertriglyceridemia – from 81.8% in menopause, versus 70.9% of fertile age in the I-th group and 91.7% vs. 88.3% – in the II-nd group]. Such RF as AH is much more common in postmenopausal women, in comparison with those of childbearing age [61.4% versus 27.3% in the I-th group and 50.6% vs. 33.3% – in the II-nd group].

### Conclusions:

1. In studied women with CHD the most common RF were are AO, BMI and hypertriglyceridemia.
2. All RF, except AH occur with equal frequency in women of fertile age and menopause.
3. AH is much more common in postmenopausal women compared with those of fertile age.

**Keywords:** coronary heart disease [CHD], women, risk factors, epidemiological study, clinical examination

## Epidemiologic survey of lifestyle factors in Slovak outpatients

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Epidemiologic analysis of lifestyle factors in Slovak outpatients of hepatologic and gastroenterologic ambulances was done. 923 patients from 13 centers were included from September 1st, 2015 till April, 30rd, 2016. Data collection was anonymous. Patients waiting for examination in hepatologic or gastroenterologic ambulance collected question—form and put it to the mailbox.

Nine questions were included involving BMI, physical activity, vegetable, fruit, fish, tobacco, alcohol and coffee consumption. The time needed to filling in was 5–8 minutes. Alcohol consumption was covered by questions corresponding to AUDIT C (first 3 questions of AUDIT questionnaire approved by WHO). Six questions covered the risk occurrence of NAFLD as the trigger of metabolic syndrome: BMI, physical activity, vegetable, fruit, fish, tobacco and coffee consumption. According to the gender 59% of women and 41% of men were included. From the educational attainment point of view 39% had secondary, 24% had college and 5% primary education, 32% didn't point his education level. Overweight and obesity was present in 59% of pts. (BMI > 25). According to the region [Bratislava vs. B. Bystrica] 30% of Bystrica's patients had BMI more than 30, however total amount of included patients was higher in Bratislava [Bratislava vs. B. Bystrica 42%:28%]. In fiber consumption only 12% reached level more than 600 g/daily [recommended by WHO]. Insufficient fiber consumption [less than 400 g] was present in 87% of pts. In fish consumption only 14% of pts. had twice weekly or more. In 85% of pts. was insufficient fish consumption [once weekly or less]. However, more women as men were included, fish and fiber consumption was higher in men as in women. According to the age, pts. below 35 and over 51 years had higher fiber consumption. The highest fish consumption was in pts. older as 71 years. According to the education the highest fiber consumption was in basic, followed by college and secondary education. Fish consumption was highest by college pts, followed by secondary and basic education. According to the region higher fiber consumption was in Bystrica as in Bratislava. Physical training every other day or more was present only in 31% of pts. 68% of pts. had physical training once weekly or less, 28% had none activity. Frequency of physical training was higher in men as in women and in younger as 50 years. 35% of pts. had insufficient coffee consumption, which has hepatoprotective effect. 68% of pts. with risk alcohol consumption had BMI>25, that increases liver mortality 19-times. Risk alcohol consumption with need of whole AUDIT test and specialized treatment had 64% of pts.

Our survey showed unfavourable data of lifestyle of our pts. All mentioned factors are modifiable and preventable. Screening of risk lifestyle factors is simple, inexpensive and can be followed by short recommendation. It may save lives of our patients. Application of short lifestyle questionnaire in each practical ambulance is recommended.

**Keywords:** lifestyle factors, question, consumption

## A community based study to assess the prevalence of Non Communicable Diseases and their risk factors among rural population of Sri Lanka

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**Background:** Existing epidemiological data on prevalence of Non Communicable diseases (NCDs) among rural Sri Lankan population is inadequate and inaccurate. We carried out a descriptive cross sectional study in a rural village; denoting most of the Sri Lankan population.

**Objectives:** The general objectives were to assess the prevalence NCDs of; hypertension, diabetes, hypercholesterolemia and the risk factors; obesity, smoking habits and alcohol consumption for NCDs among rural population of Sri Lanka.

**Methodology:** Consecutive individuals aged 25–60 years were included. Informed verbal consent was obtained following providing a detailed information sheet.

Blood drawing was done in two separate days prior to the study for fasting blood sugar, total cholesterol and lipid profile for the individuals with total cholesterol > 240 mg/dl. Consecutive sampling was done.

Data were collected using pre-tested interviewer-administered questionnaire and analysed using SPSS and results were presented with percentages and chi-square.

**Results:** 767 individuals were included with 1:2 male:female ratio. One third of the study population was indicated in to each age group categorized as 25–39, 40–49 and 50–60 years.

11.9% [91] individuals were identified as diabetic, 5.3% [41] were pre-diabetic. Prevalence of diabetes was almost same among both males and females [16.7% & 17.45%]. Prevalence was not significantly associated with gender ( $p=0.16>0.05$ ). Out of this 1/3 was newly diagnosed as diabetic or pre-diabetic.

High mean systolic blood pressure (SBP>140mmHg) found in 24% [184] and prevalence among males and females were 25.2% and 23.2% respectively. 24.8% [190] had high diastolic blood pressure (DBP>90mmHg) with 26.45% female prevalence and 22.5% of male. Both prevalence of high SBP and DBP were not statistically significant with gender ( $p_1=0.08>0.05$ ,  $p_2=0.894>0.05$ ).

High total cholesterol levels (>240mg/dl) identified in 23.7% while prevalence of males and females were 22.85% [64] and 24.22% [118]. 81.4% [44] of them had diabetes. Prevalence was not statistically significant with gender ( $p=0.865>0.05$ ) and was significantly associated with diabetes ( $p=0.01<0.05$ ).

7% [54] had high LDL levels and 22.2% [12] of them had diabetes. 6.5% [50] had high triglyceride levels (>150 mg/dl) and 36% of them had diabetes.

36.2% [278] was overweight and 5.3% [41] was obese. Prevalence of overweight among males and females were 28.57% and 33.26% respectively. Prevalence of obesity was 30.18% and 2.0% among females and males. Prevalence of high BMI was not significantly associated with gender ( $p=0.213>0.05$ ). 35.1% [85] individuals with high BMI (>23kg/m<sup>2</sup>) had diabetes while 45.4% [145] had high total cholesterol levels and 38.5% [123] had hypertension. Prevalence of hypertension was significantly associated with high BMI ( $p=0.009<0.05$ ).

There were 70.4% [540] non-smokers, 5.1% [39] current smokers and 3.1% [24] ex-smokers. 31.7% [20] of smokers had high blood pressure. 12.4% was current alcohol consumers and 2.0% were ex-consumers. 15.4% of alcohol consumers had diabetes; 34.5% had high blood pressure and 26.36% had high total cholesterol levels.

**Conclusion:** The prevalence of selected NCDs and their risk factors are relatively high among the Sri Lankan rural population surveyed requiring urgent public action. Health education and population screening should be focused to identify and treat at early stages.

**Keywords:** Community based study, Prevalence, Non communicable diseases, Risk factors, Rural population of Sri Lanka

## Descriptive study to evaluate the risk of Metabolic Syndrome among health staff members at District General Hospital Ampara, Sri Lanka

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**Introduction:** Metabolic Syndrome (MS) is common among Sri Lankan adults affecting nearly one-fourth of the adults in Sri Lanka. It is a cluster of risk factors including obesity, dysglycemia, dyslipidemia and hypertension that occur together, increasing the risk of cardiovascular diseases, stroke and diabetes. If more than one of these conditions occur in combination, the risk is even greater. Insulin resistance plays a central role in the pathophysiology of Metabolic Syndrome. Very few studies were done to identify the risk of MS in health staff members

**Objective:** To identify the risk of Metabolic Syndrome among health staff members at DGH Ampara.

**Methods:** 100 staff members were chosen by simple random sampling. In each individual Fasting Blood Sugar (FBS), Total Serum Cholesterol(TC)/Lipid Profile(LP) and Electrocardiograph(ECG) were performed, and their BMI (body mass index), abdominal circumference(AC), Blood Pressure(BP) were measured. Structured self-administered questionnaire was given. The data was categorized and analyzed using EXCEL with the aid of WHO, JNC 8 and ATP3 guidelines.

**Results:** Majority were females (63%) and the mean-age of the sample is 37.56years (female 39.46, SD-7.6 and male 34.75, SD-9.5). 96% had normal FBS, 4% had impaired blood glucose. 55% of the population had TC >200mg/dl and the mean TC is 203mg/dl. (males SD-30.6, females-32.3) Majority had normal BP and 37% of them were in pre-hypertension category. 2.77% of the males have abdominal circumference >102cm and 62.5 % of the females have abdominal circumference >88cm. The mean female abdominal circumference is 90.74cm (SD-11.25 and male is 86.70cm.(SD-11.21)

Overall 37% are at risk of developing metabolic syndrome. In which 8% are male and 29% are female.

**Conclusions:** A significant proportion is at risk of developing metabolic syndrome and majority were females. Mean serum cholesterol was significantly high and female had higher abdominal circumference. Strict lifestyle modifications are needed in health staff members.

**Keywords:** Metabolic syndrome, syndrome X, Risk for Health staff, Sri Lanka, abdominal circumference, Impaired FBS

## A community based study to assess the awareness of Non-Communicable Diseases among rural population of Sri Lanka

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**Background:** It is well-known that poor knowledge on NCDs leads to increased prevalence of these diseases among population. As none of the studies published in Sri Lanka on this, a descriptive cross-sectional study was conducted in a rural village.

**Objectives:** To assess the awareness of NCDs, their risk factors and complications among rural population of Sri Lanka.

**Method:** Individuals between 25–60 years of age who attended to the health screening program were included. An interviewer administered questionnaire was given to consecutive individuals.

The questionnaire contained twenty five stems and each of them marked according to five point likert scale; “Strongly agree” “Agree” “No opinion” “Disagree” and “Strongly disagree”

Individual who responded the correct answer with confidence [“Strongly agree” for positive stem or “Strongly disagree” for negative stem] was considered as having “Good knowledge”.

Individual who responded the correct answer with doubt [“Agree” for positive stem or “Disagree” for negative stem] was considered as having “Some knowledge”.

Individuals who selected incorrect answers [either for sure or in doubt] were considered as wrong interpreters.

**Results:** From a target population of 764 individuals, 452 were interviewed in this study which consisted of 164 [36.28%] males and 288 [63.71%] females.

Out of this population, 220 [48.67%] had a good knowledge about types of NCDs. 77 [17.03%] had some knowledge. 73 [16%] had no opinion and 82 [18%] were mis-interpreters.

224 [49.55%] individuals had a very good idea about causes of NCDs. 63 [13.93%] had some idea. 104 [23%] had no idea, 62 [14%] had wrong interpretation.

205 [45.35%] individuals had a good knowledge on identifying complications of NCDs, While 68 [15.04%] had some awareness, 128 [28.32%] were clueless, 51 [12%] were wrong interpreters.

Results revealed that 254 [56.19%] individuals had a good idea regarding diabetes while 80 [17.69%] had some knowledge, 68 [15%] responders had no opinion and 50 [11%] individuals had wrong interpretation.

Individuals had lesser awareness on hypertension related questions; 185 [40.92%] had a good idea, 70 [15.48%] some idea, 139 [31%] no opinion 58 [13%] were wrong interpreters.

Awareness regarding cancers; 241 [53.31%] individuals had a good knowledge, 76 [16.81%] had some knowledge. 46 [10%] responded that they have no opinion on cancer and related questions 89 [20%] were found to be having wrong interpretation.

Analysis on the knowledge of food habits and the occurrence of NCDs revealed that 228 [50.44%] was well aware of the relationship. 71 [15.70%] had some idea, while 116 [26%] had no opinion on the topic. 37 [8%] individuals were wrong interpreters.

302 [66.81%] and 242 [53.53%] had a good knowledge respectively, regarding smoking and alcohol. 59 [13.05%] had some idea on smoking 65 [14.38%] had some idea on alcohol related problems. 63 [13.93%] were clueless and 28 [6%] were misinterpreted the effects of smoking. This is 92 [20%] and 54 [12%] respectively for alcohol.

Regarding obesity and exercise 256 [56.63%] individuals had a good knowledge, 62 [13.71%] had some knowledge. 88 [19%] had no opinion and 51 [11%] were wrong interpreters.

**Conclusion:** According to the results of the study, the awareness and the knowledge among studied population is inadequate. It is important to have basic awareness among the population to implement programs to uplift the knowledge and practices.

**Keywords:** Community based study, Non communicable diseases, Awareness, Rural population, Sri Lanka

# ATHEROSCLEROSIS

## Analysis of risk factors and characteristics of genetic predisposition and clinical-angiographic manifestations of atherosclerosis in patient with ischemic organ damage without stenotic vascular damage

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**Relevance:** Heart and brain are interrelated target organs of vascular pathology, clinical variants which [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, arteries are intact.

**Scientific novelty:** We will summarize risk factors, clinical and angiographic, genetic testing in patients with myocardial infarction or ischemic stroke, but no 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, VEGFR [epidermal growth factor receptor].

**Materials 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 No 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 was studied contingent 55; 47 women [31%], 113 men [69%]; 101 of which have a history of coronary artery disease [67%], and 17 [11%] revealed stroke, repeated history of myocardial infarction had 9 people. Operations on the coronary arteries in 52 [35%] patients. The total duration of CHD was on average 1.2 years. Risk factors: smoking 88 [59%] patients, 43 [29%] patients with obesity according to BMI calculation. Dyslipidemia is revealed in the evaluation lipid 46 [31%], 89% have a history of hypertension, 77 [51%] diabetes. In assessing lipid: average total cholesterol level was 5.2 mmol/l, LDL 3.15 mol/l, TG 1.81 mmol/l. 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.

**Keywords:** atherosclerosis, gene polymorphism, heart stroke

## Atherosclerosis and Chronic Kidney Disease

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Atherosclerosis represents one of the major causes of premature death, and it is frequently associated with, exacerbates, and is aggravated by chronic kidney disease (CKD). Atherosclerosis integrates the response to a number of insults, and consequently, the accelerated atherosclerosis found in CKD patients is associated with activation of a variety of humoral and tissue mechanisms. Hypertension, diabetes, dyslipidemia, obesity, metabolic syndrome, and additional non-traditional risk factors can damage the kidney directly and by promoting intrarenal atherogenesis, even in the absence of obstructive lesions in the renal artery. Evidence indicates that increased oxidative stress and inflammation may mediate a large part of the effects of risk factors on the kidney. In turn, progressive deterioration of renal function in CKD may lead to dyslipidemia or accumulation of uremic toxins, which can induce production of free radicals and activate proinflammatory and fibrogenic factors, leading to vascular endothelial cell dysfunction and injury, and favoring development of atherosclerosis. Therefore, the kidney can be a villain or a victim during atherogenesis. The purpose is to provide new insights into the mechanisms by which atherogenic factors may instigate early renal injury. CVD is up to 20× more common in ESRD patients and accounts for 40–50% of all deaths; accelerated atherosclerosis has been consistently implicated, partly because of a higher prevalence of established CVRFs, such as diabetes, hypertension, and dyslipidemia. Established CVRFs are associated with the development of new-onset kidney disease. Therefore, it is important to assess conventional CVRFs in patients with kidney disease to allow early intervention. CKD in turn is a marker for elevated CVD risk in elderly adults. In addition to conventional CVRFs, novel CVRFs such as inflammation, oxidative stress, and hyperhomocysteinemia, among others, are associated with cardiovascular risk. However, establishing the role of individual CVRFs in CKD may be difficult because they may coexist, share similar mechanisms, and possibly interact synergistically. Despite recent advances in renal revascularization techniques and stenting, it remains unclear why the kidney affected by atherosclerosis often does not improve or continues to deteriorate after revascularization. This observation led to the speculation that atherogenic factors induce direct renal injury. Indeed, growing clinical and experimental evidence has demonstrated that several deleterious intrarenal pathways are activated during atherogenesis. Before development of plaques, atherosclerosis elicits micro and macrovascular dysfunction and tissue structural modifications, favored by traditional and non-traditional CVRFs, which likely activate similar mechanisms, interact, and often exacerbate renal injury. Their pathophysiological mechanisms include oxidative stress and inflammation, with several downstream sequences of feed-forward interactions, activating transcription factors that lead to vascular, tubulointerstitial, and glomerular injury. Moreover, atherosclerosis may blunt intrinsic defense mechanisms designed to preserve renal structural integrity, and thereby facilitate renal scarring. This hierarchical sequence triggers and likely perpetuates downstream mediators that are involved in the progressive renal compromise in atherosclerosis. Therefore, controlling oxidative stress and inflammation in CKD may interrupt this cycle of atherosclerosis-induced renal injury. Future research efforts are needed to uncover additional deleterious interactions in the atherosclerotic kidney and to design effective interventions to slow this process.

**Keywords:** Kidney, Atherosclerosis, Oxidative stress, Inflammation, Fibrosis

## Internist's view on the problem of cardiovascular patient's preparation for operations

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**Relevance:** in some cases, cardiovascular patients faces with the inevitability of surgical care [critical ischemia, crescendo transient ischemic attacks, etc.].

**The aim** of this research was to evaluate the metabolism correction features in patients with peripheral atherosclerosis before upcoming surgery.

**Materials and methods:** the research is based on monitoring of 57 patients with widespread atherosclerosis, which were performed reconstructive surgery on the great vessels. Patients were divided into main and control groups, according to presence or absence of infectious complications after surgery produced. The main group [34 people] consisted of patients with surgical site infection [SSI]. The control group included 23 patients without the such complications. We analyzed the characteristics of metabolism [dyslipidemia, hypertension, carbohydrate disorders, weight change], the severity of ischemic changes and the results of surgical interventions.

Statistical processing of the data was performed using "STATISTICA-10" software package. The research results are presented as  $M \pm m$ , the difference was considered significant at  $p < 0.05$ .

**Results:** SSI significantly more frequently recorded in patients with decompensated type 2 diabetes, which opens up prospects for stabilization of carbohydrate disorders, as a mean of prevention of infectious complications.

The prevalence of patients with essential hypertension stage 3 in the main clinical group [ $p < 0,05$ ] determines preventive actions for the restoration of the microcirculation in the preoperative period.

Obesity [as a component of the metabolic syndrome] is important in the development of surgical site infection [ $p < 0,05$ ].

**Conclusions:** adequate metabolism correction in the preparation of patients with cardiovascular pathology to reconstructive surgical interventions, is an important measure to prevent dangerous complications.

**Keywords:** surgical site infection, decompensated type 2 diabetes, hypertension stage 3, Obesity

## HEART FAILURE

### Left ventricular end systolic and diastolic volumes and ejection fraction in patients with heart failure and preserved ejection fraction – meta-analysis, graphic presentation and their relation with concentric hypertrophy

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**Background:** Previous studies showed that ejection fraction (EF) was greater in heart failure and preserved ejection fraction (HFPEF) than it was in healthy controls (HC). This study aimed to reveal whether differences between the components of EF, namely end systolic and diastolic volumes (ESV, EDV), in HFPEF compared to HC, explain why EF in HFPEF is greater.

**Methods:** We searched the literature for studies reporting EF, and indices of EDV [EDVi] and ESV [ESVi] until May 2015. The pooled difference between HFPEF and HC was estimated with weighted and standardized mean differences. In addition to the standard meta-analysis, a graphical presentation was developed demonstrating how ESVi and EDVi during HFPEF differed from ESVi and EDVi at health. For this end the normalized mean difference of X,  $NMD[\langle X \rangle] = [\langle X \rangle^{HC} - \langle X \rangle^{HFPEF}] / \langle X \rangle^{HC}$ , where X=EDVi or ESVi and  $\langle X \rangle$  is the mean of X, was plotted as a function of the difference between EF in HC ( $EF^{HC}$ ), and HFPEF ( $EF^{HFPEF}$ ), for each study included.

**Results:** Fourteen studies were analyzed; HFPEF patients were 3.6 years older and 3.2 BMI units heavier than HC ( $P < 0.001$ , for both);  $EF^{HFPEF}$  was 1% smaller than  $EF^{HC}$  (WMD 95%CI: -1.66, -0.5;  $p = 0.057$ ).  $EDVi^{HFPEF}$  and  $ESVi^{HFPEF}$  were not different from their HC counterparts. Graphical analysis revealed that when  $EF^{HFPEF} > EF^{HC}$ , both  $EDVi^{HFPEF}$  and  $ESVi^{HFPEF}$  were smaller than their HC counterparts (i.e.  $NMD[ESVi] > 0$ ), and the absolute difference between  $ESVi^{HC}$  and  $ESVi^{HFPEF}$  was greater than that observed between  $EDVi^{HC}$  and  $EDVi^{HFPEF}$ . When  $EF^{HFPEF} \leq EF^{HC}$ , both  $EDVi^{HFPEF}$  and  $ESVi^{HFPEF}$  were either greater or smaller than their HC counterparts.

**Conclusions:** Meta-analysis showed agreement between changes in EDVi and ESVi and the value of EF. On average, the changes demonstrated in EDVi and ESVi (from HC to HFPEF) were not characteristic of concentric hypertrophy. Graphical analysis showed that when  $EF^{HFPEF} > EF^{HC}$ , changes in EDVi and ESVi were characteristic of concentric hypertrophy, and when  $EF^{HFPEF} < EF^{HC}$  changes were characteristic of eccentric hypertrophy.

**Keywords:** Heart failure preserved ejection fraction, end diastolic volume, end systolic volume, meta-analysis

# HYPERLIPIDEMIA AND DYSLIPIDEMIA

## Common polymorphisms as strong predictors of hypertriglyceridemia in Czech population

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Hypertriglyceridemia (HTG) is a common lipid disorder. It is supposed, that really high plasma levels of triglycerides (over 10 mmol/L) have strong genetic background. Rare mutations within the genes for LPL, APOA5, APOC2, GPIHBP1 and LMF1 explain some cases, but in majority of the patients, the disease seems to be polygenic. Accumulation of risky alleles can lead to the increased disease penetrance.

Using PCR-RFLP we have analysed common polymorphisms within the genes *APOA5* (rs96484), *FRMD5* (rs2929282), *GCKR* (rs1260326), *CAPN3* (rs2412710) and *TRIB1* (rs2954029) in 145 patients with plasma TG values over 10 mmol/L and 515 control subjects with plasma TG below 1.8 mmol/L.

In all cases, we have found highly significant risk [all  $P < 0.01$ ] of hypertriglyceridemia development associated with the minor alleles of the above mentioned SNPs. The risky alleles increased the risk [OR, 95%CI] of HTG for 1.62 [1.09–2.40; *TRIB1*], 2.74 [1.19–6.33; *CAPN3*], 2.56 [1.64–4.00; *GCKR*] and 2.05 [1.19–3.53; *FRMD5*]. The extreme association has been observed in the case of the *APOA5* gene, where the GG homozygotes exhibit more than 15-times higher risk to develop HTG [OR 15.16, 95%CI 6.40–36.04;  $P < 0.000001$ ]. The mean of the risky alleles per person was 1.03 in HTG group vs. 0.48 in controls [ $P < 0.01$ ].

Our results clearly confirm that the common SNPs in distinct genes are strong predictors of the HTG development.

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# STROKE

## Amidolytic activity of haemostasis factors activated from zymogens in plasma under influence of stroke peptide pool

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**Objective:** The activation of thrombin from its predecessor prothrombin is an important regulatory process that maintains homeostasis.<sup>1,2</sup> Protein C performs anticoagulating function, modulates fibrinolysis and take place in inducing of signal pathways.<sup>5</sup> Here the idea was explored peptide pool [PP] with Mr up to 5 kDa generated in bloodstream during the acute phase and their presence past one year after stroke provokes complications or disease repetition.<sup>3,4,6-8</sup>

Investigation of the potential influence of PP formed in the bloodstream after suffering a stroke, on the amidolytic activity of Thrombin and Protein C as two of the key haemostasis factors will clarify the role of post stroke PP in the bloodstream.

**Methods:** PP fractions were obtained by the Nikolaichyk V. method<sup>9</sup> from the blood plasma of 35 healthy donors and 56 atherothrombotic [AIS] and cardioembolic [CIS] ischemic stroke patients in acute phase as well as 56 patients one year past acute phase. Isolated PP fractions were dialyzed against vehicle. Experimental mixture preparation and registration of absorption were done like previously.<sup>10</sup> An activator of prothrombin derived from the venom *Echis multisquamatus* [ecamylin] as well as activator protein C derived from the venom *Agkistrodon blomhoffi Ussuriensis* were used.<sup>11,12</sup> Control sample contained the same components but equal volume of vehicle instead of PP. Different concentrated PP fractions were tested.

**Results:** Different concentrations of PP showed various and often opposite effects. The activation of protein C amidolytic ability under influence of healthy donor's PP fraction in all tested concentrations was observed. In particular 68 mkl/ml concentrated healthy donor's PP fraction activated amidolytic ability of protein C by 19%, 34 mkl/ml by 15% and 17 mkg/ml by 26%. Different concentrated PP cause opposite effects of the study process. In particular 214 mkg/ml concentrated acute AIS as well as 99 mkg/ml concentrated year past AIS PP fractions inhibited the amidolytic activity of protein C by  $15\% \pm 2\%$  on average. However, the same fractions in concentrations half and quote less activated response by 17% and 14% respectively. Year past CIS PP fraction activated study process in concentrations of 69 mkg/ml and 34 mkg/ml by 13% and 17% respectively. The same fraction in the concentration 17 mkg/ml activated both year past as well as acute CIS by 12% and 19% respectively.

The amidolytic activity of thrombin was increased under the influence of healthy donor's PP at concentrations 34 and 17 mkg/ml by  $10\% \pm 3\%$  in average. All stroke PP fractions activated the tested process. The maximum activation was observed under the influence of quote less concentrated fractions and was equal in average 10% for both acute subtyped of ischemic strokes. For both year past strokes, the index was 7%.

**Conclusion:** Therefore results affirm that ischemic stroke accompanied by the formation of the peptide pool in the bloodstream that could take part in recurrence of the disease.

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**Keywords:** Peptide Pool, Thrombin, Protein C, Ischemic Stroke

## POSTERS

## ATHEROSCLEROSIS

**Serum chemerin and fibroblast growth factor-21 levels in acquired aorta valve stenosis patients**

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**Background:** Chemerin is an adipokine that regulates inflammation process by ensuring macrophage migration to the specific tissue. High chemerin level in blood is considered as an inflammation marker, though it is not quite clear if chemerin's mode of action is anti-inflammatory or proinflammatory. Fibroblast growth factor-21 [FGF-21] possess cardio-protective activity, there is a perception that FGF-21 levels may increase in response to different stress factors. The aim of the present study was to evaluate differences in serum levels of chemerin and FGF-21 levels, and their relationship to aortic stenosis [AoS] progression and the severity of the disease.

**Patients and methods:** Patients were allocated into two main groups: 1) with AoV stenosis 2) control group without AoV stenosis. The study group with AoV stenosis was divided into three subgroups depending on the severity of the stenosis, which was determined depending on the maximum flow rate – Vmax [m/s], average pressure gradient – avg. PG [mm/Hg], AoV aperture area – AVA [cm<sup>2</sup>]; severe: Vmax > 4,0 m/s; avg. PG > 40 mm/Hg; AVA < 1,0 cm<sup>2</sup>; medium: Vmax 3,0 – 4,0 m/s; avg. PG 20 – 40 mm/Hg; AVA 1,0 – 1,5 cm<sup>2</sup>; mild: Vmax 2,5 – 2,9 m/s; avg. PG < 20 mm/Hg; AVA 1,5 – 2,0 cm<sup>2</sup>. In this study 102 patients were included, out of which 72, 5% were females and 27, 5% were males. 13, 7% [14] had mild, 20, 6% had medium, 16, 7% [17] had severe aorta stenosis and 49% [50] were in the control group. The biochemical markers were determined using standardized clinical laboratory methods.

**Results:** Chemerin levels were higher in the aorta stenosis groups of mild and medium severity and overall decrease was observed with the increase of the severity of stenosis in comparison to the control group. Kruskal Wallis test results showed statistically significant difference between all patient groups and the controls [p=0,009]. Mann-Whitney U tests analysis showed statistically significant difference between the control group and mild stenosis group [U = 89, z = -2,855, p = 0,004]. However, FGF-21 serum levels increased as the aorta stenosis severity raised, reaching the maximum in the severe aorta stenosis patients. Results from Kruskal Wallis test showed a statistically significant difference between the aorta stenosis patient groups and the control group [p=0,041]. In the analysis between the groups Mann-Whitney U test was performed to analyse the difference between two groups, and confirmed statistically significant difference between the control and the sever stenosis groups [U = 201, z = -2,49, p = 0,013].

**Conclusions:** Our study results and literature review indicates that in the early stages of the disease inflammation is more prevalent, whereas calcification and intracellular space changes prevail in later stages. In the further course of the study analysis of the data obtained from the included subjects will be continued in order to specify the role of different biochemical marker in the pathogenesis of calcifying aorta stenosis.

**Keywords:** aortic stenosis, chemerin, fibroblast growth factor-21

# DIABETES

## Can a diabetes affect atherosclerosis?

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It is difficult to consider the combination of diabetes mellitus and atherosclerotic process to be favorable. However, the idea of fatal impact of carbohydrate disorders on the development of atherosclerosis is not generally accepted.

**The aim of** this research was to find out the relationship between impaired glucose metabolism and peculiar features of multifocal atherosclerosis development.

**Materials and methods:** Observations of 97 patients who have transferred reconstructive interventions on the main arteries in connection with the widespread atherosclerosis have formed the basis of the work.

Group I [a control group] consisted of 28 patients without disorders of carbohydrate metabolism, 29 patients with “prediabetes” [violation of prandial glycaemia] were included in Group II, Group III consisted of 40 patients with the type 2 diabetes mellitus. Such parameters as blood pressure, lipid blood spectrum, changes in the mass body index, including the presence of visceral obesity, the severity of ischemia in patients with peripheral arterial disease, the occurrence of cerebrovascular disease, complications within 30 days of the postoperative period were analyzed.

The development of surgical site infections, the adverse cardiovascular events as well as preformed amputations were considered to be primary end point.

**Statistical analysis** was performed using the software package STATISTICA 13. The results were separated on a scale mean values [mean] ± standard deviation. The difference in categorical variables was analyzed by means of Pearson’s  $\chi^2$  and Fisher’s exact test. In all statistical analysis procedures, we expected to reach the level of significance [p], while the critical level of significance was accepted at  $P < 0,05$ .

**The results:** Disorders of carbohydrate metabolism associated with the severity of essential hypertension in stage III were detected in 3, 6, 13 observations in Groups I, II and III, respectively ( $p < 0,05$ ). Occurrence of visceral obesity has been increasing from the first to the third group, which confirms the mutual influence of carbohydrate and lipid disorders [pronounced dyslipidemia, with low density lipoprotein has been increasing in the direction from Group I to Group III], ( $p < 0.05$ ). The number of patients with critical ischemia was minimal in Group I [8 patients] and it was maximum in Group III [21 patients], ( $p < 0.05$ ). Cerebrovascular disease occurrence has risen in 6 times from the control group and the frequency of stroke in the operated patients was 2.5 times higher in Group III than in Group I ( $p < 0.05$ ). The number of amputations was larger in Group III than in Group II and the control group correspondingly.

**Conclusions:** The results of these observations confirming the negative impact of carbohydrate metabolism on the development of atherosclerosis make us suggest the necessity of lifestyle changes at the stage of «prediabetes».

**Keywords:** atherosclerotic process, prediabetes, type 2 diabetes mellitus, essential hypertension in stage III, amputations

## Gliflozin as a possible cause of severe metabolic disorder – case report

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**Background:** Gliflozins belong to a new group of oral antidiabetic drugs acting on S-GLT2 receptors, increasing glucose secretion into urine. Their stimulating effect on glucagone secretion by pancreatic alpha – cells is less known.

**Case report:** 73-year old female with type 2 diabetes mellitus, treated by the combination of intensified insulin regimen and metformin, with normal renal function, and history of numerous episodes of hypoglycemia, was admitted to the hospital because of symptomatic hypoglycemia with altered consciousness. On current therapy [Novorapid 5-4-3 IU, Lantus 0-0-10 IU and metformin 850 1-1-1] hypoglycemias occurred also during the hospital stay. Therefore, gradually, the insulin therapy was withdrawn, and the patient's therapy was switched to combination of oral antidiabetics [dapagliflozin 1-0-0, sitagliptin/metformin 50/1000 1-0-1], with good effect. After 4 days the patient's clinical state became complicated by urinary infection. Despite empiric antimicrobial therapy [ampicilin/sulbactam, fluconazol] followed by prompt decrease of laboratory markers of infection, 2 days later sudden disturbance of consciousness occurred, accompanied by hemodynamic instability and serious metabolic acidosis [arterial pH = 7.007, [HCO<sub>3</sub>] = 3.7 mmol/l, pCO<sub>2</sub> = 1.75 kPa, base excess -24.8, glycemia = 24 mmol/l, [lactate] = 4.1 mmol/l] The patient was admitted to ICU requiring ventilation and circulatory support, ketoacidosis was treated symptomatically [i.v. fluid therapy, i.v. insulin, treatment of acid-base state]. Within several hours the metabolic state improved and restored to normal, patient became circulatory stable, and was extubated on the next day. 26 days later she was dismissed from the hospital in good clinical condition, on insulin monotherapy [Actrapid 3-5 IU, Lantus 6 IU], without additional oral antidiabetics.

**Conclusions:** The significance of this case report is based on the fact, that adding gliflozin to the therapy of diabetes may lead to the manifestation of serious, anion-gap positive, metabolic acidosis and diabetic ketoacidosis, especially under some circumstances [e.g. sepsis, insulin deficiency in type 2 diabetes, unstable glycemias, dehydration]. The nature of the mechanism is probably the glucagone – mimetic effect of the inhibition of S-GLT2 in alpha pancreatic cells, alteration of renal compensation mechanisms [bicarbonate reabsorption] and also maybe the loss of “warning hyperglycemia” in early stage of the development of metabolic disorder with persisting glycosuria.

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**Keywords:** diabetes mellitus type 2, S-GLT2 receptors, severe metabolic disorder, infection

## Lipid disorders in patients with diabetic foot – efficacy of therapy and relation to amputation and mortality

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**Aims:** Patients with diabetic foot (DF) have been shown to have high cardiovascular (CV) morbidity and mortality. Management of CV risk factors, particularly lipid disorders (LD) is often insufficient in patients with DF. The aim of our study was to assess the efficacy of therapy of LD and the association of these disorders with major amputation and mortality in patients with DF.

**Methods:** Two hundred and seventy patients hospitalized for DF in our centre during 1/2009–12/2012 were enrolled. The history of CV disease [peripheral arterial disease – PAD, ischemic heart disease – IHD, stroke] and LD [total cholesterol > 4.5 mmol/l, LDL > 2.5 mmol/l, HDL < 1 mmol/l, triglycerides > 1.7 mmol/l] were assessed in relation to major amputation and mortality during follow-up of  $32 \pm 14.5$  months.

**Results:** The mean age was  $62 \pm 11.1$  years, 78.5% were men, 79.6% of patients had type 2 diabetes with duration of  $20.7 \pm 11.7$  years. The prevalence of PAD was 71.1%, IHD 43%, stroke 14.4%. The incidence of major amputation and mortality were 14.8%, and 10.4%, respectively. Fifty percent of patients were on statin therapy and 7% were on other lipid lowering therapy [fibrates, ezetimib]. There was no significant difference between patients with and without lipid lowering therapy in total cholesterol levels < 4.5 mmol/l [68,3% vs. 60,8%, respectively]. Patients on statins had significantly lower LDL in contrast to patients without statins [ $2.3 \pm 0.73$  mmol/l vs.  $2.6 \pm 0.74$  mmol/l,  $p = 0.0018$ ] and significantly higher triglycerides [ $p = 0.008$ ]. Patients after major amputation had significantly lower HDL than patients without amputation [ $p = 0.04$ ]. Deceased patients had significantly lower total and LDL cholesterol [ $p = 0.013, 0.02$  respectively].

**Conclusion:** Therapy of LD in patients with DF was unsatisfactory in terms of recommended lipid levels and only one-half of patients had lipid lowering therapy. Early management of LD is necessary in patients with DF and high risk of CV morbidity and mortality.

Supported by project [Ministry of Health, Czech Republic] for development of research organization 00023001 [IKEM, Prague, Czech Republic] – Institutional support.

**Keywords:** diabetic foot, lipids, amputation, mortality

## Lipid modification in type 1 diabetic patients

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**Aim:** To identify all T1DM patients registered at a GP surgery, and to analyse whether they are on adequate statin therapy.

**Content of Presentation:** NICE guidelines (August 2015) state patients diagnosed with T1DM for over 10 years or those who are over 40 years old should be on Atorvastatin 20mg or the equivalent. This audit looks at type 1 diabetic (T1DM) patients at the practise in two age categories of 20–39 years old (considered to have diabetes for >10 years) and above 40 years old, and whether they are on statins for primary prevention of cardiovascular disease (CVD).

**Relevance/Impact:** It is well known that diabetic patients are at increased risk of CVD and that primary prevention is a key factor to reduce the burden to the patient and the NHS. The CARDS study (Colhoun et al 2004) shows the positive impact that statins have in reducing the incidence of CVD. Often young adults are lost to hospital follow up and hence need adequate primary care checks and health promotion to prevent such increase in CVD as seen in type 1 diabetics.

**Outcomes:** Only 1 patient of 8 in the 20–39 age group and 52% of patients over 40 were on a statin. The average age for starting a statin was 50 years old. The type and dose of statin varied and with that only 55% of patients on a statin were on a correct dose. Of all the patients identified, 24% were on adequate statin therapy.

**Discussion:** More patients over the age of 40 are being put on statins and this is likely due to GPs thinking about primary prevention for CVD more as patients get older. Ultimately hospital consultants need to initiate statins in anyone over the age of 20 on the annual check. Unfortunately, many young adults are lost to follow up during this period hence the opportunity lost to commence this medication. More needs to be done in primary and secondary to promote statin uptake in type 1 diabetic patients

## Prevalence of diabetic neuropathy among patients with type 2 diabetes mellitus

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**Aim:** The work was initiated to study prevalence of diabetic neuropathy among patients with type 2 diabetes mellitus as per EURODIAB questionnaire

**Materials and methods:** Autonomic neuropathy with psycho-autonomic disorders was assessed in 104 patients with type 2 diabetes mellitus undergoing clinical evaluation by means of inquiry as per EURODIAB program modified by Danilov A.B.

**Results:** In 104 patients, 52 women and 52 men among them, with type 2 diabetes mellitus with mean age  $54.6 \pm 1.04$  years mean duration of type 2 diabetes mellitus was  $10.2 \pm 0.7$  years. Body mass index was  $29.9 \pm 0.53$  kg/m<sup>2</sup>. Glycosylated hemoglobin value [HbA1c] was  $9.3 \pm 0.3\%$ . According to the findings from our study diabetic polyneuropathy syndrome occurred in 69.2% of cases, 73% of the patients had cardiovascular disorders. Disorders in hidropoiesis could be seen in 91% of the patients, gastrointestinal and respiratory dysfunctions were found in 9.6% and 44.2% of the patients, respectively. Pupillary reflex was found disturbed in 22.7%, urogenital dysfunction could be seen in 37.5%.

**Conclusions:** Disorders in hidropoiesis manifesting as hyperhidrosis or xeroderma are the most frequent type of diabetic neuropathy in patients with type 2 diabetes mellitus [91%]. Of note, cardiovascular disorders could be seen more frequently [73%] than diabetic polyneuropathy syndrome [69.2%]. Gastrointestinal disorders were the least frequent [9.6%].

**Keywords:** type 2 diabetes, diabetic neuropathy, EURODIAB questionnaire

## The impact of inherited thrombophilia on the effect of cell therapy of critical limb ischemia in diabetic patients

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**Background and Aims:** Some diabetic patients with no-option critical limb ischemia (CLI) treated by autologous cell therapy (ACT) using bone marrow-derived mononuclear cells do not increase ischemia parameters after the procedure. Inherited thrombophilia could negatively influence the clinical outcome of ACT by a re-stenosis based on microthrombosis. The aim of our study was to analyze the risk factors for impaired response to ACT in patients with CLI and diabetic foot with respect to inherited thrombophilia.

**Methods:** Seventy-two diabetic patients with CLI and diabetic foot from our foot clinic treated by ACT over 7 years were divided into responders ( $n = 57$ ) and non-responders ( $n = 15$ ). Non-responders were defined as an insufficient increase of transcutaneous oxygen pressure [TcPO<sub>2</sub>] by a maximum of 5 mm Hg at 3 months after ACT. Risk factors for the impaired response were assessed before cell therapy and divided into patient-related ones: e.g. age, sex, duration and treatment of diabetes, HbA1c, inherited thrombotic disorders, co-morbidities, product-related ones: number of leukocytes, lymphocytes, monocytes, platelets, CD34+ cell counts, and limb-related ones: e.g. severity of CLI [Rutherford classification], TEXAS classification, and infection – classified by PEDIS (up to grade 3) and WifI (up to grade 2), presence of resistant microbes [MRSA, Pseudomonas, Klebsiella ESBL], osteomyelitis [confirmed by X-ray], and CRP.

**Results:** The main independent predictors for impaired response to cell therapy were heterozygote Leiden mutation [OR 10.5; 95% CI 1.72–4] and homozygote methylenetetrahydrofolate reductase [MTHFR 677] mutation [OR 3.36; 95% CI 1.0–14.3] in stepwise logistic regression. Univariate analysis revealed that lower mean protein C [ $p = 0.041$ ] was present in non-responders compared to responders. No significant difference was found in the other tested factors.

**Conclusions:** Our study showed that the significant predictors for impaired response to autologous cell therapy by diabetic patients with CLI were inherited thrombotic disorders [Leiden mutation and MTHFR 677 mutation]. These results may support future research into adequate antithrombotic therapy after cell therapy and, also to enhance the screening for inherited thrombophilia.

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**Keywords:** critical limb ischemia, autologous cell therapy, diabetic foot, inherited thrombophilia

## GENERAL INTERNAL MEDICINE

### A Retrospective Study on Poisoning Deaths in District General Hospital (DGH) Ampara, Sri Lanka

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**Introduction:** Intentional self-poisoning is a major problem worldwide including Sri Lanka. Poisoning accounts for about 800 000 hospitalizations over 300 000 deaths per year. In District General Hospital (DGH) Ampara, Sri Lanka there is significant amount of admissions due to poisoning. Relatively little is known about the age and gender patterns of fatal and non-fatal self-poisoning in these regions. Assessing patient's clinical profile and management will give an insight as to how we could reduce the mortality.

**Objective:** To determine social demography, seasonal variation and area distribution of patients who died in DGH Ampara following admission due to poisoning, and to assess the type of poison, post ingestion time, presenting features and management of the poisoning deaths in District General Hospital Ampara.

**Method:** Retrospective descriptive study was done on deaths related to poisoning from January 2012 to May 2014 out of 1765 poisoning admissions in General Hospital Ampara. The data was retrieved from Bed Head Tickets and ICU records.

**Results:** Out of total poisoning admissions of 1765 only 25 has died due to poisoning. [1.4%] 56% of deaths were reported in 2012, 28% in 2013 and 16% in 2014. Highest number of the deaths occurred in the month of April [28%] and May [20%] of the study period. Out of 25 poisoning deaths 60% were male. Age group between 40- 49 yrs showed the highest mortality [28%] followed by the age group 30-39 yrs [24%]. Majority of patients were married [76%]. 44% were from Damana Medical Officer of Health area. 48% of the patients were direct admissions and 52% were transferred, in which the majority was from District Hospital Damana.

Pesticide poisoning was the commonest 92%, which comprised of only males. Organophosphate accounted for 36% of all deaths. All deaths were suicidal. 56% presented within 6 hours of ingestion of poison. 100% had features of toxicity. 44% had chronic illnesses and 36% had psychosocial problems. 24% were alcoholic. All of them who have died consumed alcohol at the time of presentation to the hospital.

52% of patients had GCS >12 on admission. 60% had Gastric lavage. Antidote was given for 52%. 32% of patients were intubated on admission. 44% of the patients were directly transferred to ICU. 52% patients stayed 14days. 76% of patients died at ICU and 24% at ward.

**Conclusion:** Deaths due to poisoning is common in forties and in males. Most of them were married. Occurrence of poisoning was more common during the second quarter of the year. Mortality due to poisoning was less. Organophosphate was the commonest culprit. All had features of toxicity though they presented within six hours of ingestion. Majority needed ICU care. Alcohol possibly played a role in increasing the deaths.

**Keywords:** intentional self-poisoning, Rural Srilanka, organophosphates, social demography, pesticide poisoning deaths

## A Review of Fixed Drug Eruption due to Fluconazole

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**Importance:** Fixed drug eruptions (FDE) are acute and localized cutaneous reactions that occur after exposure to a drug. The skin findings can resemble erythema multiforme or herpes simplex and therefore awareness of FDEs is key to avoiding misdiagnosis. Fluconazole is a widely prescribed systemic antifungal medication that has recently been shown to cause a FDE. Given that patients often only use this medication episodically when symptoms of candidiasis emerge, fluconazole can be missed in a drug history. FDE related to fluconazole should be considered in the differential diagnosis when a patient presents with an erythematous patch or plaque that recurs in the exact same location on the body.

**Objective:** To summarize, appraise and update the available evidence assessing fluconazole-induced FDEs.

**Data sources:** A literature search was conducted based on MEDLINE (1946–2016), EMBASE (1980–2016), Google Scholar and PubMed for publications that described the results of FDEs due to fluconazole. Further studies were identified from bibliographies of all relevant studies.

**Study selection:** All studies investigating fluconazole-induced FDE were included.

**Data extraction:** One reviewer independently appraised the selected studies and extracted data including demographics, diagnosis, anatomical location, drug rash characteristics, time to onset, biopsy histopathology, comorbidities and outcomes.

**Findings:** Of the 33 patients identified from the 33 case report studies, 27 were female (84% of patients). The medication was indicated for the following diagnoses: vaginal candidiasis (68% of patients), tinea cruris (10% patients), oral candidiasis (10% of patients) and other (12% of patients). The fluconazole-induced FDE appeared on these anatomical locations, in descending order of frequency: legs, lips, face, hands, arms, trunk, genitalia, feet, intra-oral. All 18 studies that re-challenged the patient with fluconazole resulted in a positive finding.

**Conclusion:** Fluconazole-induced FDEs should be considered in the differential diagnosis when a patient presents with an erythematous patch or plaque that recurs in the exact same location on the body.

## Cardiac complications in patients who underwent radical cystectomy

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**Background:** Radical cystectomy is a high-risk surgical procedure. The perioperative risk assessment is taking the special relevance in multi-disciplinary clinics.

**Objective:** The aim of the study is to estimate the frequency of occurrence and the structure of the cardiac complications in patients, who received radical cystectomy in our hospital.

**Materials and methods:** We performed retrospective observational research, conducted medical documents of 44 patients [13 women and 31 men] with the mean age  $66.8 \pm 9.8$  years, who underwent radical cystectomy in one hospital from 2014 to 2015 years. Every patient was evaluated using Lee Index, Gupta perioperative Cardiac Risk. We recorded comorbidities, such as: arterial hypertension, coronary artery disease [CAD], chronic heart failure [CHF], chronic kidney disease [CKD] C4-C5, diabetes mellitus on insulin, cerebrovascular disease. Also the perioperation diagnostic and treatment were analyzed. Statistical analysis was performed using BioStat 2008. P-range of 0.05 and lower was defined as significant.

**Results:** Most of patients were in an intermediate [70%] and in a high risk [22.7%] groups according to the Lee Index. A total of 33 [75%] patients occurred to perform different cardiac complications. In the structure of the cardiac complications dominated the heart ischemia – 48.5%. Heart arrhythmias were found in 24.3% of patients with complications. 4 patients [9%] died in early postoperative period: in 2 cases the cause of death was myocardial infarction, 1 patient died after the stroke and 1 suffered from acute heart failure. Total mortality was the same in both groups: 31.8% in group of patients with cardiac complications and 36.4% in no cardiac complications group. Although we found that, the causes of death were different in two groups. 30-days mortality was significantly lower in no cardiac complications group. Progression of bladder cancer was the main cause of death in no cardiac complications group. In group of patients with complications 42.8% of cases the cause of death was myocardial infarction and acute heart failure, in 14.2% was pulmonary embolism, in 7.1% was stroke and in 28.5% of cases cancer progression led to death. Among the risk factors we mentioned an intraoperative blood loss higher than 500 ml and creatinine level higher than 133 mmol/l. Cardiac complications was significantly more frequent among patients with two and more associated diseases.

**Conclusion:** Cardiac complications in patients who underwent radical cystectomy are very frequent and life-threatening. Improving perioperative management of patients, who undergo high-risk operations, we can reduce cardiac complications level and try to decrease total mortality range.

**Keywords:** perioperative risk assessment, perioperative management, cardiac complications

## Changes in the levels of cytokines in course of autoimmune hepatitis

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Cytokines [CK] play important role in controlling the degree of inflammation and fibrosis of the liver tissue. CK are biologically active mediators that regulate cell-cell interactions and are directly involved in the development of the immune response, which form the reaction of damage, inflammation and subsequent liver regeneration.

**Objective:** to assess the level of CK [IL-2, IL-4, IL-6, IL-8, IL-10, IFN- $\gamma$ , TNF- $\alpha$ ] in patients with autoimmune hepatitis [AIH].

**Materials and methods:** we prospectively included 53 people into the study – 32 patients with AIH and 21 – group of healthy controls. The diagnosis of AIH was established according to the recommendations of the IAHG. Average age of AIH patients was 42.4 $\pm$ 15.2 years, in the control group – 47.8 $\pm$ 10.6 years. Patients were divided into hepatitis (10 patients) and liver cirrhosis [LC] (22 patients). Levels of CKs were evaluated using a set of 8-plex company BioRad.

**Results:** in patients with AIH was an increase in the levels of CK – IL-4 [0,17 [0,13; 0,2]], IL-6 [1,13 [0,5; 2,6]] ( $p < 0.001$ ), IL-8 [1,5 [0,9; 2,4]] ( $p < 0.001$ ), IL-10 [0,6 [0,4; 2,7]] ( $p < 0.005$ ), and TNF- $\alpha$  [2,4 [1,65; 5,4]] ( $p < 0.001$ ) compared with control group, IL-4 [0,17 [0,15; 0,23]], IL-6 [0,4 [0,31; 0,51]], IL-8 [0,53 [0,44; 0,67]], IL-10 [0,42 [0,25; 0,98]], TNF- $\alpha$  [1,65 [1,33; 1,95]]. From IL-4 tended to increase compared with the control group. IL-2 [2,32 [1,65; 2,8]] (R 0,08) and IFN- $\gamma$  [4,6 [2,87; 17,8]] ( $p$  0,09) was in the normal range. We evaluated CK levels in hepatitis and LC staged: in hepatitis were revealed statistically significant increase in the level of IL-6 [1,18 [0,18; 0,25]] ( $p < 0.001$ ), IL-8 [1,8 [0,9; 4,02]] ( $p < 0.001$ ) compared with the control group. IL-4 [0,18 [1,8; 0,25]], IL-10 [1 [0,43; 2,7]], IFN- $\gamma$  [8,6 [3,7; 20,09]], TNF- $\alpha$  [1,6 [1,65; 2,2]] tended to be increased. In patients with LC, there was a statistically significant increase in the level of IL-6 [1,13 [0,5; 1,9]] ( $p < 0.001$ ), IL-8 [1,3 [0,9; 2]] ( $p < 0.001$ ) and TNF- $\alpha$  [3,15 [1,65; 7,4]] ( $p < 0.005$ ) compared with the control group. IL-10 [0,6 [0,43; 2,6]] and IFN- $\gamma$  [3,6 [2,5; 9,8]] tended to be increased.

**Conclusions:** patients with AIH had higher levels of CK than patients with end stage liver disease -cirrhosis.

**Keywords:** Cytokines, autoimmune hepatitis, liver cirrhosis

## Co-existent Miliary Tuberculosis and Non-Hodgkin's Lymphoma – A Case Report

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Miliary tuberculosis (TB) is often a diagnostically complex condition, both due to its non-specific presentation and its tendency to be mimicked by other clinical conditions with pulmonary involvement. Lymphoma is one such condition which may be difficult to differentiate from miliary TB due to similar presentations. Here, we discuss a case of miliary TB in the presence of newly diagnosed non-Hodgkin's lymphoma – a dual diagnosis, which has been rarely reported to date. This association raises the possibility of reactivated latent TB secondary to lymphoma-mediated immunosuppression.

We report the case of an 81-year-old gentleman presenting in acute type 1 respiratory failure with a short history of dry cough, progressive breathlessness and unintentional weight loss. He had been previously fit and well, besides from a history of treated TB at age 18. Chest imaging demonstrated numerous bilateral lung nodules, apical scarring and widespread thoracic lymphadenopathy initially suggestive of miliary tuberculosis secondary to reactivation. In view of previous TB history and positive sputum sample for Acid Fast Bacilli (AFB), empirical Anti-Tuberculous Therapy (ATT) was commenced – tuberculosis was later confirmed on AFB culture.

The decision to further investigate the widespread lymphadenopathy led to an abdomino-pelvic CT. Imaging revealed lymphadenopathy intra-abdominally as well as in the thoracic cavity, thus raising the possibility of an underlying, co-existent diagnosis of lymphoma. A new diagnosis of low-grade marginal zone lymphoma was subsequently confirmed on bone trephine.

This is a medically complex case of miliary TB, with underlying low-grade non-Hodgkin's lymphoma as a potential cause for latent TB reactivation many decades after initial treatment. Initially it posed the diagnostic challenge of differentiating miliary TB and lymphoma as a primary diagnosis due to their similarity in clinical presentation, prior to the realisation of a dual diagnosis. As such, this case illustrates that there may not be one single unifying diagnosis in each patient – it may be important, as in this case, to delve deeper and investigate for multiple diagnoses that may create the same presentation. This is particularly crucial in cases involving latent TB reactivation, highlighting the importance of investigating for potential underlying immunosuppressive causes leading to reactivation, particularly in the elderly population. An understanding of the need for thorough investigation in these patients may improve chances of successful treatment.

## Have electronic drug charts made prescribing intravenous fluids more dangerous? A quality improvement project improving the safety of intravenous prescription and administration using an electronic system

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**Background:** Experience as FY1s on the ward led us to believe there was a problem with IV fluid prescribing and administration, exacerbated by the hospital's computer system: CERNER. Multiple IV fluid prescriptions can be active simultaneously, which can make it confusing for both prescriber and administrator. This contributes to fluids being delayed, omitted, or the wrong type of fluid given.

**Aim:** We sought to obtain objective evidence of observed delays in IV fluid administration from the time of prescribing. Once the problem was confirmed, we assessed the cause and whether CERNER plays any part in it.

**Method:** Data collection was carried out over seven days from two wards: one surgical, one medical. All patients (n=44) who were prescribed IV fluids (116 prescriptions) were included. We identified if prescribed IV fluids were given, and when. Questionnaires were given to ward staff to further assess perceived reasons for any time delays (n=18).

**Results:** Quantitative data demonstrated a significant time delay between the time a bag of IV fluid was prescribed for and when it was actually given. 77% of IV fluid bags were given more than one hour after they were prescribed to be, with a >8-hour time delay in 38% of those bags. Reasons identified for this delay included 'unknown' (45%) and 'multiple bags prescribed' (34%). The most common complaint from questionnaire respondents was difficulty interpreting fluid prescriptions on CERNER (54%).

**Implementing the change:** Given our qualitative results, we discussed implementing a CERNER change with the CERNER consultant and pharmacist. We were made aware that a manual way exists to ensure fluid prescriptions automatically expire after a period of time. Thus over a two-week period we encouraged the doctors on both wards to set all fluids to expire within 48hrs of time prescribed to be given.

**Methods:** The CERNER pharmacist collects weekly data on all hospital prescriptions, including those not given. Data was collected daily over our two-week period, and used to compare fluid prescriptions that were not administered on our wards compared to the rest of the hospital.

**Results:** Across the whole hospital, the number of fluid prescriptions not administered increased by 3%. Contrastingly, the percentage of fluid prescriptions not given on our two wards decreased compared to the rest of the hospital.

There was also a noticeable decrease in the number of fluid prescriptions not administered when doctors were being more compliant with entering an expiry time of 48 hours.

**Conclusion:** Given our manual intervention demonstrated an improvement in the number of fluid prescriptions administered, we believe that an automatic expiry date on all fluid prescriptions of 48 hours would improve patient care and safety. Continuing with the manual expiry entry would be a feasible option, however this is difficult to ensure without regular encouragement. We will attend further CERNER meetings to put forward our proposal to implement this change in time for the CERNER update in November 2016.

## Pericardial Effusion: A Cause Beyond the Obvious

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**Introduction:** Pericardial effusion is one of the main manifestations of pericardial disease. The main etiologies are infectious, neoplastic and autoimmune, with the possibility of idiopathic effusion. The miliary pulmonary pattern is observed especially in the context of infections and cancers with haematogenous spread.

**Clinical case:** Male, 27 years old, with no relevant clinical personal background and no smoking history. Recent close contact with a patient with active pulmonary tuberculosis. Admitted to the Internal Medicine Service by clinical with about 20 days of evolution of coughing, hemoptysis sputum, dyspnea on moderate exertion and night sweats. Objectified only a feverish peak. Had type one respiratory failure, and analytically normocytic normochromic anaemia and slight elevation of inflammatory parameters. In imaging showed pulmonary infiltrates in miliary pattern, pericardial thickening and high volume pericardial effusion. Transthoracic echocardiography without echocardiographic signs of tamponade. It was held diagnostic and therapeutic thoracentesis, with drainage of pleural fluid with exudate characteristics. There was recurrence of effusion, with the need to create pleuropericardial window. At this stage placed the hypothesis of miliary tuberculosis with pericardial involvement. Performed microbiological study of pericardial fluid, bronchial secretions and bronchoalveolar lavage, detection of DNA Mycobacterium Tuberculosis, IGRA test and pericardial biopsy, excluding bacillary etiology. Cytology of pericardial fluid was positive for adenocarcinoma cells. Thoracoabdominal-pelvic computed tomography showed two hypodense and hypocaptant nodularity in the right lobe of the liver. Positron emission tomography showed several uptake foci suggesting secondary involvement, with no focus to suggest primary location. Liver, pulmonary and pericardial biopsies were suggestive of lung adenocarcinoma. Genetic analysis of liver metastases was conclusive of lung adenocarcinoma, with ALK gene rearrangement in 86% of cells. It was assumed the definitive diagnosis of ALK-positive non-small cell lung cancer and the patient started treatment with Crizotinib. During hospitalization presented as complications deep vein thrombosis and pulmonary thromboembolism.

**Conclusion:** The study conducted allowed to exclude the initial suspicion of miliary tuberculosis, making neoplastic etiology most likely. The ALK rearrangement is a relatively rare event in non-small cell lung cancer. This type of lung cancer is associated with specific clinical features, including never or light smoking history, younger age and adenocarcinoma histology, and is highly sensitive to ALK tyrosine kinase inhibitors. This case demonstrates that not always the diagnosis is clear, it is a challenge to the internist, and recalls its prognostic and therapeutic implications.

**Keywords:** Pericardial effusion, Miliary tuberculosis, ALK-positive non-small cell lung cancer, Crizotinib

## Psoriasis – unwanted consequence of anti TNF alpha therapy

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Anti TNF $\alpha$  inhibitors, including etanercept, are widely used in therapy of different diseases. They are used as monotherapy or in combination with other medicines which are used in treatment of rheumatoid arthritis, juvenile arthritis, ankylosing spondylitis, psoriatic arthritis, ulcerative colitis and other conditions. Anti TNF $\alpha$  inhibitors can cause different adverse effects, including skin changes. Paradoxically, though they are used in psoriasis treatment, they can cause psoriasis de novo or exacerbate existing one.

Our patient, M. R., 66 years old female has rheumatoid arthritis since year 2001. Her first symptoms were swelling, pain and stiffness of feet and hands junctions. During years, she was treated with all modalities of basic therapy [DMARD]. Because of high disease activity [high DAS28 values], in May 2011., we started therapy with subcutaneous etanercept 25mg twice a week, together with methotrexate 15mg once a week. After 6 week of therapy, we noted excellent therapy effect, with low DAS28 values and patients good condition, but we also found erythema with desquamation above left ankle on the front side and erythema with pustules on right sole. Dermatologist was consulted, psoriasis vulgaris and plantar pustulosis induced with etanercept were suspected. Patient started using topic therapy for psoriasis and etanercept was discontinued for 4 months. During discontinuation, skin changes had improved, but disease activity was high, so etanercept was given again. In following period, patient had low disease activity score, but skin changes were much worse, so in December 2012. etanercept was permanently discontinued and further therapy with rituximab was advised. Rituximab showed good therapy result in rheumatoid arthritis, but during next months it was noticed that skin erythema was still present with periodic desquamation.

There is no exact data about percentage of skin changes which are adverse effect of anti TNF $\alpha$ inhibitors therapy, but they are pretty frequent in every day practice. In our case, patient had psoriasis and plantar pustulosis, with hyperkeratosis. Although etanercept is used in psoriasis therapy, paradoxically, it can cause appearance of psoriasis de novo or exacerbating existing one, which is usually very resistant to concomitant therapy, so sometimes it is necessary to discontinue biologic therapy. Recent studies have shown that using concomitant therapy together with biologic, significantly improves skin changes in 66–79% of patients, but it was not case with our patient, so it was necessary to discontinue etanercept. It has also been found that after discontinuation of biologic therapy, skin changes persist in only 5% of patients and our patient was among them.

**Keywords:** rheumatoid arthritis, etanercept, psoriasis

## Rhabdomyolysis and Wernicke-Korsakoff Syndrome – a clinical case

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**Introduction:** Rhabdomyolysis is a syndrome characterized by muscle necrosis and the release of intracellular muscle constituents into the circulation. The severity of illness ranges from asymptomatic elevations in serum muscle enzymes to life-threatening disease associated with extreme enzyme elevations, electrolyte imbalances and acute kidney injury. On the other side of the case, we have Wernicke-Korsakoff syndrome that is the best known neurologic complication of thiamine [vitamin B1] deficiency.

**Clinical Case:** Male, 78 years old, admitted to hospitalization because of muscle weakness and myalgia. The patient stated asthenia and sense of generalized muscle weakness, myalgia and worsening of previous gait limitations. He was found slumped at home, unable to stand up due to loss of strength. He reported difficulty in starting urination and dysuria with a few days of evolution. Pathological history of ethanoic habits [157g/day]. On physical examination he was confused, with periods of transient agitation, dysarthria [aggravated compared to previous deficits], bilateral horizontal nystagmus, flapping and symmetrical loss of muscle strength of the lower limbs; dehydrated and digital rectal examination showed a hard prostate with nodular and heterogeneous texture and finger glove with brownish stools. Exams revealed discrete macrocytosis, AST 6NSL, ALT 2NSL, LDH 2NSL, CK 5NSL, PSA 4NSL, carboxihemoglobin 3% and combur test compatible with urinary tract infection; normal aldolasis and thyroid function, negative viral serology and microbiologic cultures. We admitted a severe rhabdomyolysis with myopathy induced by alcohol, compounded by immobilization, exposure to carbon monoxide and the urinary tract infection, in a patient with simultaneous manifestations of Wernicke-Korsakoff syndrome. We empirically started Amoxicillin and Clavulanic Acid, strengthened fluid therapy and supplementation with thiamine 100mg iv 3times a day, tiapride and B12 vitamin. During treatment, CK values showed a downward trend with practically standard values at discharge. The clinical improvement was evident and he stayed under treatment with enhanced oral rehydration and thiamine. We were yet not able to discard a concomitant prostate cancer but at the post hospitalization clinical appointment, patient was feeling better, still with some ataxy but no nystagmus and no flapping.

**Conclusion:** Rhabdomyolysis can be multifactorial; with multiple causes that need to be considered according to the history, evolution and gravity and if not properly treated can be fatal. The Wernicke-Korsakoff syndrome is a serious and potentially reversible condition that deserves attention to early identification and properly treatment.

**Keywords:** Rhabdomyolysis, Wernicke-Korsakoff syndrome

## Secondary failure of etanercept therapy in case of good drug level and anti-drug antibodies absence

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Anti TNF $\alpha$  inhibitors have brought significant success in rheumatoid arthritis therapy. However, some patients are not responding to therapy, which is known as primary failure. In other patients, after initial therapeutic success, secondary failure is following and they are not responding to the same therapy any more.

Patient P.M., born 1950. was diagnosed seropositive rheumatoid arthritis in year 2006. after suspicion on carpal tunnel syndrome and unsuccessful decompression procedure. Disease started with pain and limited movements of both wrists and MCP's on both hands. He had moderate disease activity score [DAS28 4.97]. Classic DMARD were included in therapy, resochin 250mg/d and methotrexate 12.5mg/w. Till 2010. he was treated with these medicines in combination or methotrexate alone, with very humble success, because disease activity was always in moderate activity level [DAS28 4.43. – 4.48]. Methotrexate dose never was more than 15mg/week, because high transaminase levels were detected several times after dose increase. By the end of 2010. DAS28 reached high activity level [5.52] and it was decided to switch the patient to biologic therapy – etanercept in weekly dose of 50mg together with methotrexate 12.5 mg/w. Few weeks after starting etanercept disease activity was significantly lower [2.8] and during following period it has reached remission level [2.4]. Year 2014. almost 4 years after starting etanercept, disease got worse and DAS28 was again in moderate to high activity level [4.32 – >5]. Analyses showed detectable medicine serum level [serum level ETA 1.0 mcg/ml] and drug antibodies could not be detected [pAb ETA <3.2 ng/ml equivalents]. Because patient was not responding anymore to etanercept therapy, he was switched to tocilizumab. Patient follow up since starting tocilizumab, showed good therapy effect, with low disease activity score and good patient's condition.

Our patient has experienced worsening his symptoms after almost 4 years period of good therapy response. It is estimated that up to 50% of patients with rheumatoid arthritis experience secondary failure in anti TNF $\alpha$  therapy. All known explanations are applicable in case of low drug level. Some cases are explained by individual differences in drug bioavailability and pharmacokinetics, which may lead to low blood drug level. Also, increased clearance of drug may be the reason. The most often reason of low drug level are drug antibodies in serum due to immunogenicity. It is proven that subcutaneous administration of drugs is more immunogenic and there are frequent cases of antibody presence. But, in case of our patient antibodies were not present and drug level was normal. What are the reasons for such change in responsiveness still needs to be discovered. Did immunological profile of disease changed? Are there some other kinds of antibodies that are eliminating therapy effects, anti-idiotypic or other? Has dominant pathologic mechanism of disease changed? If yes, was it spontaneously or induced by therapy? Or change of responsiveness can be some kind of escape phenomenon? In cases of good drug level and absence of anti-drug antibodies, it is recommended to switch to another group of biologic therapy, like tocilizumab in our case, IL-6 inhibitor.

**Keywords:** etanercept, anti-drug antibodies, drug level, secondary failure, rheumatoid arthritis

## Spontaneous coronary artery dissection

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Spontaneous coronary artery dissection (SCAD) is a rare emergency condition associated with high mortality. SCAD can slow or block blood flow in a coronary artery, causing a heart attack, heart rhythm abnormalities and sudden death. It frequently affects young females ages 30–50. Current knowledge of SCAD is limited and the proposed mechanisms are coronary arteritis, connective tissue defect and underlying atherosclerosis. Other risk factors include physical exertion, cocaine abuse and pregnancy. Angiography is the gold standard diagnostic test. Treatment options include conservative approach, percutaneous coronary artery intervention (PCI) or cardiac surgery. We describe a case of 33-years old woman with SCAD.

### Case report

A 33-years old woman was admitted to our hospital with symptoms of myocardial infarction. No diseases or regular treatment were revealed in the patient's history. She has been a smoker. Family history of myocardial infarction was found. Physical examination as well as chest X-ray was within normal limits. ST segment elevation in leads V2–V4 was documented on the electrocardiogram (ECG).

Standard treatment of acute coronary syndrome was administered. A coronary angiography was performed as a further diagnostic procedure. It confirmed a spiral dissection type C of the ramus interventricularis anterior (RIA) extending from the ostium to the middle part of the artery. Distal and apical part of RIA were with no signs of dissection.

Lesion was unsuitable for percutaneous coronary artery intervention (PCI). Patient suffered with no symptoms of myocardial ischemia after nitrate therapy administration. Also ECG finding normalized, therefore conservative treatment approach was selected. Patient could have been discharged from hospital one week later. Coronary angiography was performed six weeks later. It confirmed persistence of RIA dissection and also coronary artery dextra dissection. An attempt to solve the lesions was not successful. Moreover, iatrogenic dissection of coronary artery sinistra and ramus circumflexus was caused. Patient underwent urgent coronary artery bypass. Left ventricular systolic dysfunction was proved by echocardiography. Ejection fraction was established on 35–40%. Patient could have been discharged later.

Patient must have been admitted for recurrence of chest pain few weeks later. Coronary artery bypass on ramus interventricularis posterior was proved to be closed by computed tomography angiography. There was high risk of iatrogenic dissection, therefore conservative approach was selected. Histological testing of coronary artery revealed no abnormalities. Rheumatic diseases screening proved only elevated level of antinucleosome antibodies. Importance of this finding remains unclear and patient will be examined by rheumatologist. Results will be mentioned in final text.

**Keywords:** coronary artery dissection

## Tuberculosis during infliximab therapy – latent infection activation or unwanted therapy consequence?

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Before initiating biologic therapy in patient, it is necessary, among other, to exclude existence of latent and chronic infections. In order to exclude latent tuberculosis, tuberculin skin test (TST) is still in wide usage. Also, tuberculosis is one of unwanted consequences of some biologic agents, such as infliximab, as noted in user’s manual and literature.

Our patient, B.M. born 1949. suffered rheumatoid arthritis for many years. Year 2013. she was on methotrexate therapy, 20–25mg/week, when high activity score was noted [DAS28 7.08]. She presented with pain and tender small hand joints, synovitis of right wrist and MCP joints. It was decided to start infliximab therapy, so patient went through necessary checkups. Physical examination, laboratory analyses, lung rtg and anti-viral tests [HBV, HCV] were normal and TST was < 5mm. She started infliximab in dose of 600mg as recommended [0, 2, 4 and 8<sup>th</sup> week i.v.] in June 2013. In next 3 visits, DAS28 was decreasing [7.08...6.1...3.82] and the patient felt better. In August 2013. about 4 weeks after last therapy, she reported subfebrile temperature 37.8C, enlarged lymph nodes on neck, armpits and both inguinal regions. Rheumatologic status was in normal range, except right wrist tenderness. Laboratory analyses showed increased sedimentation rate [76], CRP was 57, blood count in normal range. Immunoglobulins, tumor markers and virology analyses were in normal range. Blood culture samples were taken. Ultrasound showed cervical, axillar and inguinal lymphadenopathy, nodes were up to 35mm. Chest CT scan detected lymphadenopathy in supraclavicular, pretracheal, subcarinal, prevascular and preaortic region, which were partially organized in conglomerates. Abdominal CT scan showed slightly enlarged liver. Hematologist examined bone marrow and found granulocyte hyperplasia. Extirpation of supraclavicular node was done and pathohistological diagnosis was lymph nodes tuberculosis. Patient started anti-tuberculosis therapy and after six months of treatment, she showed significant improvement. After one year, she suffered generalized lymphadenopathy without fever. Biopsy showed nonspecific lymphadenitis. She was under regular rheumatology control, with satisfying DAS level, without active synovitis, on methotrexate therapy.

In this case, patient was examined for all recommended chronic infections, including tuberculosis, before introducing biologic therapy. She excluded all risk factors for any of chronic infections. TST result was < 5mm, which excluded latent tuberculosis. After 3<sup>rd</sup> round of infliximab, patient showed up with advanced signs of infection. It is questionable how valuable is TST in patients on immunosuppressants for a long time and also are suffering disease which is causing immunologic impairment. Some authors are advising repetition of TST 1–3 weeks in patients with risk factors. Also, it is recommended to repeat TST every 6 months in patients receiving biologic therapy. Due to nature of the test and disease immunopathology, it is more secure to use some other tests before introducing biologic therapy, such as QuantiFERON and IGRA test. Recent studies have shown cost-effectiveness of QuantiFERON testing over TST. However, tuberculosis is mentioned as unwanted consequence of biologic agents, so we cannot definitely distinct if our TST testing was right or wrong and if tuberculosis was latent or acute.

**Keywords:** infliximab, tuberculosis, tuberculin skin test, rheumatoid arthritis

## Unrecognized and untreated chronic hypoxia – case report

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In this paper, we will present unrecognized and untreated case of chronic hypoxia, which led to development of chronic respiratory failure with severe symptoms and physical signs, together with expansive radiographic lung changes.

In April year 2013. on Pulmonology department of Clinical center of Montenegro, a patient with clinical presentation of partial respiratory failure was admitted. He was 72 years old at the time of admission and he presented with severe dyspnea, instability, low effort tolerance, heart palpitations. He explained that he is being treated for respiratory failure in last 3 years with inhalation bronchodilators, theophylline and LTOT 16h/d. Also, he said that he is diabetic type 2 for 12 years, on insulin for 8 last years. In socio epidemiological anamnesis we noted that he worked for 40 years on metal lathe machine and that he is allergic to penicillin. He smoked up to 10 cigarettes/d, for more than 20 years. He said that he had regular medical checkups during working years and that he was regular on GP and endocrinology controls periodically and that he noticed changes on his fingers about 20 years ago. Family history didn't discover any significant diseases.

Physical examination discovered periphery cyanosis – cyanotic nose peak, ears, lips, finger tips, which were severely changed into drumstick fingers. Auscultation of lungs, found on both sides diffuse late expiratory crackles, rhythmic, tachycardic heart action, without pathological sounds. Detailed laboratory analyses showed hypoxia [Sat.O<sub>2</sub> -87.7] polycythemia, respiratory alkalosis, partial respiratory failure. Cardiology checkups showed signs of pulmonary hypertension, right ventricular overload, RSVP +90, EF 50%, IRBBB. Recent CT images showed severe pulmonary fibrosis and bullous emphysema. New lung RTG didn't show acute changes, although parameters of inflammation were elevated. Spirometry wasn't performed, because of the patient's condition.

During hospitalization, patient was treated with antibiotic, oxygen therapy, inhalation bronchodilators, inhalation and i.v. corticosteroids, inhalation cholinergic, theophylline, calcium channels blocker, cardiotonics and other symptomatic therapy. His condition approved, oxygen saturation raised up to 92 %, he felt better.

Other modalities of therapy were not taken in consideration, because biopsy and pathohistological verification were never performed, so we did not know the real diagnosis in this case. Also, patient's condition did not allow biopsy and lung changes were terminal, so it is questionable if any therapy would be successful. Empirically, we can assume it was fibrosis due to chronic metal exposure. This case is not interesting in therapeutical sense, but maybe more in ethical, because patient's chronic hypoxia rested unrecognized for decades, although he was under regular medical care. Physical and radiographic changes are documented by images, that are showing a case which can't be seen often in nowadays ambulances. What is even more interesting, he lived and worked for 35 years in Sweden, which has one of the most developed medical systems in the world.

**Keywords:** hypoxia, chronic, respiratory, failure

# HEART FAILURE

## Psychoemotional changes at chronic heart failure

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**Objective:** to establish the presence and severity of anxiety and depressive stress and assess the impact it produces on the life quality of patients with chronic heart failure [CHF].

**Materials and methods:** A total of 130 patients with NYHA FC II and III CHF secondary to post-infarction atherosclerosis, mean-age  $60.66 \pm 0.64$  yrs. The age of infarction was  $4.09 \pm 0.29$  yrs, left ventricular ejection fraction was  $50.1 \pm 3.78\%$ . The signs of FC II CHF was registered in 58.5% subjects, and FC III was noted in 41.5% subjects. All individuals received common clinical examination. Medical treatment was represented by standard therapy. The assessment of the presence/absence of anxiety and depressive stress was performed using Hospital Anxiety and Depression Scale [HADS], and life quality [LQ] was evaluated using Minnesota questionnaire [MLHFQ].

**Results:** According to HADS, anxiety and depressive stress was present in 46.9% subjects. The signs of depression alone was seen in 22.3% cases, anxiety alone in 24.6% cases. LQ in patients with co-disorders was 1.5 times worse compared to patients with normal psychoemotional status. A correlation was revealed between LQ and depression severity [ $r=0.46$ ,  $p<0.001$ ], LQ and anxiety severity [ $r=0.48$ ,  $p<0.001$ ], as well as between depression and anxiety severity [ $r=0.51$ ,  $p<0.001$ ]. Additionally, 10.8% of patients suffer from both depression and anxiety, and LQ of this group was 1.6 worse as compared to subjects with no depression and anxiety.

In patients with FC II CHF anxiety and depressive stress was established in 30.3% subjects, 9.2% patients experience both depression and anxiety; the signs of isolated depression and anxiety were noted in 4% & 26.3% cases, correspondingly. As for this group, a correlation between LQ and depression severity and anxiety was mild. A for FC III CHF, anxiety and depressive stress was noted in 70.4% subjects, and the signs of isolated depression and anxiety were established in 48.2% & 22.2% cases, correspondingly. This group showed a correlation between LQ and depression severity [ $r=0.49$ ,  $p<0.001$ ], LQ and anxiety severity [ $r=0.57$ ,  $p<0.001$ ]. The severity of anxiety and depression in patients with FC III CHF exceeds HADS normal values by 1.4 & 1.7 times, correspondingly. In 11.1% subjects, signs of both anxiety and depression were revealed, and LQ here is worse compared to those who had isolated anxiety or depression [ $p<0.01$ ].

**Conclusion:** In conclusion, our study showed the rate of anxiety and depression stress detection in patients with CHF that is 46.9%. The life quality of patients with post-infarction atherosclerosis complicated by CHF becomes significantly worse in the presence of anxiety and/or depression, and this worsening is more evident in the combination of anxiety and depression. Deterioration of FC of HF is associated with the increased number of patients with anxiety and depression disorders; depressive stress prevails in FC III CHF where as anxiety does so in FC II CHF.

**Keywords:** chronic heart failure, anxiety, depression, life quality

## The study of neurohumoral factors in patients with chronic heart failure

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**Objective:** The study of neurohumoral factors in patients with chronic heart failure (CHF).

**Methods:** Examined 92 patients with CHF. Determining the level of brain natriuretic peptide (BNP) and aldosterone was performed on ELISA immunoassay analyzer using reagents of company «Biomedica».

**Results:** Analysis of the study results showed that patients with CHF, activation of the neurohumoral factors were marked which characterized by increasing concentrations of BNP and aldosterone in all examined patients. Established that in CHF levels of BNP and aldosterone were significantly increased and these changes correlate with disease progression. Patients with FC II had increased amount of BNP by 181.8% [ $p < 0,001$ ], and patients with FC III by 319.5% [ $p < 0,001$ ] compared with the control group. Accordingly, BNP level was 2.8-fold in FC II and 4.1-folds higher in FC III, compared with the values of the control group. There was also a significant increase of aldosterone in both groups of patients: in patients with FC II, level of aldosterone increased by 36.8% [ $p < 0,001$ ] compared with the control group. In patients with FC III it was 66.4% [ $p < 0,001$ ]. Aldosterone levels increased by 1,3-fold in FC II and 1.6-fold in FC III. There was a direct correlation between BNP and AL in patients with FC II, which made up  $r = +0,91$ , and FC III  $r = +0,98$ , in both cases,  $P < 0,001$ . Fluctuations of BNP in patients with FC II ranged from 430.5 to 912.6 fmol/ml, and in patients with FC III from 675.5 to 1423.1 fmol/ml. Similar changes were observed while analyzing aldosterone level. Fluctuations of aldosterone in FC II were from 180.2 to 361.1 pg/ml, in FC III from 219.1 to 435.7 pg/ml. In consideration of the changes of these indices, we study the distribution of the examined patients on basis of the content of the investigated hormone levels within the lower values of the median [mid-high level] and high values of the median [high level]. Analysis of the study results showed that mid-high increase in BNP was noted in 54.3% of examined patients, aldosterone in 62.8% of patients. High level of BNP, i.e. values above the median, was observed in 45.7% and aldosterone – in 37,2% of patients with FC II CHF. Studying the distribution of patients by the level of increase in neurohumoral factors in patients with CHF FC III showed that this group had high levels of BNP increase – 57.6% and aldosterone – 63.6% of the patients with III FC.

**Conclusions:** As is obvious from the data of patients with FC II dominated mid-high levels of neurohumoral factors, whereas in patients with FC III noted the predominance of high levels of BNP and aldosterone.

**Keywords:** chronic heart failure, brain natriuretic peptide, aldosterone

## HYPERLIPIDEMIA AND DYSLIPIDEMIA

### Associations between equivalent radiation dose and blood lipids

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Many studies have explored associations between radiation exposure and cancer among atomic bomb survivors in Japan, Chernobyl rescue workers, workers of nuclear industry in Germany and in a historical cohort of people who were exposed to the radiation from the Semipalatinsk nuclear weapons test site in Kazakhstan. Non-cancer consequences of radiation exposure have been less studied.

**Objective** is study assessed associations between equivalent radiation dose and blood lipids among population of East Kazakhstan and Pavlodar regions who permanently live in close proximity to Semipalatinsk nuclear weapons test site.

**Methods:** in this population-based cross-sectional study (n=1755) we studied total cholesterol, low- and high density lipoproteins as dependent variables across quartiles of the equivalent radiation dose using multiple linear regression with adjustment for gender, smoking, alcohol consumption, body mass index and region of residence.

**Results:** Individuals with a higher dose of radiation were significantly older ( $p < 0,001$ ), and had a higher body mass index ( $p < 0,001$ ). Statistically significant differences in the prevalence of smoking and drinking on the effective equivalent dose is not found.

Bivariate analysis of the average values of the dependent variables using analysis of variance revealed a pronounced directly proportional relationship between the dose of ionizing radiation, and total cholesterol ( $p < 0,001$ ), and low-density lipoproteins ( $p < 0,002$ ), while the relationship between the effective equivalent dose and lipoproteins high density not revealed ( $p < 0,154$ ).

After correcting for factors konfaunder received higher doses of ionizing radiation, had higher mean values of both total cholesterol and LDL cholesterol independently of region of residence, gender, body mass index, smoking and alcohol consumption. No statistically significant relationships between the effective equivalent doses and HDL cholesterol have been identified.

We observed significant positive association between equivalent dose and total cholesterol and low density lipoproteins, but not high density lipoproteins. Our results contribute to the understanding of the mechanisms between low dose radiation exposure and cardiovascular diseases.

**Keywords:** cardiovascular diseases, radiation exposure, the Semipalatinsk nuclear weapons test site, ionizing radiation, cholesterol

## Generalized Lipodystrophy as a Rare Cause of Heart Failure

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Lipodystrophy syndromes comprise a group of rare, heterogeneous disorders characterized by progressive loss of fat tissue. The disorder, which has been reported in just 300 to 500 people worldwide, can be inherited or acquired and is characterized by near complete absence of fat tissue from birth or disappearance of fat during childhood. Patients with lipodystrophy are deficient in the hormone leptin, that is made by fat cells and regulates energy intake and expenditure.

We present the case of a 25 years old female patient admitted at the Cardiology Department on September 2014 due to worsening heart failure NYHA class IV. At eight y.o she was first diagnosed with hypertriglyceridemia (Triglycerides > 1000 mg/dl) and at eleven y.o she started showing first signs of lipodystrophy. Only at 19 y.o the diagnose of generalized lipodystrophy due to leptin deficiency was made and at the time she had already developed diabetes mellitus type 2 and severe dyslipidemia (TG > 2300 mg/dl) both refractory to treatment with insulin and statins. In 2011 the patient began treatment with analogue recombinant leptin replacement therapy (42 IU daily sc) started at the National Institutes of Health (NIH) USA as an experimental drug. At the time she had in concomitance: Diabetes type 2, Hyperandrogenism, Polycystic Ovary Syndrome, Osteoporosis, Liver steatosis and Heart failure. After beginning the treatment the lipid and glycemic profile slowly turned to normal.

At admission in our clinic the patient was cachectic (BMI 15 kg/m<sup>2</sup>) with fat tissue absent in her body. She had irregular heartbeats, holosystolic murmur at the apex radiating at the back, S3 gallop sound, BP 80/60 mmHg, diminished sounds in both lung bases, abdominal fullness due to ascites and lower limbs and perineal edema. The most pertinent significant finding was the patient's cardiac function. The echocardiography showed dilation, diffuse hypokinesia of the left ventricle and a severely decreased left ventricular systolic function (EF ~30%), with a moderate to severe mitral regurgitation, mild enlargement of the right chambers, right ventricle systolic dysfunction, moderate tricuspid regurgitation with pulmonary hypertension (PAP of 48 mmHg). High dose i/v diuretics, inotropic drugs, digoxin 0.125 mg/daily and rivaroxaban for newly installed atrial fibrillation were started. Her therapy also included atorvastatin 20 mg/d, fenofibrate 150 mg/d, aspirin 100 mg/d, metoprolol 25 mg/d, metformin 1000 mg/d, omega 3, leptin 42 UI/d and calcium carbonate. She was discharged in a stable condition. However the prognosis remained poor despite supportive treatment. On December 2015 the patient died due to a severe respiratory infection.

Lipodystrophy syndromes are characterized by progressive loss of fat tissue, mainly from subcutaneous compartment and occasionally affecting visceral fat. Mechanisms for adipocyte deficiency include: defects in adipogenesis pathway, increased destruction of adipocytes. This may result in: Inability to store triglycerides, leading to abnormal deposition in other tissues (liver, heart, skeletal muscle and pancreas), absent or immature adipocytes leading to inability to synthesize and release adipocytokines (leptin, adiponectin).

Lipotoxic mechanisms are possibly the cause of impaired cardiac efficiency and lipoapoptosis. Generalized congenital lipodystrophy and heart involvement is extremely rare.

**Keywords:** hypertriglyceridemia, lipodystrophy, leptin, heart failure

## The analysis of HDL-cholesterol quantity among middle aged Lithuanian adults

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**Aim of the study** was to compare HDL-C values among different groups of middle aged Lithuanian adults participating in Lithuanian High Cardiovascular Risk [LitHiR] primary prevention programme from 2009 to 2015 as the programme has showed that dyslipidemia is common risk factor among middle aged Lithuanians [89,7%] although many individuals have elevated HDL-C levels.

**Materials and methods:** During 2009–2015 period a total of 83.376 people were examined. Data of 63.573 patients with dyslipidemia; data of 11.265 patients with severe dyslipidemia [LDL-C >6 mmol/l, or total cholesterol >7.5 mmol/l, or triglycerides >4.5mmol/l], and data of 8538 patients without dyslipidemia were used for statistical analysis.

**Results:** HDL-C was within the normal range for 42.66% of population. The prevalence of very high HDL-C values [ $\geq 1.55$ mmol/l] was 43,74% while HDL-C was lower than the normal value [male <1.0mmol/l, female <1.2mmol/l] for 13.61% of the examined. In very high HDL-C group mean value was 1.94 mmol/l  $\pm$  0.37 comparing with normal HDL-C group with 1.31 mmol/l  $\pm$  0.14, p

**Conclusions:** Elevated HDL-C levels are common among the participants of LitHiR primary prevention programme. The highest concentration of HDL-C was noticed among severe dyslipidemia group. That might suggest that antiatherogenic qualities of HDL should be measured by quality of the particle and further studies are needed.

**Keywords:** HDL- cholesterol, prevention programme, dyslipidemia

## The dynamics of serum lipid profile among middle aged Lithuanian adults with dyslipidemia from 2009 to 2015

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**Aim of the study** was to assess the dynamics of serum lipid profile among middle aged Lithuanian adults with dyslipidemia participating in Lithuanian High Cardiovascular Risk (LitHiR) primary prevention programme from 2009 to 2015.

**Materials and methods:** During 2009–2015 period a total of 83.376 people were examined. Data of 63.573 patients [59% female and 41% male] with dyslipidemia and data of 11.265 patients [67% female and 33% male] with severe dyslipidemia [LDL-C >6mmol/l, or total cholesterol >7,5mmol/l, or triglycerides >4,5mmol/l] were used for statistical analysis.

**Results:** The prevalence of dyslipidemia remains stable and high, affecting about 76.3% of middle-aged adults, while the prevalence of severe dyslipidemia increased from 12.5% to 13.2%,  $p < 0.001$ . In general, there are almost 90% of people who have dyslipidemia in LitHiR programme. Mean age of dyslipidemia group decreased from  $52.82 \pm 5.97$  to  $51.54 \pm 6.27$ ,  $p < 0.001$ . Concentrations of LDL-C increased from  $3.77 \pm 0.74$  to  $3.84 \pm 0.73$ ,  $p < 0.001$ , HDL-C – from  $1.52 \pm 0.44$  to  $1.53 \pm 0.45$ ,  $p = 0.007$  and triglycerides decreased from  $1.48 \pm 0.73$  to  $1.46 \pm 0.71$ ,  $p = 0.001$  in dyslipidemia group. Mean age of severe dyslipidemia group decreased from  $53.95 \pm 5.98$  to  $52.58 \pm 6.42$ ,  $p < 0.001$ . Concentrations of LDL-C increased from  $5.25 \pm 1.17$  to  $5.29 \pm 1.27$ ,  $p = 0.002$ , HDL-C – from  $1.56 \pm 0.52$  to  $1.61 \pm 0.55$ ,  $p = 0.011$ , triglycerides – from  $2.69 \pm 2.2$  to  $2.76 \pm 2.51$ ,  $p < 0.001$  in severe dyslipidemia group.

**Conclusions:** The prevalence of dyslipidemia is increasing and it is attributed to the growth in severe dyslipidemia frequency. The mean age of people affected in both groups is decreasing with increasing values of LDL-C and HDL-C.

**Keywords:** dyslipidemia, prevention programme, lipid profile

## HYPERTENSION

### Assessment of factors for adherence to treatment in hypertensive patients

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The present time the effective control of hypertension is an actual problem in Kazakhstan. The efficacy of treatment in the hypertensive patients depends not only on the choice of drug, dosage of medication, but also on patient compliance with medical recommendations.

**Objective:** analysis of the main factors of adherence to treatment in hypertensive patients.

**Design and method:** The cross-sectional study included 162 patients with hypertension II degree [63 men and 99 women] aged 45 to 65 years. The duration of the disease was at least 3 years; all participants have been constantly taking antihypertensive drugs for at least 1 year. The mean age was  $59.8 \pm 6.4$  years. We have calculated such rates: Importance of updating of a way of life – IUWL, Importance of medicinal therapy – IMT, Importance of medical support – IMS, and Index of Importance of treatment – IIT. Then we have analyzed rates of Adherence to updating a way of life – AUWL, Adherence to medicinal therapy – AMT, Adherence to medical support – AMS, and Index of Adherence to treatment – IAT. Based on these data we estimated the following indices of expected efficacy: Efficiency of updating of a way of life – EUWL, Efficiency of medicinal therapy – EMT, and Efficiency of medical support – EMS.

**Results:** IUWL index was  $20.1 \pm 1.4$  for males,  $18.3 \pm 1.3$  for females; IMT –  $19.2 \pm 1.6$ ;  $22.4 \pm 1.3$  respectively; IMS –  $19.3 \pm 1.9$ ;  $21.4 \pm 1.9$  respectively. Analysis of the total indexes of willingness for complex treatment revealed that AUWL index was  $20.8 \pm 1.9$  for males,  $22.1 \pm 1.6$  for females; AMT was  $16.8 \pm 2.4$ ;  $17.7 \pm 2.2$  respectively; AMS was  $20.4 \pm 2.2$  and  $21.8 \pm 2.1$  respectively. EUWL was  $2.4 \pm 0.3$  points for males,  $2.7 \pm 0.3$  for females; EMT was  $3.7 \pm 0.4$ ;  $2.6 \pm 0.4$  respectively; EMS –  $3.08 \pm 0.4$  and  $2.4 \pm 0.3$  respectively. The index of expected effectiveness of treatment for men was  $3.15 \pm 0.6$  points, for women –  $2.62 \pm 0.6$  indicating a satisfactory efficacy of medical intervention for all participants.

**Conclusions:** Factors affecting adherence to treatment are associated with the patient's attitude to the necessity of the treatment, and the quality of medical support. Women show greater willingness to comply with medical recommendations than men.

**Keywords:** the hypertensive patients, patient compliance, willingness, efficacy of treatment

## Blood pressure components and lipids: acquainted traits of cardiovascular disease development

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**Introduction:** In recent years, it has become clear that although BP is one of main risk factors for cardiovascular disease (CVD) and premature death, several studies found superiority of different hemodynamic characteristics compared with conventional BP in prediction of CVD events. The new statements target evidence with almost higher precision of craftsmanship of drawings and impose decision for each difficulty that did not previously exist in order to preclude severe complications. To meet this challenge, we initiated our research.

**Methods:** We evaluated EPOGH follow-up (n=204), assessed maximal and minimal BP, calculated primary amplitude (PrAmp, maximum minus minimum of BP), used clock-time-dependent method narrow-approach for ambulatory BP.

**Results:** While all of us believe in dominating magnificence of allegation that BP level is key determinant for CVD, actually, researchers conducted the dedicated work and discovered fortunate circumstances concerning waveform analysis. What is interesting is that it is expressed so in theory (meta-analysis) that explanation of waveform appearance remains unresolved and diverged, underlining the following reasonings: wave reflection performs at sites of impedance mismatching at arterial branches, arterial compliance is complimentary sound of hypothesis, etc. With doctrine in mind, in partial pattern with age inclusion we found association of PrAmp of systolic day BP with TC (r=0.115), TG (r=0.084), LDL-C (r=0.103), HDL-C (r=0.019); PrAmp of diastolic day BP with TC (r=0.046), TG (r=-0.013), LDL-C (r=0.019), HDL-C (r=-0.018); PrAmp of systolic night BP with TC (r=0.164, p=0.024), TG (r=0.173, p=0.017), LDL-C (r=0.198, p=0.006), HDL-C (r=-0.030); PrAmp of diastolic night BP with TC (r=0.137, p=0.058), TG (r=0.123), LDL-C (r=0.143, p=0.048), HDL-C (r=0.011). To gain better insights, office central exceeds peripheral BP, 24-h surpasses central BP (C. Huang). As we amble towards arterial wall models, perspectives of increasing significance of vascular wall composition and function are established, solace may be broken off in relationship between BP and arterial elasticity, arterial viscosity in addition to elasticity. Rest assured, there are a lot of exciting new components of hemodynamic load to look forward to – and they're just singing competitions of mechanistic properties. The appropriately quoted assets, pressure waveform consists of discrete hemodynamic parameters derived from measured central BP and flow, which is conjecturing of investing in risk of adverse outcomes. Attention has reached the point where it is a major topic of interest was incremental contributions to CVD risk of mean and various pulsatile components of BP. In particular, we were also fascinated by several kinetic characteristics of vascular realignment (Framingham Heart Study) – for instance, forward BP wave amplitude, which being effectively reduced by antihypertensive drug therapy is accompanied by restriction of CVD events as authors noted, global reflection coefficient, primary pressure wave amplitude, etc. – have been granted most for purposeful compelling evidence, according to requirements. This was widely acclaimed that hemodynamic load increases with aging.

**Conclusions:** Series of findings left us on spectacular cliffhanger – which we sure, as ever, likely reaps greatest benefit for CVD prevention – but many questions are uncovered insufficiently and awareness of hypertension-related risk of complications is promoted haywire.

**Keywords:** lipids, blood pressure components, hypertension, age

## Mortality rates by ethnicity among patients suffering from hypertension

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**Objective:** Examine the outcomes of patients who died during the lifetime of suffering from hypertension, depending on the ethnicity according postmortem study.

**Material and methods:** A retrospective study was conducted according to autopsy protocols of deceased persons during 16 years [from 1999 to 2014] who suffered during the lifetime from hypertension carried out by “Postmortem Bureau” in Semey, the Eastern Kazakhstan region of the Republic of Kazakhstan and Semey branch of the State Enterprise “Centre of Forensic Medicine of the Ministry of Health of the Republic of Kazakhstan”. The protocols were selected with an indication of the presence of hypertension during the lifetime and confirming the results of the autopsy data. The criteria for non-inclusion to the evaluation group were: presence of respiratory disease, heart disease, obesity, heart failure. Therefore, the protocols were selected for autopsy of dead who during the lifetime did not have any associated pathology, leading to heart remodeling besides hypertension. We studied the causes of death in the research sampling groups.

**Results:** While studying the data obtained on the basis of postmortem study we elaborately selected 674 patients with autopsy, suffering from hypertension during the lifetime and died suddenly. The median age was  $56.78 \pm 12.39$  years old. By gender, male and female are respectively 60.4% and 39.6%. By ethnicity the number of Kazakhs is 208 [30.9%], Russian – 437 [64.8%], and others – 29 people [4.3%]. Given the paucity of other nationalities, in the further study only Russians and Kazakhs were included.

It was revealed that the main causes of death of patients suffering from hypertension was the development of acute cardiovascular disease [60.4%], acute myocardial infarction [1.2%], acute stroke [37.2%], and other causes of cardiovascular origins [1.2%]. All these causes of death were categorized into two groups, depending on the organ damage: Group 1 was accompanied by heart damage [the development of cardiovascular disease, acute myocardial infarction], and Group 2 – brain damage [acute cerebrovascular accident]. It was found that among the Russian group the causes of death by heart and brain damage determined at 299 and 134 people respectively, among Kazakhs – 99 and 106 respectively. Among the Russians, heart disease was observed in 69% of cases, while among Kazakhs – only 48% of cases. The odds ratio of the outcome of heart disease compared with brain damage in 2.39 times higher [95% CI: 1.70, and 3.36] among Russians compared with the Kazakhs. Pearson’s chi-square is 25.55,  $df = 1$ ,  $p < 0.0001$ .

**Conclusion:** Among the main reasons for the outcomes of death patients suffering from hypertension during their lifetime development of acute heart failure. Identified ethnic differences in outcomes of death indicate that the probability among the Russian population for the outcome of primarily heart damage is 2.38 times higher compared to the Kazakh population, were brain damage is dominated.

**Keywords:** cardiovascular disease, hypertension, pathoanatomical research, ethnicity, mortality

## INTENSIVE CARE

### Ethical aspects of enrolling cardiac arrest victims into a research project

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**Introduction:** Enrollment of patients who are being actively resuscitated to a clinical study is an ethically challenging issue. However, lack of similar studies warrants such an approach to prove effectiveness of novel therapies and approaches.

Our study is an ethical substudy of an ongoing randomized study on refractory out-of-hospital cardiac arrest. The aim of our current study is to provide a deeper patients' perception of the fact of being enrolled into a cardiac arrest study and randomized into one of the treatment arms without providing an informed consent. Similarly, their relatives are being also audited for their perception of the fact, that their close person might have been enrolled into a cardiac arrest clinical study and even randomized.

**Methods:** A written survey has been offered to cardiac arrest survivors, to their relatives and also to relatives of cardiac arrest victims, who did not survive their cardiac arrest. As a comparison groups, similar survey has been offered to populations of myocardial infarction survivors and patients with chronic heart failure.

**Results:** Currently, we collected answers from 28 cardiac arrest survivors and 31 patients with chronic heart failure. All patients agreed on a need to perform research projects on cardiac arrest victims while being unconscious and not able to provide informed consent. Twenty-six out of 28 cardiac arrest survivors agreed with the fact to be enrolled into such a project. Other 25 agreed on the fact of being randomized to one of the treatment arms.

**Conclusions:** Cardiac arrest survivors do not perceive negatively the fact of being enrolled into a clinical study while not being able to provide an informed consent. Majority of them even agree with the possibility of being randomized into one of the treatment arms.

**Keywords:** out-of-hospital cardiac arrest, clinical study, ethics, randomization, consent

## METABOLIC SYNDROME

### Antihypertensive therapy using two free dosed combination of drugs with calcium channel blocker and angiotensin receptor blocker in patients with metabolic syndrome

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**Background:** Metabolic syndrome [MetS] is considered as a strong and significant risk factor for Ischemic heart disease and other atherosclerotic vascular events. The prevalence of MetS gradually increases with obesity, diabetes and hypertension. Identifying optimal drug combinations to treat of hypertensive patients with metabolic syndrome is one of the actual problems. Aim of this study was to optimize antihypertensive therapy in patients with MetS, using two free dosed combinations of drugs.

**Material and methods:** The present study was carried out in the «Republican specialized scientific-practical medical center of therapy and medical rehabilitation». We have examined 112 patients [aged 47–70 years, mean 59±8.0] who have hypertension and metabolic syndrome dividing into two groups by 56. In the first group patients were given 5 mg amlodipine, 20 mg telmisartan per day. In the control group patients were given 5 mg amlodipine, 25 mg losartan per day. Patients underwent all baseline investigations like complete blood count, liver function tests, kidney function tests, blood sugar level, ECG, total cholesterol [mg/dl], serum creatinine [mg/dl], SGPT [U/L] and ambulatory blood pressure monitoring test. Above investigations were done at the start of the study and at the end of the study. We have examined the patients' office systolic [SBP] and diastolic blood pressure [DBP] every 2 weeks during the 8 weeks.

**Results:** In the first group patients the mean systolic blood pressure decreased after 8-weeks i.e. from visit-1 to visit-4 [162.8 ± 14.72 to 126.8 ± 8.80 mm Hg] and the mean diastolic blood pressure also decreased after 8-weeks i.e. from visit-1 to visit-4 [104.2 ± 4.32 to 82.2 ± 3.92 mm Hg] [p < 0.05]; in the control group patients the mean systolic blood pressure decreased after 8- weeks i.e. from visit-1 to visit-4 [163.2 ± 6.72 to 129.8 ± 6.84 mm Hg] and the mean diastolic blood pressure decreased after 8-weeks i.e. from visit-1 to visit-4 [104.2 ± 4.12 to 83.8 ± 4.72 mm Hg] [p < 0.02].

**Conclusion:** Amlodipine + telmisartan in free dosed combination have showed significant blood pressure control in hypertension patients with MetS and the antihypertensive effect was greater than amlodipine + losartan study group.

**Keywords:** metabolic syndrome, hypertension

## Correction of infectious-inflammatory process in experimental burn disease of stage septic toxemia

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According to modern concepts of burn disease the effect of bacterial infections is one of the main causes of burns burdened course. Therefore, the aim of this work was to investigate microbiosis in samples of esophagus mucosal layer and cytokines level of immature rats serum using the model of the esophageal chemical burns of 2<sup>nd</sup> grade under the conditions of intake of melanin drug.

Immature [1-month age] white rat weight 90–110g [according to 1–4 age children] were using in the experiments in compliance with general ethical principles of animal experiments. The animals were experimentally simulated with the alkali esophageal burn [AEB] with 20% NaOH. The animals were divided into 2 groups: group 1<sup>st</sup> – AEB of 2<sup>nd</sup> grade, which was injected with melanin start from 2nd day of the experiment at a dose of 1 mg / kg for 14 days, group 2<sup>nd</sup> – AEB of 2<sup>nd</sup> saline was injected in the appropriate dose and time. In our investigation we used the melanin that produced yeast-like fungi *Nadsoniella nigra* strain X1 which obtained from cliffs Halindez island. The materials were selected for the research at 15<sup>th</sup> day, according to septic toxemia stage of burn disease. Selected culture of organism was characterised and identified with commonly used microbiology methods according to microorganism taxonomy data base. Serum cytokines level were analysed by ELISA. Statistical analysis was performed used mathematical function of Microsoft Excel and Student's t-test. Investigate of the bacteriological samples of esophagus mucosal layer in rats with the AEB of was shown priority *S. aureus* and *Streptococcus salivarius* strains. Interesting but melanin injects to rats with the AEB led to growth inhibition of above-indicated microorganisms. Research shown dramatically increase of inflammatory cytokines IL-1 $\beta$ , IL-12 respectively 18% and 36% and significantly decrease of anti-inflammatory IL-4 and IL-10 cytokines respectively 44% and 25% in rats with the AEB. Melanin induce negligible increase of inflammatory cytokines IL-1 $\beta$ , IL-12 respectively 3% and 14% and slight decreased of IL-4 and IL-10 cytokines respectively 10% and 5% in rats with the AEB.

Therefore, it was investigated that during modeling alkali esophageal burn of 2<sup>nd</sup> grade in immature rats takes place infectious inflammation of bacterial causes that the function of the immune system in the stage septic toxemia. Results of Melanin consume was growth inhibition of *S. aureus*, *Streptococcus salivarius* and affect on the level of proinflammatory and anti-inflammatory cytokines of immune system. We considered that melanin can be used as a promising tool for burn disease prevention and treatment.

**Keywords:** alkali esophageal burn, melanin, septic toxemia

## The Metabolic syndrome and Lipids

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The main cause of the metabolic syndrome lies in the influence of the environment. The absence of sufficient movement, excessive energy intake, stress and smoking. These factors act primarily in individuals who have a family history of the metabolic syndrome – hypertension, diabetes and obesity. Concerning early detection of risk, patients should be medically monitored and intervention needs to happen in a timely manner.

A 10% reduction in total cholesterol level means a 15% lower death rate from cardiovascular disease.

Ambulances examined 550 patients during preventive inspections and at follow-up examination. Patients were being examined from January 2014 to May, 2014. In the study group the total observed values of cholesterol, HDL- cholesterol, LDL- cholesterol, triacylglycerol – TAG, glucoses, Thyroid stimulating hormone TSH. Ages ranged from 25 to 65 years, both men and women were included in the set of study.

Of the 550 patients examined, 380 patients had normal levels of cholesterol, 410 patients had normal values of TAG, 468 normal blood glucose, 72 patients from the whole set were in the range of hypothyroidism.

In order to start the subsequent treatment and prevention of metabolic syndrome, early detection is necessary. It is possible to rely on the five following factors:

- family history of diabetes,
- family history of arterial hypertension,
- detection limit and higher levels of TAG,
- detection of lower levels of HDL – cholesterol,
- an increase in waist circumference and a hint of androgenic obesity.

All studies agree that elderly patients with the metabolic syndrome are not at a heightened cardiovascular risk. However, the heightened risk of the 2<sup>nd</sup> type of diabetes remains. The most effective prevention of the metabolic syndrome is a suitable amount of physical activity; dietary measures, with plenty of fruit and vegetables and the restriction of animal fats. A suitable type of Mediterranean diet is recommended and consists of plenty of fish, vegetables, fruits and vegetable fats.

**Keywords:** metabolic syndrome, lipids, Thyroid stimulating hormone, cardiovascular risk

## NEPHROLOGY

### Hyporesponsiveness to erythropoietin therapy in hemodialyzed patients-single center experience

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**Background:** Renal anemia as a consequence of decreased production of erythropoietin (EPO) is a common complication of advanced chronic kidney disease and has been associated with increased mortality rate and cardiovascular events in hemodialyzed patients. Several studies have reported that 90–95% of dialysis patients responded to erythropoietin therapy in a dose-dependent manner, whereas the remaining 5–10% of patients had low or absent response. Therefore, we investigated the factors contributing to EPO hyporesponsiveness using the EPO resistance index (ERI).

**Patients and methods:** A total number of 110 patients (66 males, aged 67.27±10.52 years and 44 females, aged 65.79±11.51 years) who received EPO treatment were prospectively followed for one year. We defined ERI as the weekly dose of EPO per body weight divided by hemoglobin [U/kg/g/dl/week]. The dose of EPO was titrated to maintain a target hemoglobin level between 10 g/dl and 12 g/dl.

**Results:** Hemoglobin, dialysis adequacy index [Kt/V] and average ultrafiltration volume per dialysis session were 105.3±6.0 g/dl, 1.35±0.25 and 2710 ml, respectively. Statistically significant positive correlation with CRP [r=0.698, p<0.001], ferritin [r=0.314, p<0.001] and parathormone [r=0.408, p<0.001] were found. On the other hand, there were negative correlation with Kt/V [r= -0.453, p<0.001] and transferrin saturation [TSAT] [r=-0.204, p=0.003]. Using multivariate stepwise regression analysis, CRP, ferritin and KT/V were found to be independent predictors of ERI. ERI didn't correlate with ACE inhibitors, type of dialysis, dialysis vascular access, gender, age and dialysis duration.

**Conclusion:** This study demonstrates that appropriate control of inflammation and infections as well as adequate dialysis could contribute to low EPO dosing.

**Keywords:** hemodialysis, erythropoietin, resistance

## RHEUMATOLOGY AND CVD

### Cardiac Involvement in Systemic Sclerosis

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Cardiac involvement in systemic sclerosis [SS] can be manifested by myocardial disease, conduction system abnormalities, arrhythmias, or pericardial disease. Myocardial fibrosis has been documented to be a common finding in pathology and autopsy studies. The presence of cardiac involvement in SS is often underestimated due to the occult nature of the signs and symptoms.

We reported a 38-year-old male with anti-Scl-70 positive scleroderma referred to our center for worsening dyspnea, paroxysms of nocturnal dyspnea, and pedal edema.

Cardiac examination revealed regular rhythm with a S3 sound at the apex cordis. ECG showed sinus rhythm with right bundle branch block [RBBB] and left anterior hemiblock. The patient's serum concentration of NT-pro-BNP was 2335 pg/ml. Echocardiography demonstrated left ventricular systolic dysfunction with a left ventricular ejection fraction of 30–35%, biatrial enlargement, right ventricular enlargement with systolic dysfunction [TAPSE 14mm] and moderate to severe tricuspid regurgitation with right ventricular systolic pressure of 20 mmHg.

Computed tomography did not show any evidence of interstitial lung disease.

A diagnosis of SS-related cardiomyopathy New York Heart Association functional Class III-IV was reached. The patient was monitored in hospital and commenced on furosemide 80 mg/d, spironolactone 50 mg/d, enalapril 10 mg/d and carvedilol 6.25 mg/d. The patient developed sustained ventricular tachycardia [VT], he became symptomatic with dizziness and nausea and his BP dropped to an unrecordable level. An emergency synchronized direct current cardioversion [DCCV] re-established sinus rhythm. Since the patient had developed haemodynamically sustained VT whilst on betablocker therapy, an ICD implantation was performed. His carvedilol was increased to 12.5mg daily. A repeated 12-lead EKG revealed a first degree atrioventricular block. Holter ECG monitoring showed nonsignificant ventricular ectopic beats, but no VT. After six months following his initial admission he received an appropriate shock from his defibrillator for VT, but unfortunately after a year the patient died due to global heart failure symptoms.

At present, no treatments have been demonstrated to alter the natural history of primary cardiac involvement in patients with SS. The involvement of both right and left ventricle in patients with SS is a rare finding and is associated with a poor prognosis.

**Keywords:** Systemic sclerosis, Cardiac involvement, Heart failure

## Cryoglobulinemic vasculitis in a Systemic Lupus Erythematosus patient

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Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease presented with multiple clinical manifestations. Its pathogenesis is very complex and involves both humoral and cellular immunity. Formation and later circulation of immune complex leads to blood vessels inflammation, which is responsible for various clinical manifestations. Our presentation is about a Caucasian patient, diagnosed with SLE, cryoglobulinemic vasculitis and hepatic impairment.

**Case report:** 30 y.o. patient, female, refers for periodic subfebrile temperature for the last seven months, weight loss, fatigue, polyarthralgia, Raynaud Phenomenon, photosensitivity, painful vasculitic elements in her extremities.

During physical examination, IPP, MCF, MTF joints are painful from pressure and no synovitis sign, Allen’s test positive both phases, are seen purple vasculitic elements with necrotic periungual areas. On the skin over articulation cubiti and genu are observed atrophic areas combined with hyper pigmented areas.

Laboratory tests: CBC presents leucopenia, chronic inflammatory anemia and increase of ESR. Urinalysis shows microalbuminuria with no pathologic urinary sedimentation rate. Renal function was normal. Increased level of AST, ALT, GGT and mild increase of ALP and direct bilirubin. Normal CK, LDH, aldolase. Total protein and albuminemia normal. Immunologic tests: ANA positive 1:640 homogeneous pattern, anti ds-DNA positive [430], FR positive with low titer, anti CCP negative[-], ENA screen positive[189], anti-Sm positive[7.5], anti-RNP positive[78], anticardiolipin antibody negative, anti phosphatidylserin/colin negative, anti  $\beta_2$ GP-I negative, LKM-1 negative, anti-LC1 negative, SMAs negative, increased CRP, ANCA p/c negative, low decrease of complement level  $C_3$ ,  $C_4$ , Cryoglobulines resulted positive[+]. Immunoelectrophoresis: Increased level of IgG and light chains  $\kappa$  and  $\lambda$ , but normal rate. Viral markers for HIV, HBsAg, HCV, EBV, CMV resulted negative[-]. Thoracoabdominal CT identified increase of normal size of liver, but no structural impairment and minimal pericardial effusion, other data were normal. Echocardiography: minimal pericardial effusion, PsAp 30mmHg. Biopsy of skin elements: Leukocytoclastic vasculitis and DIF: vascular deposit of IgG,  $C_3$  and  $C_4$ .

According to clinical, immunologic, radiologic and immunohistologic findings to this patient was determinate the diagnosis: SLE, cryoglobulinemic vasculitis type II and hepatic impairment.

**Keywords:** SLE, Cryoglobulinemic vasculitis

## Electrophysiological remodeling of the heart in patients with ankylosing spondylitis

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**Relevance:** In the recent years often discussed the involvement of the cardiovascular system and increased cardiovascular risk in patients with rheumatic diseases, including ankylosing spondylitis [AS].

**The purpose of the work:** The study of early pre-clinical parameters of myocardial electrical instability and lesions of the anatomical structures of the heart in patients with AC and their relationship to activity and duration of the disease.

**Materials and methods:** Study of 94 patients: 66 males (70.2%) and 28 females (29.8 per cent) of reliable AC without diagnosed cardiovascular disease clinically and/or medical documentation [average age  $46 \pm 2.76$  years]. Disease duration from onset of first symptoms before the examination was less than 10 years – in 18 (19.1 per cent), more than 10 years – 76 (80.9 per cent). According to BASDAI in patients with low activity was 11 (11.7%), moderate in 14 (14.9%), high and very high – 69 (73.4%) of the average BASDAI of  $6.01 \pm 1.12$ . To assess the geometry of the heart were used Ajax account the recommendations of the ASE and EAE (2005/2006). In vectorcardiography (VCG) has produced the calculation of the area of QRS loop and T loop.

**Results:** 13 (13.8%) patients with were found changes in the geometry of the heart according to Ajax: concentric remodeling – in 2 (2.12%), eccentric hypertrophy – in 11 (11.7%) patients, concentric hypertrophy was not detected. The area of the QRS loop in patients with disease duration less than 10 years was  $1084.13 \pm 132.42$  mV, and in the group with disease duration more than 10 years, the average loop area of the QRS –  $2840.56 \pm 224.41$  mV ( $p < 0.05$ ). The area of a loop T in the group with duration up to 10 years –  $675.48 \pm 85.52$  MB, and in the group over 10 years –  $704.02 \pm 29.44$  MB. Also studied vectorcardiographic change depending on disease activity. The area of the QRS loop in the group with low activity amounted to  $895.13 \pm 37.19$  MB, with moderate –  $1084.13 \pm 132.42$  mV, and with high and very high –  $3017.73 \pm 235.86$  mV ( $p < 0.001$ ). The area of a loop T in the group with low activity amounted to  $190.53 \pm 82.44$  MB, with moderate –  $675.48 \pm 85.52$  MB, and with high and very high –  $713.35 \pm 32.14$  mV ( $p < 0.001$ ).

**Conclusion:** In patients with disease duration more than 10 years there was a significant increase in the area of QRS loop according VCG, suggesting a more pronounced electric activity of the myocardium and the tendency to the development of left ventricular hypertrophy. Also we have identified that with the increased activity of the disease was on the increase as the square of loop QRS ( $p < 0.001$ ) and area of the loop T ( $p < 0.001$ ). These changes suggests that the increase in the activity of the AS was accompanied by increased electrical activity of the ventricles and extension of the process of repolarization, in other words, diastolic dysfunction. Thus, the duration and activity as are the factors leading to electrophysiological remodeling of the heart, despite normal geometry of these entities.

**Keywords:** spondilitis, electrophysiological remodeling, heart, hypertrophy

# STROKE

## Secondary Prevention Following Acute Ischaemic Stroke or Transient Ischaemic Attack (TIA) in Hospital

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**Introduction:** Acute stroke is the third leading cause of death in the UK and a significant contributor to morbidity. Following an initial stroke, 25% of patients will develop a second stroke within 5 years and nearly 40% within 10 years. This audit aims to investigate the timely implementation of secondary prevention within a hospital setting – in particular, the identification of known risk factors for acute ischaemic stroke or TIA and initiation of appropriate management in the presence of these risk factors, as recommended by the National Clinical Guidelines for Stroke from the Royal College of Physicians (RCP) [2012].

**Methods:** RCP National Clinical Guidelines for Stroke were used as the standard for this audit. Based on these guidelines, a specifically designed form was created to collect data on all patients admitted to the Stroke Unit in Kent & Canterbury Hospital with a diagnosis of acute ischaemic stroke or TIA as confirmed on MRI over a 30-day period. Information was retrieved from patient notes and database regarding the identification of risk factors for stroke and whether these were addressed within the recommended time period. Results were then analysed to establish if the recommended standard had been achieved.

Initial audit identified several areas of poor compliance to recommended guidelines and changes were implemented. Audit results and steps for secondary prevention were both provided to Junior Doctors on the Stroke Unit and presented at the Trust Neurovascular meeting. The Hospital Admission Stroke Pro-forma was notably underused; hence it was made mandatory at every stroke call and its use highlighted at the Junior Doctors Induction. A tick-box prompt on providing lifestyle advice was introduced into the stroke discharge document as a mandatory activity prior to patient discharge. The audit was repeated at 6 months to determine if there were any improvements.

**Results:** Results of each investigated risk factor will be presented with the post-intervention re-audit result followed by the initial audit result in parentheses. Blood pressure was measured in 100% [100%], cholesterol in 100% [83%], cardiac rhythm analysed in 100% [91%] and appropriate neck imaging performed in 84% [94%]. Smoking history was obtained in 76% [26%], alcohol history in 10% [0%], dietary habits in 33% [0%] and exercise in 0% [0%].

Results for appropriate risk factor modification will be presented with the above format. Hypertension was addressed in 70% [56%] and hypercholesterolaemia in 86% [79%]. Cardiac imaging was requested in 76% [35%] and carotid artery stenosis addressed in 100% [100%]. Anti-platelet medication was prescribed in 64% [94%] of patients in sinus rhythm, and anticoagulation for those in atrial fibrillation in 100% [55%]. Advice was given regarding smoking cessation in 100% [100%], alcohol intake in 100% [0%], diet in 33% [9%] and exercise in 19% [13%].

**Conclusion:** This audit demonstrates that significant improvements in compliance with secondary prevention measures may be achieved through the introduction of a mandatory Pro-forma coupled with raising awareness of National Guidelines at a local level. Further improvement may be obtained through implementation on a wider scale with National Stroke Pro-forma.

## VARIA

### A Doctor's Dilemma Solved by the Patient

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Adult cardiac congenital anomalies are associated with an increased risk of complications during pregnancy for both mother and child. Among congenital heart diseases, incidence of atrioventricular canal defects is reported to be 4–5% in patients born with a congenital heart defect. Occurrence is estimated to be 0.19 in 1000 live births.

We report the case of a 42 y.o asymptomatic female patient who in the last days of her first pregnancy coincidentally was diagnosed with a partial atrioventricular canal defect.

At the time of the visit the patient seemed in good health and until then the pregnancy was going normally. In the last week before giving birth the obstetrician requested a cardiological evaluation to assess the risk because of the patient's age and the fact that it was her first pregnancy.

On physical examination a pansystolic murmur was present at the left sternal border and the apex cordis. The ECG showed first-degree atrioventricular block, left axis deviation and voltage evidence of right ventricular hypertrophy.

As a result a transthoracic echocardiogram was performed. It showed an ostium primum atrial septal defect of 26 mm, accompanied by a cleft in the anterior leaflet of the mitral valve with significant mitral regurgitation and common atrioventricular valve. Left ventricle was with normal function. Left atrium and right cavities were dilated with moderate tricuspid regurgitation and pulmonary hypertension [pulmonary artery pressure 50 mmHg].

The diagnose of a partial atrioventricular canal defect was made.

The patient being asymptomatic did not receive any treatment. A general consultation with an obstetrician, cardiologist and anesthesiologist was scheduled to decide the best labor option for both mother and baby. The next day the labor contractions started. The patient was admitted immediately in the hospital and 2 hours later she gave birth naturally to a healthy boy, weighing 2.5 kg, without any congenital anomaly. After 48 hours in observation care both mother and child were discharged in good condition. Two years after the patient still refuses surgical treatment and is on metoprolol 100 mg/daily, furosemide 40 mg/d, spironolactone 25 mg/d and aspirine 100 mg/d. She remains in sinus rhythm and has signs of heart failure NYHA class II. Best treatment strategies for such cases are a challenge for physicians because nowadays pregnancies in adults with unrepaired congenital anomalies are rare. In general a pregnancy is well tolerated by patients with an unrepaired cardiac heart defect and is allowed to go on. Cardiac care is recommended to prevent paradoxical embolism, stroke, arrhythmia and heart failure and such patients should be followed in a tertiary care center. Pregnancy is not recommended in women with unrepaired atrioventricular canal defects with heart failure symptoms or pulmonary hypertension, and the operative delivery is the best solutions in such patients.

The team decision was to deliver through planned C-section, but fortunately everything solved naturally, without complications. Preventing maternal death must be the prime aim of all cardiologists involved in the care of pregnant women.

**Keywords:** pregnancy, atrioventricular canal defect, delivery

## Analysis of drug induced liver injury at internal department

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**Introduction:** Drug induced liver lesion (DILI) is the common cause of acute liver lesion especially in older people of developed countries. Together with increasing life expectation and amount of drugs used the frequency of DILI is increasing.

**Aims & Methods:** The analysis of DILI in the 1-year follow up of all inpatients at Internal Clinic is given. The clinical approach was essential for determining of suspected drug. Type of lesion [hepatitic, cholestatic, mixed] according to the enzyme [ALT, AST, ALP, GMT] and bilirubin levels, time of onset, duration of medication, presence of jaundice were determined. Age, gender, alcohol consumption, concomitant drugs, nutritional supplements, excessive physical training were considered. RUCAM scale for objective valuation of diagnosis was rated and correlation with the clinical consideration was done.

**Results:** During 1-year follow up eleven cases of DILI among the 1509 inpatients was recorded. Using the clinical approach with the liver enzymes and bilirubin statement the diagnosis was done in all patients. Hepatitic type of DILI in 8 patients (73%), cholestatic in 2 (18%) and mixed in 1 patient (9%) was present. Hepatitic type was more often in younger, but cholestatic in older people. Jaundice occurred in 54% of patients. The most common drugs responsible for DILI in our series were: analgesics (46%), contraceptives (27%), antibiotics (18%) and hypolipidemics (9%). From the used drugs the following were responsible for hepatitic lesion: contraceptives (3), flupirtine (2), atorvastatin (1), chondroitin/sulphate (1). Cholestatic lesion occurred after amoxicillin/clavulanate, vancomycine and metamizol. Mixed lesion was recorded after ibuprophen. According to the scoring system RUCAM scale the definitive diagnosis of DILI was done in 5 cases, probable in 4 and possible in 2 patients. Median age of series was 55 years. From the gender point of view higher predominance in women was determined (91%). All patients were occasional alcohol consumers. In 3 of them excessive physical training and in 2 energetic drinks and nutritional supplements were recorded. The incidence of DILI in our series was 0,73% to 100 inpatients. After drug cessation the liver function was completely restored in all patients.

**Conclusion:** Correlation between the clinical approach and RUCAM scale was poor. RUCAM scale is nowadays the only quantitative scale for DILI diagnosis determining. Accurate history taken on concomitant treatment, alcohol, drug and nutritional supplements, excessive physical training or massage procedures are needed. The incidence of DILI in our study was comparable with the date from the literature (1% to 100 inpatients). The consistent drug combination together with monitoring of liver and kidney function especially in patients over 60 with more than 4 drugs is needed for prevention of DILI.

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**Keywords:** drug induced, liver injury

## Experimental model of an acid esophagus burn and its main clinical biochemical parameters

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**Objective:** There are a number of experimental models of an acid esophagus burns (AEB) which require the use of chemicals affecting the certain biochemical parameters, which complicates the interpretation and analysis of the experimental results. Therefore, we elaborate a guideline to develop a new model of burn, which could be used for broad spectrum research of burns pathogenesis especially in children ages from 1 to 8 years.

**Methods:** There were used nonlinear immature white rats [1 month] weighting 90–110g, which were kept on a standard vivarium diet. The animals for experimentally simulating AEB were treated by 30% solvent of CCl<sub>3</sub>COOH; it was injected into the esophagus via the broach. The broach was placed on 4.0 cm from mouth and 0.2 ml of solution was slowly injected. The control rats were administered of 0.2 ml water. We used slices of esophageal length of about 1.5 cm for visual and morphological studies at 1, 3 and 7th day after injection of acid. The biochemical parameters [total protein, albumin, the level of urea, creatinine, K<sup>+</sup> ions and ALT, AST activity] were determined with analyzer Humalyser 3000 at the same time point of experiment.

**Results:** It was revealed edema, congestion, damage to the superficial layers of the esophagus epithelium, hemorrhages into submucosa after 30% CCl<sub>3</sub>COOH treatment. The micrography of the esophageal mucosal lesions demonstrates damage to the esophagus tissues in rats under experimental simulation of AEB through 30% CCl<sub>3</sub>COOH: fibrinous, erosive esophagitis [damage to the mucosa and submucosa]. It was defined that the experimental burns of the esophagus through 30% CCl<sub>3</sub>COOH accompany by the significant changes of blood protein content. On the 1, 3 and 7 day of supervisions it showed decrease of total protein in 1.4 – 1.2 times and albumin content in 2.3; 1.8 and 1.7 times respectively comparing with control values. We observed an increase the levels of urea [in 2.2 – 1.6 times] and creatinine in blood serum in the course of the whole period of the study, on the 1, 3 and 7<sup>th</sup> days in 1.98; 1.93 and 1.63 times compared with control values. The research of the level of K<sup>+</sup> ions in blood serum of the rats with an acid esophagus burns permitted to determine its increase in 2.7; 2.6; 1.5 times at all time. The description of aminotransferase activity in blood serum of the rats under modeling esophageal burns showed that the ALT was raised in 3.2; 2.7 and 2.5 times as well as the activity of the AST increased in 1.2; 1.1; and 0.9 times, respectively, on the 1, 3, 7 day of the experimental acid esophagus burns of 2nd degree.

**Conclusions:** Thus, we have reproduced the model of 2nd degree AEB using 30% CCl<sub>3</sub>COOH which was accompanied by corresponding morphological lesions of esophageal mucosa and changes in basic biochemical parameters. This approach may be used in the study of biochemical and immunological mechanisms of pathogenesis of the 2nd degree an acid esophageal burns of animals.

## Chromosome 15 breakage: A strongly possible cause of both ostium secundum atrial septal defect and acute promyelocytic leukemia in a 22 years old female

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Chromosomal aberrations that involves DNA breaks result in structural chromosomal instability, massive loss of genetic information and chromosomal rearrangements. They lead in chromosomal translocations, inversions or sequence deletions and drive through a tumor genesis and an increased predisposition to leukemia and other cancers.

We report the finding on the karyotype of a chromosomal breakage on the chromosome 15 involving the genomic regions 15q14-22 in a 22-year-old female treated in 2009 with Amplatzer device for isolated Ostium Secundum Atrial Septal Defect, whom diagnosed in January 2013 with an Acute Promyelocytic Leukemia.

There are many genetic conditions related to changes on the chromosome 15, and Acute Promyelocytic Leukemia is one of them, caused by the translocation  $t[15;17][q22;q21]$  in which the PML gene localized on 15q22 provides the material for the PML protein that block cell growth and proliferation and induces apoptosis in combination with other proteins.

Mattson et al [2008] mentioned the importance of the chromosomal aberrations in the chromosome 15 and suggested the gene locus ACTC1 [ASD5] [Phenotype MIM 612794], located on 15q14, as very important for the cardiac septal formation. The reduced levels or impaired function of this gene at some crucial stage of development leads to a delayed looping of the heart preventing so the normal septal development and resulting in ASD5.

This strongly suggests the chromosome breakage 15q14- 22 founded, as the possible cause of an isolated ADS 5 in our patient, triggering a chromosomal instability and generating so the start point of the Acute Promyelocytic Leukemia. Further genetic researches are still on going and we are waiting for the results.

**Keywords:** Ostium secundum atrial septal defect, Acute Promyelocytic Leukemia, Chromosome breakage

## Role of mycobacterium tuberculosis MPT63 and MPT83 antigens in mechanisms of immune cells activation *in vitro*

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**Introduce:** Tuberculosis – is a dangerous infectious disease that causes death of approximately 2 million persons each year. The ineffectiveness of current methods to control the epidemic situation of tuberculosis associated with lack of understanding of the molecular mechanisms pathogenesis of mycobacterial infection. Study of diagnostic properties of *Mycobacterium tuberculosis* antigens important in order to clarify the molecular mechanisms of infection and for the further development of subunit vaccines and diagnostics is an urgent task of modern molecular and cellular biotechnology.

**Aim:** Investigate the ability of antigens *M. tuberculosis* MPT63 and MPT83 to binding with cells of different origin and study the effect of these proteins on immune cell activation *in vitro*.

**Methods:** We used different methods in our work. There are DNA cloning, PCR [Polymerase Chain Reaction], obtaining of recombinant proteins in prokaryotic expression system *E. coli* BL21 Rosetta [DE3], immobilized metal ion affinity chromatography, electrophoresis in polyacrylamide and agarose gels, Western blot assay, flow cytometry, confocal microscopy. The specific binding of *M. tuberculosis* antigens MPT63 and MPT83, fused with a red fluorescent protein *mCherry*, with different types of cells was researched with help of specialized programs for data processing with flow cytometry FSC Express v3.0.

**Results:** During the experiment was investigated the binding of fluorescently labeled derivatives of mycobacterial proteins MPT83 and MPT63 with a number phagocytic-like cells lines. It is shown that protein MPT63 binds to the surface of mouse spleen cells separate subpopulations. There was no binding to the intracellular targets MPT63 with peritoneal mouse macrophages. With help of flow cytometry and confocal microscopy was shown that mycobacterial antigen MPT83 binds to surface macrophage-like cell line U2149.

Established that MPT63 and MPT83 can specifically induce activation of macrophages. Was shown increases the percentage of cells expressing markers of macrophage activation CD11b and F4 / 80, and increases the proportion of cells with increased phagocytic index on peritoneal murine macrophages after incubation with MPT63 and MPT83.

**Conclusion:** Our results suggest that on the surface cells of monocytic origin at a certain stage of differentiation appear molecules which specifically interacts with mycobacterial protein MPT63 and MPT83 and make that population of cells targeted by their effect. Research of target cells for MPT63 and MPT83 is an important step involvement of these proteins in the pathological process. The data is a prerequisite for determining the target cells of the human body to the *M. tuberculosis* proteins MPT63 and MPT83 and for a better understanding of molecular mechanisms of tuberculosis development.

**Keywords:** Tuberculosis, MPT63, MPT83, macrophages

## The impact of CYP4F2 G1347A genotype on patients` plasma metabolic activity after stent implantation

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**Introduction:** The member of hepatic P450 enzymes – CYP4F2 monooxygenase has a significant effect on antiplatelet therapy. This enzyme participates in a biosynthesis of 20-hydroxyeicosatetraenoic acid (20-HETE) from arachidonic acid. 20-HETE inhibits platelet aggregation by binding to its target-thromboxane/prostaglandin H2 (PGH2) receptor. The aim of this study was to determine the impact of CYP4F2 genotype on plasma enzyme activity and 20-HETE concentration in patients hospitalized due to acute coronary syndromes.

**Materials and Methods:** Totally 41 patients, who had been hospitalized due to acute coronary syndromes at the Department of Cardiology of Lithuanian University of Health Sciences (LUHS) from 2014 to 2015 and who continued clopidogrel and aspirin therapy after PCI and stent implantation for at least of 28 days, were included into the further study. A standard 75 mg/day clopidogrel and 100 mg/day aspirin doses were prescribed to all of the represented patients. Blood samples were collected twice: immediately after PCI and stent implantation and 28 days after this procedure. Genotyping and ELISA tests were performed at the Laboratory of Molecular Cardiology of the Institute of Cardiology of Lithuanian University of Health Sciences. The polymorphism CYP4F2 G1347A [rs2108622] and plasma CYP450 and CYP4F2 activity were measured by using commercial kits. Mass spectrometry analysis was done at the Department of Pharmacognosy of LUHS. Commercially available external and internal standards were used. This study was done according to the Declaration of Helsinki. Written informed consent was obtained from all patients included in the study. Permission for this study was obtained from Regional bioethics committee of Kaunas [Lithuania]. The permission number is BE-2-42.

**Statistical analysis:** Non-parametric data was analyzed by using independent samples Kruskal-Wallis test.

**Results:** Plasma P450 enzyme concentrations did not differ significantly during acute phase [immediately after stent implantation] [median 693 ng/ml] and 28 days after this procedure [long-term treatment] [median 823 ng/ml]. CYP4F2 activity was significantly higher [median 4.2 ng/ml] during acute phase than compared to long-term treatment [median 1.4 ng/ml], pCYP4F2 [G/G] polymorphism [n=26] had lower CYP4F2 enzyme concentrations during acute phase, as well as during long-term treatment vs. A allele carriers [n=15]: [median 3.7 and 0.2 vs 6.8 and 3.4, respectively], p

**Conclusion:** Our results showed that plasma CYP4F2 concentrations were significantly higher during acute phase than compared to long-term treatment after PCI and stent implantation. Also, the carriers of wild-type [G/G] polymorphism had lower CYP4F2 enzyme concentrations during acute phase and during long-term treatment than A allele carriers.

**Keywords:** CYP4F2 G1347A, Antiplatelet therapy, Acute coronary syndrome, 20-HETE, ELISA

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