II Sympozjum Naukowe Wydziału Lekarskiego w Katowicach

2nd Scientific Symposium of School of Medicine in Katowice

W dniach od 3 do 14 grudnia 2012 r. odbyło się II Sympozjum Naukowe Wydziału Lekarskiego w Katowicach, ponownie zorganizowane z inicjatywy Kierownika Centrum Medycyny Doświadczalnej oraz Dziekana Wydziału Lekarskiego w Katowicach.
Podobnie jak rok wcześniej, Sympozjum miało formę sesji plakatowej zorganizowanej w holu głównym budynku Wydziału Lekarskiego w Katowicach.
Tematyka Sympozjum koncentrowała się na osiągnięciach naukowych Wydziału w 2012 roku, stanowiąc podsumowanie aktywności badawczej w tym okresie. Została ona zilustrowana 37 plakatami prezentującymi prace zarówno o charakterze klinicznym, jak i dotyczące podstawowych zagadnień biomedycznych.
Zebrane w niniejszym numerze „Annales Academiae Medicae Silesiensis" streszczenia pozwalają zapoznać się z zakresem realizowanych na Wydziale Lekarskim w Katowicach badań naukowych.
Mamy nadzieję, iż Sympozjum w podobnej konwencji będzie kontynuowane.

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1

Rational nutrition and physical activity among medical, physiotherapy, nursing and midwifery students at Medical University of Silesia

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Background: Cardiovascular diseases, diabetes and obesity are major health problem of the 21st century. Proper eating habits and moderate exercise are the best way to reduce the risk of cardiovascular diseases. The objective of this study was to assess the awareness of proper nutrition and physical activity of students beginning their first year of studies at various medical faculties.
Methods: A survey was conducted on a group of Polish first year students of medical, physiotherapy, midwifery and nursing faculties at the Medical University of Silesia (N = 239, aged 19–22 years, mean age: 19.82 ± 1.23 years). Daily meals, poor eating habits such as consumption of fast food, drug usage, and weight-loss diets were evaluated. The questions were related to the subjective assessment of the health of the student, knowledge of the consequences of physical inactivity, type of physical activity practiced and reasons for failing to exercise. The significance of the differences between the groups was assessed by the $\chi 2$ test.
Results: Comparing students of the four different fields of medicine, only 40% of medical students, nursing and midwifery rated themselves as physically active, whereas among the students of physiotherapy this percentage was over 70. Analyzing the responses of students of all the faculties, 5% of students believed that regular physical activity was not necessary for being healthy and a significant proportion of nurses (22%) believed that a lack of exercise and healthy diet had no detrimental effect on health. The most frequently marked reason for the most common cause of students' inactivity was lack of time (60%) and lack of energy (26%), indicated by the students of nursing and medical faculties. Analysis of the dietary habits of students indicated that mainly students of the medical faculty neglect breakfast and mid-morning meal, and 40% of students did not eat a hot meal every day. A significant proportion of students, mainly of the medical faculty snacked between meals (70%), ate ready-made meals and more than 40% consumed energy drinks every day.

Discussion: Proper dietary patterns and physical activity were more frequently observed among the students of physiotherapy. Our study has shown that 19-year-old young people who are studying medical sciences in college, although in theory possess higher awareness of the importance of healthy eating and undertaking regular physical activity, do not implement the knowledge in their everyday life.

2

Influence of incretinomimetics on adhesion molecules ICAM-1 and VCAM-1 expressed on artery endothelial cells

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World statistics demonstrate the epidemic nature of diabetes. This disorder carries an increased risk of heart attack, stroke, and complications related to poor circulation. Furthermore, diabetes is associated with significant changes to the structure and function of cardiac and vascular tissue. Recent studies indicate that in addition to the ability to control glucose levels, incretinomimetics – a novel therapy used in diabetes, have a beneficial effect on the cardiovascular system. This novel group of drugs can affect the activity of endothelial cells through the GLP-1 receptor leading to improved glycemic control. However, still little is known about the related mechanisms.

The aim of the study was to assess the influence of incretinomimetics (natural GLP-1 and synthetic exendin-4) on endothelial cells function. The coronary artery endothelial cells function was determined by measuring the expression of adhesion molecules (ICAM-1 and VCAM-1) under dysfunction conditions induced by TNF-α and glycated albumin. Both TNF-α (proinflammatory cytokine) and glycated proteins contribute to progression of atherosclerosis among diabetics. In such conditions, expression of the tested molecules was measured by ELISA.

Results: Both GLP-1 and exendin-4 have potent anti-inflammatory properties mediated through diminished expression of adhesion molecules ICAM-1 and VCAM-1. Moreover, the possible effect is related to their influence on the NFκB signaling pathway.

Conclusions: A novel group of drugs used in diabetes therapy, incretinomimetics, possesses not only the ability to modulate glycemia but also anti-inflammatory action. These properties may be important in the prevention of atherosclerosis, which is one of the main causes of death in western countries.

3

Influence of incretin mimetics on matrix metalloproteinases expression in TNF-α or glycated albumin-stimulated vascular endothelial cells

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Nowadays, diabetes mellitus is a major global problem. It is closely related to the progression of hypertension and dyslipidaemia, which lead to accelerated development of coronary atheroma and generalized vascular atherosclerosis. These complications are mainly caused by the dysfunction of smooth muscle cells and endothelial cells. TNF-α and glycated proteins contribute to the progression of atherosclerotic changes among diabetics. Incretin mimetics are new drugs used in diabetes therapy. These compounds act through GLP-1R by stimulating postprandial insulin secretion and increasing glucose uptake by peripheral tissues. They also cause a decrease in glucagon secretion from the pancreas and increased glycogen synthesis in peripheral tissues. Recent studies indicate that in addition to the ability to control glucose levels, they have a beneficial effect on the cardiovascular system. The related mechanisms are not known yet. It is believed that among other functions, these drugs can affect the activity of vascular endothelial cells. In atherosclerosis, these cells exhibit increased production of matrix metalloproteinases (MMPs). MMPs are involved in all stages of the atherosclerosis process, from the initial lesion to plaque rupture. The project assumed that GLP-1 receptor agonists alter the expression of matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) in vascular endothelial cells.

Aim: The aim of the study was to assess the influence of GLP-1 receptor agonists on mRNA expression and the concentration of matrix metalloproteinases protein: MMP-1, MMP-9 and their inhibitors: TIMP-1, TIMP-2 in TNF-α or glycated albumin-stimulated human iliac artery endothelial cells (IAEC). The choice of this cell

line was dictated by the high incidence of atherosclerosis in this location.

Results: The results of the presented study have shown significant changes in basic and TNF-α or glycated albumin-stimulated expression of the tested molecules. The tested incretin mimetics decreased MMP-1 and MMP-9 expression stimulated by proinflammatory factors. On the other hand, they slightly induced the expression of tissue inhibitors of metalloproteinases (TIMP-1 and TIMP-2). This may result in the inhibition of TNF-α or glycated albumin stimulated metalloprotease activity, and thereby inhibiting the degradation of ECM.

Conclusion: The tested incretin mimetics exert protective effects on vascular endothelial cells by antagonizing the negative action of TNF-α and glycated albumin and reducing extracellular matrix degradation. This may play an important role in atherosclerosis prevention among patients with diabetes.

4

Effects of incretin agonists on eNOS expression and nitric oxide synthesis in human endothelial cells

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Cardiovascular diseases are a predominant cause of death in type 2 diabetes. Numerous vascular dysfunctions may be caused as a complication of metabolic disorders. The tumor necrosis factor (TNFα) is a cytokine involved in systemic inflammation. Evidence suggests that TNFα plays a pivotal role in the injury of macro- and microvascular circulation both *in vivo* and *in vitro*. TNFα-mediated signaling initiates and accelerates atherogenesis, vascular remodelling, oxidative stress and impaired NO bioavailability, resulting in vascular dysfunction. The TNFα level is elevated in diabetic patients. The incretin hormone, glucagon-like peptide 1 (GLP-1) is a gut-derived hormone that stimulates insulin and suppresses glucagon secretion, inhibits gastric emptying, and reduces appetite and food intake. The GLP-1 receptor is expressed in pancreatic islet α and β cells and in peripheral tissues, including the heart, kidney, lung, gastrointestinal tract and vasculature. The pleiotropic actions of GLP-1 and its synthetic agonist – exenatide, on the control of blood glucose are of interest in the use of these agents for the treatment of type 2 diabetes. Some experimental and clinical data have suggested a considerable protective role of GLP-1 analogs in the cardiovascular system. Human vascular endothelial cells from the coronary artery (CAEC), aorta (AOEC) and iliac artery (IAEC) were used in this experiment. Nitric oxide synthase gene expression was assessed by Real-Time PCR. Protein quantity was assessed by western blot and ELISA. Nitric oxide production was assessed by flow cytometry using DAF-FM/DA. Each cell line was stimulated with TNFα, GLP-1 and exenatide. The project aims to assess the influence of incretin receptor agonists during the stimulation of TNFα on: endothelial nitric oxide synthase (eNOS) mRNA expression, eNOS protein expression and nitric oxide synthesis. Potential differences in the influence of the tested substances on endothelial cells from different vascular locations were assessed.

The highest basic eNOS protein synthesis and NO production was detected in CAEC cells, lower in AOEC cells and the lowest in IAEC cells. TNFα significantly decreased the expression of eNOS on mRNA and the protein level. GLP-1 and exenatide did not change eNOS mRNA expression. Both GLP-1 and exenatide increased the eNOS protein level only in IAEC cells. The incretin agonists decreased NO production compared to TNFα stimulated cells. We suppose that this effect is caused by the anti-inflammatory action of incretins.

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Detection of changes in DNA of genes encoding procollagen type I in patients diagnosed with osteogenesis imperfecta (*OI*): An analysis of 83 cases

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Although studies on the genetic background of osteogenesis imperfecta have been conducted for more than half of a century and resulted in a large number of mutations identified in both genes encoding

procollagen type I as well as pointed to several new candidate genes, the complex mechanism of this disorder has yet to be elucidated. New technologies for sequencing nucleic acids provide a powerful tool for the identification of new mutations and other nucleotide changes in order to create a more complex picture of sequence difference in the genes of unaffected and *OI* individuals. Here we used directional sequencing in *COL1A1* and *COL1A2* from 83 patients diagnosed with different types of *OI*. OI Type I constituted 51 patients of whom 27 were from 8 unrelated families represented by more than one member and the remaining 24 were all unrelated patients. With type II there were 4 unrelated patients and 3 related. With type III, 9 unrelated patients and five from 2 unrelated families were diagnosed. Seven patients were diagnosed with type IV. The remaining patients seemed to be diagnosed with *OI* type I/IV (2 unrelated and two related). In 14 patients with *OI* type I, no mutational changes were detected in the coding sequences of *COL1A1,* and furthermore in 10 of them there were no significant changes in the *COL1A2* exon sequences. Among the 51 patients with OI type I, 27 patients have had sequenced exons of *COL1A2*. Overall, there were 71 different changes in the exons and surrounding introns of the *COL1A2* gene. Moreover in 37 patients, the diagnosis was verified by assay of the thermal stability of collagen type I. In 32 patients the collagen thermal stability (Tm) was decreased. In two cases there was no significant change in the stability of collagen monomers and in two cases the thermal stability of collagen type I was increased, suggesting the role of other genes in the molecular pathogenesis of *OI*.

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Cell therapy of patient with type III osteogenesis imperfecta caused by G23569A (p.Gly517Asp) *COL1A2* gene mutation and unstable collagen type I

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This report presents the clinical case of a newborn girl diagnosed with *osteogenesis imperfecta* type III, with multiple bone fractures, deformities and extreme shortness of limbs, treated at the age of 4 and 6 weeks with the transplantation of allogenic bone marrow derived from mesenchymal stem cells. The diagnosis of *osteogenesis imperfecta* was confirmed by the biochemical analysis of collagen type I recovered from a culture medium of cultivated skin fibroblast, which revealed an unstable triple helical structure at a temperature of about 2°C lower than normal. Subsequent sequencing of both genes encoding procollagen type I revealed G23569A substitution in the *COL1A2* gene causing missense mutation by changing glycine at position 517 to aspartate. To obtain skin fibroblasts for procollagen type I production and DNA isolation, a skin biopsy was performed. The donor of the mesenchymal stem cells was the girl's father. She received two intravenous infusions of suspended cultured mesenchymal cells 16 days apart without any side effects. Analysis of procollagen type I secreted to the culture medium by bone marrow-derived mesenchymal stem cells obtained from the patient 3 months following transplantation revealed normal triple helix stability. During the subsequent two years of follow-up, two new bone fractures were noted. Currently the two-year-old girl presents extreme growth and weight deficiency. The motoric development is also retarded, but the patient is constantly improving and making progresses.

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Zmiany w cyklu włosowym pod wpływem wybranych leków u szczurów w okresie dojrzewania

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Wstęp: Ważne zagadnienie z punktu widzenia klinicystów i leczonych pacjentów stanowią niepożądane działania polekowe. Obejmują one wiele układów i narządów oraz implikują dalsze postępowanie terapeutyczne. Jednym z nich jest łysienie polekowe, którego mechanizm nie zawsze pozostaje jasny i w wyraźny sposób wiąże się ze stosowanym lekiem. Częstość występowania tego zjawiska u ludzi w skali ogólnej nie jest znana.
Cel: Celem pracy była próba odpowiedzi na pytanie: jaki wpływ na mieszek włosowy wywierają cyklofosfamid, flukonazol, atorwastatyna oraz perindopril w porównaniu ze stanem fizjologicznym?
Materiał i metody: Szczurom szczepu Wistar, podzielonym na grupy kontrolne oraz badane, podawano codziennie, dożołądkowo, przez 3 miesiące wymienione leki. Następnie oceniano makroskopowo owłosienie zwierząt oraz przebieg cykli włosowych wywołanych na podstawie trichogramów. Cykl włosowy wywołany uzyskano naprzemienną, 32-dniową epilacją pola o wymiarach 10 x 10 mm okolicy krzyżowej u wszystkich zwierząt. Dwa razy w tygodniu od każdego szczura pobierano kleszczykami Kochera ok. 100 włosów. Następnie pod mikroskopem w powiększeniu 40 x obliczano procent włosów prawidłowych (anagenowych, katagenowych, telogenowych) oraz patologicznych (dystroficznych i dysplastycznych). Uzyskane wartości porównywano z grupą kontrolną.
Wyniki: We wszystkich analizowanych cyklach w grupie otrzymującej cyklofosfamid stwierdzono zwiększony odsetek włosów telogenowych i dystroficznych oraz przedwczesną inwolucję katagenową, w pozostałych grupach w przypadku obserwowania zaburzeń przebiegu cykli włosowych odpowiednio przedwczesną inwolucję katagenową i wzrost liczby telogenowej.
Wnioski: Uzyskane wyniki dowiodły, iż wszystkie wybrane do badania leki wpływają na przebieg cykli włosowych i odpowiadają za rozwój łysienia polekowego o przebiegu zależnym od stosowanego leku oraz czasu ekspozycji.

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Eplerenone promotes alternative activation in human monocyte-derived macrophages

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In this study, we have analyzed the response of human monocyte-derived macrophages to modulators of the mineralocorticoid axis. Recently, a few studies have shown that inflammation, macrophages and their phenotype may be the effectors of aldosterone. Aldosterone is a mineralocorticoid hormone and is synthesized by adrenal gland cortices. It is a ligand for a nuclear receptor, known as the mineralocorticoid receptor. Mineralocorticoid activity is classically described in relation to its effects on kidney epithelium, salt and water retention. Human monocytederived macrophages were incubated with aldosterone alone, eplerenone alone, and a combination of aldosterone and eplerenone. Eplerenone, along with spironolactone, belong to a class of mineralocorticoid receptor antagonists, also known as aldosterone antagonists. The analyzed variables were nitric oxide and reactive oxygen species production, the expression of genes and proteins belonging to inducible nitric oxide synthase, arginase I, and the mannose receptor. We have shown that aldosterone promotes classic inflammatory response in macrophages, whereas its antagonist – eplerenone – attenuates aldosterone--induced activity. However, eplerenone did not quantitatively weaken the response of macrophages to aldosterone but qualitatively changed their behavior. Eplerenone alone did not change the release of toxic molecules in macrophages, it affected the gene and protein expression in these cells. Notably, it affected the expression of arginase I and mannose receptor mRNA as well as protein levels. Both of them are markers of alternative activation of macrophages. Alternative activation is an anti-inflammatory phenotype of macrophages that is opposed to the pro--inflammatory and toxic one. In summary, the inhibition of mineralocorticoid activity with the aldosterone antagonist eplerenone promotes the alternative activation of macrophages. The resulting phenotype may prevent macrophages from producing toxic molecules in the presence of aldosterone.

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Adenosine-monophosphate activated protein kinase (AMPK) – independent effects of Metformin on rat primary microglial cultures

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The results of recent studies suggest that metformin, in addition to its efficacy in treating type 2 diabetes, may also have therapeutic potential for the treatment of neuroinflammatory diseases in which reactive microglia play an essential role. However, the molecular mechanisms by which metformin exerts its anti-inflammatory effects remain largely unknown. Adenosine-monophosphate-activated protein kinase (AMPK) activation is the best-known mechanism of metformin action, however, some of the biological responses to metformin are not limited to AMPK activation but are mediated by AMPK-independent mechanisms. For this reason, we attempted to evaluate the effects of metformin on unstimulated and LPS-activated rat primary microglial cell cultures. Our evidence supports the conclusion that metformin-activated AMPK participates in regulating the release of TNF-α. Furthermore, the effects of metformin on the release of IL-1β, IL-6, IL-10, TGF-β, NO, and ROS as well as on the expression of arginase I, iNOS, NF-κB p65 and PGC-1α were not AMPK-dependent, because the pretreatment of LPS-activated microglia with compound C, a pharmacological inhibitor of AMPK, did not reverse the effect of metformin. Based on the present findings, we propose that the shift of microglia toward alternative activation may underlie the beneficial effects of metformin observed in animal models of neurological disorders.

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Copeptin – a new prognostic biomarker of degenerative aortic stenosis

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Purpose: Copeptin is a new biomarker of cardiovascular diseases. Its diagnostic value in degenerative aortic valve stenosis (AS) with preserved left ventricle systolic function is unknown. We aimed to assess the association of serum copeptin levels with the AS severity and coexistence of coronary artery disease (CAD).

Methods: Sixty-four patients with AS and preserved left ventricle systolic function including 40 with severe degenerative AS (sAS group, effective orifice area EOA = 0.67 cm^2), 24 with moderate degenerative AS (mAS group, EOA = 1.40 cm^2) were enrolled in the study. 23 patients without AS and heart failure, matched for age, sex and CAD occurrence served as the control group (group C). The serum levels of copeptin and NT-proBNP were measured using the ELISA method.

Results: The mean serum copeptin concentrations were significantly higher in patients with AS: sAS (405 pg/ml) and mAS (351 pg/ml; sAS vs mAS $p < 0.05$) compared to group C (302 pg/ml, $p < 0.05$). Serum copeptin levels correlated inversely with EOA ($r = -0.55$; $p < 0.001$) in AS patients. There was no correlation between copeptin and NT-proBNP or association with coexisting CAD. ROC analysis showed that copeptin was a good marker of severe/moderate AS (sensitivity 71%; specificity 87%), with an optimized cut-off value of 354 pg/ml.

Conclusions: Serum copeptin concentration constitutes a novel biomarker of degenerative AS. Coexisting CAD does not interfere with the copeptin level.

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Aortic valve replacement and non-invasive assessment of arterial stiffness in patients with degenerative aortic stenosis

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Arterial stiffness constitutes a part of total left ventricle afterload defined as valvulo-arterial impedance as well as corresponds to the risk of cardiovascular diseases. Arterial stiffness is of special interest in degenerative aortic stenosis (AS). It may be influenced by aortic cannulation during aortic valve replacement (AVR). The aim was to assess the influence of AVR procedure on noninvasive markers of arterial stiffness in patients with severe degenerative AS. 80 patients (M/F: 43/37, mean age: 68.9 ± 9.1 years) with severe AS and preserved left ventricle systolic function were enrolled in the study. All the patients were admitted to AVR (artificial prosthesis n = 32/bioprosthesis n = 48) with ascending aorta cannulation according to the standard protocols. Clinical data as well as PWV-pulse wave velocity (PWV), aortic pulse pressure (PP), augmentation index (AIx) estimated by applanation tonometry were examined pre- and postoperatively: on 7 days and 1month after AVR. The mean values of PWV measured preoperatively, on the 7th day and 1 month after AVR were comparable (6.75 ± 0.4 m/s vs 7.31 ± 0.2 m/s vs 7.23 ± 2.4 m/s, p = 0.27, respectively). The mean values of aortic PP were significantly lower on the7th day (40.71 ± 1.6 mmHg) as compared to the baseline data and data obtained 1month after AVR (48.53 ± 2.2 mmHg, p = 0.018, 46.09 ± 2.0 mmHg, p = 0.04, respectively). Similarly, AIx was significantly lower on the 7th day (24.24 ± 1.7%) as compared to the baseline data and data obtained 1 month after AVR (32.56 ± 1.8%, p = 0.002, 29.51 ± ± 1.6%, p = 0.02, respectively). The mean PP and AIx values were comparable 1month after AVR to the baseline data. Noninvasive markers of arterial stiffness remain stable in patients surgically treated for degenerative AS. Decreased values of pulse pressure and augmentation index observed in the early postoperative period are reversible and probably depend on the clinical status of patients.

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Impaired functional capacity in patients with systemic sclerodermia related to right ventricle dysfunction

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Systemic sclerodermia (SSc) is characterised by cardiovascular abnormalities, which may affect a patient's clinical symptoms. The aim was to assess whether the impaired exercise tolerance in patients with SSc without overt cardiopulmonary complications is related to left ventricle (LV) or right ventricle (RV) dysfunction and vascular remodeling. Forty-seven patients (F/M : 36/11; age 51.7 ± 9.9) with diagnosed SSc and clinical symptoms (NYHA I/II) were enrolled in the study. In all the patients, pulmonary arterial hypertension (PAH), pulmonary fibrosis, left ventricle (LV) systolic dysfunction and valvular heart diseases were excluded. The following tests were performed: echocardiography, ultrasound vascular indexes: flow mediated dilatation, nitroglycerin mediated dilatation and arterial tonometry parameters: pulse wave velocity, pulse pressure and augmentation index. The above indexes were related to the 6 minute walk test (6MWT) results. The 6MWT mean value was 440.0 ± ± 72 m. LV diastolic dysfunction parameters did not correlate with 6MWT. RV systolic dysfunction (fraction area change < 32%), decreased tricuspid annular plane systolic excursion (TAPSE < 20 mm) or low peak systolic velocity of the lateral tricuspid anulus (TDI: RV S' < 20 cm/s) were found in 1 (2.1%), 5 (10.6%), 43 (91.5%) patients, respectively. The 6MWT values correlated with TAPSE (r = 0.318, p = 0.030) and TDI: RV S' (r = -0.295, p = 0.048). There were no significant correlations between ultrasound and arterial tonometry parameters and 6MWT values. After excluding typical causes of low exercise capacity in SSC, the shortened 6MWT distance observed in this group seems to be related to RV systolic impairment, which supports regular echocardiographic screening for early detection of cardiac complications in SSc.

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Prevalence of hydrogen cyanide and carboxyhaemoglobin in victims of smoke inhalation during enclosed-space fires: a combined toxicological risk

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Smoke inhalation is a well-established cause of death in victims of fires, and carbon monoxide (CO) and hydrogen cyanide (HCN) are two of the main noxious gases involved. During pre-hospital medical intervention of persons rescued from a fire who are demonstrating symptoms of smoke inhalation distress, insufficient attention is paid to the potential harm caused by HCN. Likewise, during medicallegal examinations and when determining the probable cause of death of bodies recovered from fire-damaged buildings, the possible role of HCN as a sole or contributing toxin is considered far too infrequently.

Against this background, we undertook an investigation to assess the prevalence of toxic HCN exposure in victims of enclosed-space fires, either found dead at the scene or rescued alive. We also examined factors that may have influenced the toxicity of HCN in victims who died, specifically the co-presence of carboxyhaemoglobin (COHb) and ethanol in blood samples.

A retrospective observational study was conducted at the Medical University of Silesia in Katowice between 1995 and 2011. Medical or post-mortem records from persons exposed to smoke during enclosed-space fires were reviewed. In all the cases, whole blood samples were analysed by the following methods: a) microdiffusion technique in a Conway chamber and employing a calorimetric method based on the König reaction with Nedoma modification (for HCN assessment), b) Wolff method using a Hitachi 2001 spectrophotometer (for quantitative assessment of COHb level) and c) 'headspace' technique using a FISONS-HRGC 5300 gas chromatograph and enzymatic method (for ethanol assessment).

Of the 285 available blood samples, 78 were from females and 207 from males. The most common fire location was an apartment/flat (200 victims), followed by a house (69), car (15) and laboratory (1). A positive result for HCN (mean concentration 16.83 mg/l) was detected in blood samples from 169 of the 285 fire-related deaths (59%). Ethanol was present in 91 (65%) of 139 samples with a coincident presence of HCN and carboxyhaemoglobin (COHb). HCN (mean 4.0 mg/l) was also detected in 20 of the 40 (50%) fire survivors.

The high prevalence of coincident CO and HCN in enclosed-space, fire-related deaths should alert clinicians to suspect toxic HCN exposure in all persons rescued from fire with symptoms of respiratory distress. Medical procedures in persons rescued from enclosed-space fires should be augmented to cover the possibility of toxic HCN exposure, particularly in individuals who do not respond to standard supportive therapy. Post-mortem investigations should routinely include assays for HCN.

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Forensic entomotoxicology – first Polish experiences from Upper Silesia Region

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Forensic entomotoxicology is a relatively new branch of forensic entomology, which uses insects, mainly fly larvae, as an alternative to routinely collect (blood, urine, organs) material for post-mortem toxicological analyses. It is also interested in the influence of different xenobiotics on the life cycles of insects of forensic significance. Forensic entomotoxicology may be useful especially in the cases of human cadavers discovered long after death, changed by decomposition processes.

In Poland, so far, forensic entomotoxicological studies have not been performed, so to gain the first experiences in this field, we decided to collect and analyze fly larvae in two cases of significantly decomposed and even partially skeletonizated bodies revealed in a building (case 1) and forest (case 2).

During medical-legal autopsies, tissue samples of organs – muscle (case 1 & 2), liver and kidney (case 1) – with feeding larvae were collected. Until the time of analyses, the larvae were kept alive in a refrigerator on muscle tissue. The samples of larvae were morphologically identified as the 3rd instar larvae of Protophormia terraenovae and Calliphora vomitoria (case 1), and Stearibia nigriceps (case 2). The samples

of tissues and homogenized larvae were analyzed using the volatiles screen method, that simultaneously detects and quantitates ethanol, isopropanol, acetone, acetaldehyde and n-propanol by headspace gas chromatography equipped with capillary columns Rtx--BAC1 and Rtx-BAC2 and flame-ionization detectors, using t-butanol as an internal standard. Additionally, because there was suspicion that the deceased from case 1 was a drug addict, analysis towards the presence of drugs and other organic xenobiotics, using high performance liquid chromatography coupled with mass spectrometry with electrospray ionization, was performed. Extraction was done with ethyl acetate, acetonitrile or chloroform. Separation was conducted in a mobile phase of acetonitrile and ethyl formate (1:1). The ion trap mass spectrometer operated in the total ion monitoring mode, in the range of 100––700 m/z.

Ethanol, acetaldehyde, isopropanol and n-propanol were identified and quantified by GC-FID in both cadaverous and entomological matrices. Acetone was present in the human tissue samples, but was absent in the larvae. The analysis, both in the human and larval material, did not reveal any drugs or other xenobiotics. Fly larvae may be used in some forensic cases as an alternative source of toxicological information, but now more studies, including studies on the metabolism of xenobiotics by insects, standardization of analytical procedures and guidelines for forensic toxicologists and also forensic medical examiners and forensic investigators, who are first present at the crime scene, are needed.

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Stężenie cystatyny C w surowicy noworodków z objawami zakażenia

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Wprowadzenie: Wyniki opublikowanych badań dowodzą, że oznaczanie cystatyny C w surowicy może stanowić lepszy marker czynności wydalniczej nerek niż stężenie kreatyniny w surowicy. Jednakże znaczenie tego markera w diagnostyce upośledzonej czynności nerek u noworodków nie zostało jednoznacznie wyjaśnione. Celem badania jest analiza stężeń cystatyny C w surowicy u noworodków leczonych z powodu sepsy.

Materiał i metodyka: Do badań włączono 21 noworodków (wiek płodowy 36–42 tygodnie, masa urodzeniowa ciała: 2070–4440 g; 7 dziewczynek i 14 chłopców) przyjętych na Oddział Intensywnej Terapii i Patologii Noworodka w pierwszym miesiącu życia z powodu zakażenia (3 zapalenia płuc, 8 zakażeń układu moczowego i 10 zakażeń uogólnionych). Stężenie cystatyny C oznaczono metodą ELISA w 3 kolejnych dobach leczenia oraz po zakończeniu leczenia zakażenia.

Wyniki: W chwili włączenia do obserwacji średnie stężenie cystatyny C wynosiło 1,60 mg/L (95%CI: 1,46–1,73). Stwierdzono ujemną korelację z masą urodzeniową noworodka ($R = -0,36$, $p < 0,05$ w dobie pierwszej; $R = -0,48$, $p < 0,05$ w dobie drugiej i $R = -0,31$, $p < 0,07$ w dobie trzeciej), lecz nie z wiekiem płodowym. W drugim dniu pobytu stwierdzono silną ujemną korelację pomiędzy stężeniem CRP i cystatyny C ($R = -0,59$, $p = 0,01$) oraz pomiędzy stężeniem prokalcytoniny i cystatyny C ($R = -0,45$, $p < 0,05$). Podobnych zależności nie stwierdzono w dobach pierwszej i trzeciej. W dobach kolejnych nie obserwowano istotnych zmian stężeń cystatynyC, natomiast w trakcie obserwacji oraz po zakończeniu leczenia stężenia cystatyny C nie zmieniły się istotnie.

Wnioski: Nasilenie stanu zapalnego nie powoduje podwyższenia stężenia cystatyny C u noworodków leczonych na oddziale intensywnej terapii.

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Stężenie NGAL 2 surowicy i moczu u noworodków leczonych w oddziale intensywnej terapii

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Wprowadzenie: Lipokalina neutrofilowa związana z żelatynazą (NGAL) jest opisywana jako nowy marker diagnostyczny ostrego uszkodzenia nerek (AKI). Jest ona wydzielana przez komórki nabłonka różnych

narządów oraz neutrofile i szybko usuwana z krążenia. Jej rola w diagnostyce u noworodków nie została ustalona. Celem badania było przeanalizowanie stężeń NGAL w surowicy i moczu noworodków w różnych sytuacjach klinicznych w trakcie leczenia na oddziale intensywnej terapii (OITN).

Materiał i metodyka: Do badania włączono 28 noworodków przyjętych do OITN z podejrzeniem zakażenia. U 3 zdiagnozowano zapalenie płuc, u 10 zakażenie układu moczowego, a u 2 ciężkie niedotlenienie wewnątrzmaciczne z zakażeniem wrodzonym. U 7 noworodków rozpoznano zakażenie wewnątrzmaciczne, u kolejnych 6 zakażenie nie potwierdziło się w trakcie obserwacji klinicznej. Stężenia NGAL w surowicy i moczu oceniano w kolejnych 3 dobach.

Wyniki: W chwili przyjęcia najwyższe wartości NGAL w surowicy stwierdzono u noworodków z wrodzonym zapaleniem płuc (231 ± 308 ng/ml) i po przebytym niedotlenieniu okołoporodowym (208 + 31 ng/ml). Natomiast najwyższe stężenia w moczu (wyższe niż w surowicy)
obserwowano w zakażeniu dróg moczowych (181 + 246 ng/ml) i niedotlenieniu. W trakcie hospitalizacji, gwałtowne obniżenie wartości NGAL w surowicy pojawiło się u pacjentów z zakażeniem wewnątrzmacicznym, a pozostało podwyższone u noworodków niedotlenionych i z zakażeniem układu moczowego. Równocześnie wartości NGAL w moczu obniżały się najwolniej u noworodków z zakażeniem układu moczowego.

Wnioski: Podwyższone wartości NGAL w surowicy nie powinny być przypisywane wyłącznie uszkodzeniu nerek. Podwyższone stężenia NGAL w moczu mogłyby być obiecującym markerem ostrego uszkodzenia nerek, po uprzednim wykluczeniu zakażenia układu moczowego. Pomiary seryjne są bardziej wiarygodne niż pojedyncze oznaczenia.

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Ultrasonographic reference brain measurmenets in preterm newborn infants

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Background and aims: Ultrasonography is noninvasive, commonly used neuroimaging in premature newborns. Studies on brain measurements are lacking. This paper aimed to determine the average measurements of the cerebral ventricles, brain and cerebellum in preterm infants and to describe the differences on the left and right side, taken with sector and convex transducers, and to assess the relationships between the measurements and gestational age, head circumference, birth length, birth weight and gender.

Methods: Each of the 132 newborn infants enrolled had 34 measurements taken (5285 in total) and 6 ratios calculated (784 in total). The area of cavum septum pellucidum (ACSP), ventricular index (VI), ventricular width (VW), brain width (BW), third ventricle width (3VW), frontal horn width (FHW) were assessed in the coronal plane. Evans (ER) and Johnson (JR) ratios were calculated. The midbody of the lateral ventricle (MLV) and thalamo-occipital distance (TOD) were studied in the parasagittal plane. Transverse cerebellar diameter (TCD), width (4VW) and length of the 4th ventricle (4VL) were assessed via the mastoid fontanel.

Results: The sector probe gave significantly smaller measurements than the convex transducer. The left side measurements were significantly greater than the right ones. VI, VW, BW and TCD and 4VW depended on birth weight, length, head circumference and gestational age. ACSP, FHW, TOD and JR were independent of the above mentioned factors. No relationships were found between gender and measurements. Reference values for cranial measurements and ER, JR for the examined population of premature newborns were determined.

Conclusions: The above mentioned values may be used in every-day clinical practice in neonatal units.

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Quantitative cranial ultrasound prediction of severity of disability in premature infants with post-haemorrhagic ventricular dilation

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Background: Infants with post-haemorrhagic ventricular dilatation (PHVD) have a high risk of severe disability and parenchymal infarction increases this risk. Existing cranial ultrasound (CUS) markers of neurodevelopmental outcome are based on categorical features.
Objective: To investigate to what extent quantitative CUS measurements correlated with the severity of developmental outcome and the need for a ventriculoperitoneal (VP) shunt at 2 years of age.
Method: 69 premature infants with PHVD had lateral ventricle area, intraventricular echodensity and parenchymal lesion dimensions measured at the start of treatment for PHVD. The outcome measures were the Bayley Scales of Infant Development-II and functional ability at 2 years of age. Bayley developmental quotients (DQ) were used in preference to index scores to enable the inclusion of severely disabled children.
Results: Quantitative CUS measurements of the parenchymal lesion area correlated significantly with later mental and motor DQ. The intraventricular echodensity area correlated with motor DQ in infants with grade 4 intraventricular haemorrhage (IVH). Neither the ventricular area nor ventricular width correlated with DQ in grade 3 IVH. Infants who ultimately required a VP shunt had a significantly larger intraventricular echodensity area.
Conclusions: CUS measurement of parenchymal lesions in infants with PHVD can increase the precision of predicting severe mental and motor disability, but ventricular size at the start of treatment is not predictive of the outcome in infants with PHVD following grade 3 IVH.

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The diagnostic value of neuroimaging in recognising encephalitis and meningitis in children

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Background and aims: Neuroinfection is an entity with possible serious subsequent complications. Early and precise diagnosis can help in purposeful treatment and accurate prognosis. The aim of the study was the analysis of principles and value of neuroimaging in the diagnostic process in pediatric neuroinfection.
Methods: The retrospective analysis comprised 74 patients diagnosed with encephalitis and/or meningitis. The cohort was divided into two groups: A (meningitis; n = 45) and B (encephalitis and meningoencephalitis, n = 29). Data obtained from medical records (medical history, signs and symptoms, results of laboratory tests and radiological imaging) were investigated. Computer tomography (CT) or magnetic resonance (MR) were performed in the study group.
Results: In group A, the first CT examination revealed abnormalities in 9.7% of patients, in group B – in 28% of children. MR examination showed a pathological brain area in 79.3% of patients in group B. A high signal in SE/T2 was observed in 95.7 % and in FLAIR in 86.9%. In 90% of analyzed group B, disturbances in DWI were noted.
Conclusions: CT examination performed in the initial stage of meningitis and/or encephalitis has limited diagnostic value for recognizing inflammation. The characteristic of the abnormalities revealed by MR enables one to recognize inflammation changes in the central nervous system and their localization can direct the diagnostic process. The presence of brain tissue alterations in the MR image has significant correlation with clinical symptoms like seizures, consciousness disturbances and neurological deficits. The most sensitive sequences in the estimation of the inflammation activity process are DWI and FLAIR.

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Brachytherapy of head and neck cancers with application of individual inserts – – authors' own experience

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The aim of study is to present the authors' own experience in brachytherapy of head and neck tumors, with particular emphasis on some rare methods, i.e. radiation with the application of a tracheostomy tube and an individual insert of a hearing aid. The study was conducted on 4 patients with surgically-treated laryngeal cancer (pharyngolaryngectomy), in whom an intra- and postoperative brachytherapy applicator has been inserted. In two patients, neoplastic infiltration in the area of the tracheostomy was observed and in 2 cases cancer of the external auditory canal was found. 3 patients suffered from massive cancers of the maxilloethmoidal complex. A tracheostomy tube and an individual insert of a hearing aid as a vector for brachytherapy were used in the study. There was no recurrence observed in the patients with neoplastic infiltration in the area of the tracheostomy nor with cancer of the external auditory canal in the 5-year follow-up. One and two years after the pharyngolaryngectomy and tumor resection of the maxillo-ethmoidal complex, no recurrence was found. The authors recommend brachytherapy as an important method of adiuvant radiotherapy, especially if applied in the region of critical areas, such as facial nerve or meninges. They emphasize its importance as a method of adiuvant radiotherapy after a full-dose teletherapy.

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Kuttner's tumor- a rare cause of enlargement of submandibular gland

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Introduction: Chronic sclerosing sialadenitis- Kuttner's tumor- is a rare benign pseudotumoral lesion of the salivary gland, which predominantly affects the submandibular gland. The course of this disease mimics the neoplastic process, however, its microscopic image indicates an inflammatory origin. The etiology remains controversial, but IgG-4 overexpression seems to play a key role in Kuttner's tumor pathogenesis.
Our work is a case presentation of a patient suffering from Kuttner's tumor.
Methods: We analysed the medical records of a patient manifesting chronic sclerosing sialadenitis within the submandibular gland.
Results: Our case is a 62-year-old female with a submandibular mass, rapidly growing over 5 months, treated by surgery. The histopathological examination revealed preserved lobular architecture with thickened septa, dense lympho-plasmacytic infiltration, periductal fibrosis and loss of acini-features characteristic for Kuttner's tumor.
Conclusions: Although chronic sclerosing sialadenitis was first described in 1896, this clinical entity is underdiagnosed by many surgeons. There is not enough evidence to support any diagnostic procedure helpful in differential diagnosis of this benign condition. Given the high rate of malignancy in firm, painless lesions of the submandibular region, surgical excision is recommended. Thus Kuttner's tumor is usually diagnosed by a pathologist.

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Tuberculous infection within Warthin's tumor of parotid gland

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Introduction: Warthin's tumor is the second most common lesion seen in major salivary glands. There are only about 200 cases of tuberculosis within the parotid gland mentioned in literature. In our work, we present a case of comorbidity of Warthin's tumor with tuberculosis of the parotid gland.

Methods: We analyzed medical records of a patient suffering from mycobacterial infection within Warthin's tumor.
Results: a 74-year-old female with a 2-year history of a non-tender lump located behind the left mandibular angle was the subject of a superficial parotidectomy. Neither signs of active pulmonary tuberculosis nor systemic symptoms were visible. The istopathological examination showed adenolymphoma with epithelioid cell granulomas typical for tuberculosis. The patient received antimycobacterial treatment.
Conclusion: There are two paths of mycobacterial spread to the salivary glands. Infection might reach the parenchyma or lymphatic tissue of the parotid gland from sputum through ducts or afferent lymphatic vessels. Mycobacteria might also reach the gland by heamatogenous or lymphatic metastases from origin in the lungs.
Inclusions of salivary ducts in intraparotid or paraparotid lymph nodes seem to be the main factor in the pathogenesis of Warthin's tumor. Adenolyphomas with inflammatory changes are rarely seen. Patey and Thackray considered the cystic component of the tumor as a medium for bacteria. Nowadays infarction of the tumor stroma is taken to be the cause of inflammation within Warthin's tumor.
In the presented case, it remains unclear whether tuberculosis or neoplasm was the primary lesion.

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Modification of surgical approach to massive carcinomas of maxillo-ethmoidal complex

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The classical approach to advanced carcinomas of the maxillo-ethmoidal complex was first reported by Dieffenbach, Weber and Zange. It enabled resection of the maxilla and wide access to the orbit. The scission ranged from the lower labium oris through the nasomalar fold, horizontally to the inferior orbital rim. However, in case of penetration to the pterygopalatine fossa, the above approach is insufficient. Therefore, an extension has been performed using Fairbanks--Barbosa's approach (a common pterygopalatine fossa approach) prolonged horizontally to the front side. The modification provides access to half of the craniofacial and an en-block resection of maxillo--ethmoidal complex tumors and those located in the pterygopalatine fossa. Moreover, in the case of orbital and anterior cranial fossa penetration of tumors (with a scission in the supraorbital arch instead of an inferior orbital rim scission) the modified approach is advantageous. The aim of the study is to create a satisfactory approach to advanced carcinomas of the maxillo-ethmoidal complex with orbital penetration and/or penetration to the pterygopalatine fossa.
The study was conducted on 11 patients with advanced carcinoma of the above region, surgically treated in the years 2006–2010.
Survival rates in the examined group were as follows: 2 patients died within one year from the operation, 4 patients died within the 5-year observation period, without recurrence, 5 patients died within 3 years from surgical treatment (one with local recurrence).
According to the authors, the discussed modification is recommended due to good visualization of the tumor topography providing the possibility of their radical resection.

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Badanie kontrolne za pomocą aparatu do wizualizacji graficznej przebiegu rozwarcia zwieracza ust przełyku u pacjentów po laryngektomii

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Laynx w 1881 r., a Struebing i Londois w 1889 r. opisali pojedyncze przypadki pacjentów po laryngektomii z wykształconą mową przełykową. Twórcami metody diagnostycznej opartej na badaniu rozwarcia zwieracza ust przełyku byli Seeman i Van Den Bergh. Metoda w początkowym okresie była przeznaczona do określenia poziomu, z jakim pacjent może opanować mowę przełykową. Podczas dalszych badań zauważono dodatkowy element diagnostyki, umożliwiający wczesne wykrycie nawrotów procesu nowotworowego w okolicach ust przełyku. Materiał dotyczy 96 pacjentów leczonych w latach 2008–2010 w Klinice Laryngologii Śląskiego Uniwersytetu Medycznego w Katowicach. Wszystkich chorych zakwalifikowano na

podstawie TK krtani oraz wyniku badania histopatologicznego z wycinka pobranego z guza krtani do całkowitej laryngektomii. Stopień zaawansowania w skali TNM wynosił T3N0M0–T4N2M0 w skali złośliwości histologicznej od G1 do G3. U 74 chorych przeprowadzono uzupełniającą radioterapię z powodu niskozróżnicowanego raka krtani lub potwierdzonych histopatologicznie dodatnich marginesów chirurgicznych. 16 pacjentów miało wcześniej wszczepioną protezę głosową typu Provox. Wszyscy pacjenci zostali poddani badaniu urządzeniem do pomiaru ciśnienia rozwarcia zwieracza ust przełyku.W trakcie dwuletniej obserwacji w 28 przypadkach (29%) ciśnienie otwarcia ust przełyku wyniosło ponad 80 mmHg. 22 pacjentów (79%) było poddanych laryngektomii całkowitej z uzupełniającą radioterapią, u 6 (21%) wykonano całkowitą laryngektomię bez leczenia uzupełniającego, 2 chorych miało wszczepioną protezę głosową typu Provox. Po przeprowadzonym TK szyi oraz badaniu histopatologicznym wycinka wznowa raka krtani potwierdziła się w 23 przypadkach (82%). Zastosowanie aparatu do pomiaru oraz wizualizacji graficznej przebiegu otwarcia zwieracza ust przełyku u chorych po laryngektomii całkowitej może być użyteczne w doborze odpowiedniej metody rehabilitacji głosu i mowy oraz we wczesnej diagnostyce wznów raka krtani i/lub gardła dolnego.

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Mięsaki tkanek miękkich regionu głowy i szyi w materiale Kliniki Laryngologii Śląskiego Uniwersytetu Medycznego w Katowicach

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Wprowadzenie: Celem pracy była ocena skuteczności leczenia mięsaków tkanek miękkich (Soft tissue sarcoma – STS) u dorosłych w materiale Katedry i Kliniki Laryngologii Śląskiego Uniwersytetu Medycznego w Katowicach (do 2007 Śląskiej Akademii Medycznej w Katowicach).
Materiał i metody: Retrospektywna analiza została przeprowadzona dla 22 pacjentów z rozpoznaniem STS w głowie i szyi, leczonych w Klinice Laryngologii Śląskiej Akademii Medycznej w Katowicach, w latach 1980–2010. Najczęstszym rozpoznaniem histopatologicznym był włókniakomięsak. Preferowaną metodą leczenia było postępowanie zabiegowe w połączeniu z radioterapią. Pomimo intensywnego leczenia wyniki są niezadowalające.
Wyniki: Najczęstszą przyczyną niepowodzenia leczenia była wznowa miejscowa, którą stwierdzono w 7 przypadkach. U 2 chorych wykazano przerzuty metachroniczne w węzłach chłonnych, natomiast u kolejnych 4 pacjentów uogólniony rozsiew nowotworu. Spośród 22 pacjentów objętych badaniem 13 zmarło. Kompletne 5-letnie przeżycie w badanej grupie uzyskano w przypadku zaledwie 3 pacjentów.
Wnioski: Zastosowanie leczenia zabiegowego w połączeniu z radioterapią może poprawić jakość życia i przedłużyć życie chorych. Niestety, odsetek wznów miejscowych nadal pozostaje wysoki. Wyniki leczenia STS nadal nie są zadowalające.

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Diagnosis and treatment of head and neck phlegmons – authors' own observations

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[4]Helimed Diagnostic Imaging w Sosnowcu

Introduction: Head and neck phlegmons are rare diseases and they are associated with a high risk of mortality. They derive from different structures of the described anatomical area. Although their etiology might be unknown, they are often odontogenic. Diagnosis of phlegmons is based on imaging studies, especially computerized tomography. A surgical incision and drainage as well as analgesia are usually performed in the treatment.
A retrospective analysis was conducted on 11 patients from three different ENT centres: ENT Department of the Medical University of Silesia in Katowice, ENT Department of the Municipal Hospital in Sosnowiec and ENT Department of the Hospital No.1 in Bytom.

The authors analysed the laboratory results, imaging results, treatment and other factors influencing the course of the disease.
Most of the patients were males and the average age was 50.8. In most cases the phlegmons were diffused and located in different regions of the head and neck. The phlegmons were mainly located in the carotid and parapharyngeal space. Streptococci and staphylococci were mostly found in the examined material. The administration of antibiotics and metronidasol were effective in all cases. Two types of surgical procedure were undertaken-either common abscess incision or a broad incision along the sternocleiodomastoid muscle.
Head and neck phlegmons are rare and they affect patients at any age. The dominating location of the phlegmons depends mainly on the starting point. CT plays the most important role in diagnosis. The treatment is based on surgical procedures and antibiotic therapy.

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Head and neck cancer tissues in transmission electron microscope with high magnifications-ultrastructure – preliminary report

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The aim of the study was to receive a pioneering diagnostic imaging method of head and neck cancer tissues with the application of a transmission electron microscope with high magnifications. The study was performed on the tissues of 16 patients with head and neck cancer. Endogenic normal tissues acted as the control group. Preparation of the tissue specimens was based on a two-hour fixation of the specimens in a 2.5% glutaraldehyde solution in a 0.1 M phosphate buffer (pH = 7.4). Then, the tissues were immersed in a phosphate-buffered osmium tetroxide solution. Following fixation and rinsing in the buffer, the tissues were dehydrated in alcohol and propylene oxide series for embedding in an Epon mixture. Ultrathin specimens were collected on carbon film coated grids and then examined with the application of a transmission electron microscope with an operating voltage of 300 kV and a magnification of 800 000x. Promising results were revealed. Images of a structure containing atoms of structural elements in the examined tissues were found. The prospective study will focus on the assignment of the described structure (cross-linking of atoms) in the tissues before and after radiotherapy and its reference to clinical conditions (early and late recurrences).

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Piezosurgical osteotomy may limit complications associated with anterior skull base lesions by subcranial approach

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The subcranial approach was originally developed by Raveh in 1978 for the management of severe skull base injuries. At present, this approach is used in cases of tumors and other lesions involving the anterior skull base. The bone drill represents a rather aggressive cutting instrument, which intra-operatively is more difficult to control and is more damaging to the soft tissue, especially to the nerve endings, consequently delaying the process of bone healing (Schaller B.J., Gruber R., Merten H.A. et al. Piezoelectric bone surgery: a revolutionary technique for minimally invasive surgery in cranial base and spinal surgery. Technical note. Neurosurgery 2005; 57(4 Suppl): E410). The piezoelectric drill is a more precise cutting instrument, offering better control in all anatomical situations. Piezoelectric surgery facilitates the performing of precise osteotomy lines, micrometric and curvilinear, with absolute confidence, particularly in close proximity to vessels and nerves and other important facial structures (dura mater). (Crosetti E., Battiston B., Succo G. Piezosurgery in head and neck oncological and reconstructive surgery: personal experience on 127 cases. Acta Otorhinolaryngol Ital. 2009; 29(1): 1–9). Piezosurgery is only active

in mineralized tissue. It facilitates very gentle and careful cutting of the bone, without any damage to the dura mater, arteries or nerves. We recommend this system for use in subcranial and combinative skull base approaches. Both subcranial approaches described by Fliss D.M. et al. were used in our patients. The purpose of this paper is to report an initial clinical experience with piezosurgical osteotomy in the subcranial approach. We present two patients with anterior skull base lesions; the case of *Tumor gigantocelullarae* caused by weak trauma of the frontonasal region, and a patient with *Carcinoma planoepitheliale*. The subcranial approach was used in our patients (in the first case Type A, and in the second case Type B). No complications were observed after the surgery. Piezosurgery offers excellent exposure with good functional results as well as improves the outcome by limiting potential complications, particularly in oncological cases. Reconstruction of the anterior skull base is technically challenging and may be further complicated by several factors. We believe that the use of piezosurgical osteotomy may prevent complications and improve the overall outcome. Furthermore, the cosmetic result in the subcranial approach becomes vastly improved, especially when the frontal sinus is opened.

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Piezoelectric System may improve functional and cosmetic effects associated with Resection of large orbital tumors especially in sphenoorbital meningiomas

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Sphenoorbital meningiomas are complex tumors involving the sphenoid wing, the orbit and the cavernous sinus, which makes their complete resection difficult or impossible. (Shrivastava R.K., Sen C., Costantino P.D., Della Rocca R. Sphenoorbital meningiomas: surgical limitations and lessons learned in their long-term management. J Neurosurg. 2005 Sep; 103(3): 491–497). Total removal of sphenoorbital meningiomas with a view to cure and preserve vision should be the goal of treatment (Bikmaz K., Mrak R., Al-Mefty O. Management of bone-invasive, hyperostotic sphenoid wing meningiomas. J Neurosurg. 2007 Nov; 107(5): 905–912). However, according to some authors, total resection was not achieved in such patients due to the impossibility to resect the dura mater in the superior orbital fissure without causing significant complications (Scarone P., Leclerq D., Héran F., Robert G. Long-term results with exophthalmos in a surgical series of 30 sphenoorbital meningiomas. J Neurosurg. 2009 Nov; 111(5): 10; 69––77). Similar problems can occur in the case of large tumors of the deep retrobulbar compartment, especially if they involve the orbital apex and the optic canal. Another issue is improvement of the cosmetic result in the orbitofrontal approach, especially when the frontal sinus is opened. The Piezoelectric System is only active in mineralized tissue. This method, with a saw thickness of only 0.5 mm facilitates very gentle and careful cutting of the bone, without any damage to the dura mater, arteries or nerves. We suggest using this system in orbitofrontal and skull base approaches and the early results were compared with classic craniotomy. The paper shows the results of total resection of a giant optic nerve *Sheath Meningioma*, a giant *Neurofibroma* by the classic approach and *Angioma cavernosum* removal with use the Piezosurgical System. The Piezoelectric System offers excellent exposure and cosmetic results. Furthermore, it improves the outcome and often makes complete resection possible especially in optic nerve sheath meningiomas and sphenoorbital meningiomas.

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Rehabilitacja wzrokowa w chorobie Stargardta z wykorzystaniem funkcji biofeedback mikroperymetru MP1 – opis przypadku

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Choroba stargardta to najczęściej występująca dystrofia plamki. Związana jest z postępującym uszkodzeniem warstwy nabłonka barwnikowego (RPE) i warstwy fotoreceptorów. W 90% przypadków dziedziczenie jest autosomalne recesywne. Najczęściej choroba ujawnia się między 7 a 12 rokiem życia. Prowadzi do utraty widzenia centralnego, przy zachowanym widzeniu obwodowym.

Wykorzystanie standardowej perymetrii jest mało przydatne do oceny progresji choroby Stargardta ze względu na brak centralnej fiksacji u tych pacjentów. Zastosowanie mikroperymetrii wyposażonej w automatyczną funkcję kontroli ruchów oka (*automatic eye-tracking*) umożliwia otrzymanie wiarygodnego wyniku, nawet przy niestabilnej fiksacji. Badanie mikroperymetryczne pozwala na obrazowanie stopnia zaawansowania choroby Stargardta, monitorowanie jej przebiegu oraz ocenę stopnia progresji choroby. W pracy prezentujemy przypadek 26-letniej kobiety z chorobą Stargardta z dnem żółtoplamistym, pozostającej w naszej obserwacji od 12 roku życia. U pacjentki zastosowano rehabilitację wzrokową z wykorzystaniem funkcji *biofeedback* mikroperymetru MP1. Po dwukrotnej serii ćwiczeń przeprowadzonej w lutym i wrześniu 2012 r. uzyskano poprawę parametrów fiksacji obu oczu – większą centryczność i stabilność oraz niewielką poprawę ostrości wzroku do bliży z Sn OP, OL = 1,5 do Sn OP, OL = 1,0. Ostrość wzroku do dali nie zmieniła się w obu oczach i wynosiła V OP, OL = 0,3.

Fiksacja poprawiła się w oku prawym z 37% (*poor central*) do 52% (*predominantly central*), a w oku lewym z 9% (*predominantly eccentric*) do 38% (*poor central*). Badanie mikroperymetryczne pozwala na ocenę zaawansowania choroby Stargardta oraz monitorowanie jej przebiegu. Zastosowanie funkcji biofeedback mikroperymetru MP1 umożliwia rehabilitację wzrokową pacjentów dotkniętych tym schorzeniem. Rehabilitacja wzrokowa może reorganizować obszary kory wzrokowej, co tłumaczy się zjawiskiem remapowania. Badania te jednak wymagają dalszych obserwacji, a efekty wydają się obiecujące.

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Wyniki leczenia jałowej martwicy głowy kości udowej za pomocą zogniskowanej fali uderzeniowej – doniesienie wstępne

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Jałowa martwica głowy kości udowej stanowi duże wyzwanie dla lekarza ortopedy i traumatologa. Jak dotąd, nie wprowadzono w pełni skutecznej metody leczenia. Gdy dojdzie do zapadnięcia się głowy kości udowej, jedynym ratunkiem dla pacjenta jest endoprotezoplastyka stawu biodrowego.

Celem naszej pracy jest wczesna ocena wyników leczenia jałowej martwicy głowy kości udowej za pomocą zogniskowanej fali uderzeniowej.

Wykonano prospektywne badanie obejmujące pacjentów z rozpoznaną w badaniu MRI jałową martwicą głowy kości udowej w stadiach I–III wg klasyfikacji ARCO. Zabieg aplikacji fali uderzeniowej jest stosowany pod kontrolą RTG. Za pomocą markera wyznacza się 4 punkty na skórze nad zmianą chorobową. Każde miejsce otrzymuje dawkę 1500 impulsów o gęstości energii 0,4 mJ/mm^2, z częstotliwością 4 Hz. U każdego pacjenta wykonuje się 5 aplikacji. Przed terapią i po jej zakończeniu chory poddawany jest badaniu posturometrycznemu i stabilometrycznemu. Oceniane są także siła leczonej kończyny (metodą tensometryczną), nasilenie dolegliwości bólowych (skala VAS) oraz funkcja stawu biodrowego (skala Harrisa). Kontrola odbywa się po 6 tygodniach oraz 3, 6, i 12 miesiącach.

U leczonych pacjentów zaobserwowano wyraźne

zmniejszenie dolegliwości bólowych oraz zwiększenie ruchomości w leczonym stawie (VAS spadek 6,75 ± ± 0,71 do 2,5 ± 1,7; skala Harrisa wzrost z 55,21 ± ± 15,45 do 89,21 ± 8,26). Spośród parametrów mierzonych na platformie tensometrycznej po terapii zanotowano istotną statystycznie różnicę między średnią prędkością przemieszczenia COP (środka nacisku) podczas marszu, zarówno z oczami otwartymi, jak i zamkniętymi ($p < 0,05$) oraz średnim przemieszczeniem COP wzdłuż osi x (marsz z oczami zamkniętymi) oraz y (swobodne stanie z oczami zamkniętymi).

Wstępne wnioski:

1. Leczenie zogniskowaną falą uderzeniową po 6--tygodniowej obserwacji przynosi wyraźny wzrost komfortu życia pacjentów.
2. Po 6 miesiącach u niektórych pacjentów obserwowano wzrost dolegliwości bólowych i pogorszenie funkcji stawu biodrowego. Wyniki te jednak ciągle były lepsze niż te przed leczeniem.

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Improvement of cognitive functions in depressive patients treated with tianeptine in monotherapy

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The authors put forward hypotheses that during a three-month pharmacological treatment with tianeptine in patients with depressive disorders, there is improvement in: 1) the short-term memory mechanism; 2) the reaction time; 3) the attention mechanism. Twenty patients meeting the ICD 10 criteria for depressive disorders (F32, F33), aged between 18 and 50, were included in the study. Patients with mild-to-moderate depression as measured by their HDRS score were included in the study. During the entire research period, all the patients met the monotherapy requirement (tianeptine). Cognitive functions measurements were performed using Signal, CORSI and RT tests, being a part of the computer-based Vienna Test System (VTS).

Our study showed an improvement in the assessed cognitive functions. It is interesting that the cognitive processes studied by the authors showed no significant correlation with depression scores (HDRS). Lack of such a correlation may suggest that cognitive function improvement in patients treated with tianeptine is effected not exclusively by the subsidence of depression symptoms. That may suggest that tianeptine not only improves depression but also affects the improvement of cognitive functions.

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Analysis of attitude of young people in Poland to the mentally ill

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The stigma of being dangerous, socially incompetent and useless has been carried by the mentally ill for centuries. The aim of the study was to analyze the attitudes of young people towards the mentally disordered and to find which factors determine these attitudes. A specially designed questionnaire was posted on a website particularly popular amongst young users. The questionnaire was composed of 12 questions and consisted of two parts, one of which was concerned with demographic data (respondents' age, gender and place of residence), while the other with the respondents' knowledge of different mental disorders and their views regarding the mentally ill. It contained mainly yes/no questions. The factual knowledge of mental disorders was checked using a list of 8 exemplary illnesses. The respondents were asked to say if each of those 8 illnesses was or was not a mental disorder. A specially designed survey engine had a built-in cookie-based mechanism to avoid re-participation of the respondent. 11.900 people were questioned, including 71% women. 30% of the interviewees were under the age of 19, while 34% of them were between 19 and 24 years old and 36% were over 24. 39% of the interviewees stated they closely knew at least one mentally ill person. 44% of those questioned believed a lot of criminal offenders were mentally ill. 66% of interviewees would not mind sharing a flat with a mentally disordered person, 64%

would agree to work with one. Those who personally knew a mentally disordered person were more inclined to share a flat or start a relationship with such an individual, than the rest of the participants (51% vs. 37% for flat sharing and 38% vs. 26% for starting a relationship, $p < 0.001$). More of those questioned under the age of 19 believed that a significant number of criminal offenders were mentally ill, than those over the age of 24.

Our study shows that many young Poles believe the mentally disordered are inclined to break the law and behave aggressively. These opinions seem to be related amongst others to age and gender, and they result in unwillingness to have relations with the mentally disordered. The better the knowledge of mental disorders and the mentally ill, the more positive the attitude towards them, shows that there is a great need for educational anti-stigma interventions.

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Influence of cannabis abuse on selective neuropsychological tests in schizophrenia patients

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The aim of the study was an assessment of cognitive functioning in abstinent schizophrenia patients with various previous patterns of psychoactive substance abuse. The study was performed on a group of 80 schizophrenia patients (74 male, 6 female), aged 18––40 (mean 25) years, of whom in 40, a co-morbid psychoactive substance abuse was diagnosed. The latter group was subdivided, based on their predominant type of substance (opioid, amphetamine, or cannabis). All the patients were examined during clinical improvement, and the patients with comorbid substance abuse, after a six-week period of detoxification in a therapeutic community. A battery of neuropsychiatric tests was used, which included subtests of the Trail Making Test, Stroop test and Verbal Fluency Test. No significant differences in the clinical factors or cognitive functioning between the two examined groups were found. However, when the patients were divided according to their pattern of substance addiction, it turned out that the group of patients with cannabis, despite the shortest duration of disease and that of addiction, and the highest percentage of using atypical antipsychotics, performed worse on all cognitive tests, significantly so on Stroop's and Fluency tests, compared to the groups with predominant opioid or amphetamine abuse. A statistically significant effect for the Stroop RCNb test was found when comparing the three groups with ANOVA ($p < 0.05$) as well as in individual comparisons between the cannabis and opiates group ($p = 0.03$) and between the cannabis and stimulants group ($p < 0.05$). A statistically significant effect for the Stroop NCWd test was obtained in the comparison of the three groups with ANOVA ($p = 0.018$) and in individual comparisons between the cannabis and opiates group ($p = 0.009$) and between the cannabis and stimulants group ($p = 0.02$). A statistically significant effect for the Phonological fluency test was obtained in a comparison of the three groups with ANOVA ($p < 0.05$) and in individual comparison between the cannabis and amphetamine group ($p = 0.013$). Finally, significant individual difference in the Categorical fluency test was obtained between the cannabis and opiates group ($p < 0.05$). Abstinent schizophrenic patients who previously abused cannabis have worse cognitive functioning compared to other schizophrenic patients with comorbid substance abuse. The possible role of previous cannabis use or cannabis withdrawal in this phenomenon is discussed. We believe that the results of our study may add to the ongoing controversy concerning the effect of cannabis on cognitive functions in schizophrenia.

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Prezentacja pracy z pacjentką z depresją poporodową w modelu psychoterapii integratywnej systemowej

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Prezentacja dotyczy pracy terapeutycznej z 35-letnią kobietą z depresją poporodową. W środowisku medycznym problem depresji poporodowej jest często traktowany jako stan przejściowy, wywołany „huśtawką hormonów", bez wglądu w psychologiczne czy systemowe podłoże, które może być źródłem problemu, a praca terapeutyczna na tym poziomie drogą do skutecznego wyleczenia. Problem pacjentki został przedstawiony w ujęciu psychoterapii integratywnej systemowej. Depresja ujawniła się po porodzie, ale cechy depresyjne jej osobowości były obecne, jak mówiła sama pacjentka, od zawsze. Narodziny dziecka były dla niej ważnym sprawdzianem zdolności do kochania, zdolności do przepływu miłości. Pacjentka czuła, że nie potrafi kochać syna – – dlaczego?…, bo jej miłość była uwięziona i płynęła ku innym osobom, które wcześnie utraciła – ku zmarłemu ojcu i dwójce dzieci, które poroniła. Depresyjna osobowość stała się więc „kokonem" chroniącym przed życiem, w którym pacjentka funkcjonowała, godząc miłość ku zmarłym z codziennym funkcjonowaniem. Jednak w obliczu narodzin dziecka, które domaga się całym sobą uwagi i miłości – tu i teraz, mechanizm ten zawiódł. Pacjentka nie była w stanie pomieścić narastającego w niej napięcia i poczucia winy z powodu braku miłości do syna, co objawiło się depresją poporodową.

Prezentacja zawiera najważniejsze etapy i momenty kluczowe w terapii pacjentki. Punktem przełomowym była praca systemowa w hipnozie, w trakcie której pacjentka doświadczyła wglądu – zrozumiała i poczuła, jak jej depresyjność jest powiązana z nieprzyjęciem życia od rodziców. Wystąpienie ukazuje również zadania terapeutyczne i różnorodność zastosowanych technik w ramach modelu psychoterapii integratywnej systemowej. Zawarte zostały także wrażenia z relacji z pacjentką, w tym osobiste trudności terapeutki w kontakcie, a także cenne sugestie z superwizji. Najistotniejszą zmianą osiągniętą w terapii była zmiana w relacji z synem, pacjentka zaczęła czerpać radość z macierzyństwa. Efekty pracy zostały nie tylko przedstawione opisowo, ale również zostały zobiektywizowane testem CORE-OM, który wykazał zmianę na poziomie istotności klinicznej.

Problem śmierci osób bliskich, w tym poronień, nie jest zwykle łączony z etiologią depresji poporodowej, a – jak wykazuje prezentowane studium przypadku – może stanowić źródło problemu oraz drogę do odzyskania miłości i cieszenia się macierzyństwem.

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Ultrasonic vocalization (USV) depends on mouse strain genetic background

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Mice similarly to some other rodent species communicate with specialized sounds in the ultrasonic range called ultrasonic vocalizations (USV). Evaluation of this behavioral activity enables estimation of the social interactions in animal models of diseases involving psychiatric manifestations related to the social environment like autistic spectrum disorders (ASD). Because transgenic mouse models are generated in most cases on a mixed 129SV/C57Bl/6 genetic background, we were interested if the parameters that characterize USV differ between these two mouse strains and we compare them additionally with the BALB/c line. In order to analyze USV, we applied on newborn animals the standard isolation test and compared the standard parameters. The obtained results become an important hint for the selection of proper experimental controls for future studies on USV using transgenic disease models.

All the animals used for the experiments were bred in the animal facility of the Center for Experimental Medicine and are offspring of certificated strains provided by Charles River Laboratories (BALB/ /cAnCrl, C57Bl/6NCrl, 129S2/SvPasCrl). To analyze the possible differences in USV between the selected mouse strains, we applied the standard isolations test. For the test, we used 3 to 4 litters from each strain, so at least 15 pups (male and female) were analyzed from each strain. USV was recorded every second postnatal day between P2 and P14. The test duration was 7 min. Vocalizations were recorded with a condenser

ultrasound microphone Avisoft-Bioacoustics CM16/ /CMPA and the UltraSoundGate 116Hb recording interface (Avisoft Bioacoustics, Germany). The recorded vocalizations were analyzed with integrated software Avisoft SASLab Pro.
In the first instance, we analyzed three parameters:
1) Developmental time course of the vocalization rate – number of single USVs in one minute
2) Developmental time course of the call duration – – mean duration of a single USV call
3) Sonogram classification according to Scattoni and Branchi 2010
All three parameters showed significant differences between the selected mouse strains.

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Physiological role of TSC1 and TSC2 in cerebellar Purkinje cells and autistic-like behaviors

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Tuberous Sclerosis Complex (TSC), is an autosomal dominant disorder characterized by the development of hamartomatous growths throughout many organs including CNS. Many patients with TSC suffer from mental retardation, cognitive abnormalities, epilepsy and autism. Linkage studies of affected families revealed two genes responsible for TSC: TSC1 and TSC2 coding hamartin and tuberin respectively. Both proteins act as mTOR pathway inhibitors and control the translational machinery in each type of cell. Because of the confirmed role of cerebellum in autism etiology, we applied the cell specific DNA recombination system Cre/loxP to specifically knockout TSC1 and TSC2 genes in the cerebellar Purkinje cells of mice. Analysis of the transgenic animals should give answers regarding the role of hamartin in these neurons with respect to autism etiology.
Genomic sequences coding for TSC1 and TSC2 have been modified by the insertion of two loxP sites in two separate transgenic mouse lines. Using the Cre/loxP approach, we plan to switch off the expression of both genes and establish a transgenic line mutated for TSC1 and TSC2 in cerebellar Purkinje cells (PC). A PC specific switch off of hamartin and tuberin enables one to estimate if simultaneous knockout of both proteins leads to different phenotypic manifestations, than in the case of independent mutants.
Animals from the new transgenic strain will be analyzed by means of behavioral methods focused mainly on autism related traits.
Because of the cerebellum-involved mutation, we look first at the motor coordination of transgenic offspring. Detailed evaluation of the obtained results revealed severe impairment of motor coordination in the elevated runway test.