

Issued since 1920

2020

VOLUME **56** SUPPLEMENT 1

MEDICINA

- ABSTRACTS

**accepted for the International
Scientific Conference
on Medicine**

organized within the frame
of the 78th International
Scientific Conference
of the University of Latvia

Riga, Latvia

ISSN 1648-9233

**Abstracts
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Oral presentations

BASIC MEDICAL SCIENCE & PHARMACY

Pharmacists' perspective on pharmacovigilance and barriers towards adverse drug reactions reporting in Lithuania: Qualitative study

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Background. Spontaneous adverse drug reactions (ADRs) are a significant cause of morbidity and mortality. Every report of a suspected ADR by patient or healthcare professional has a substantial impact on signal detection of new, rare, or serious ADRs. The number of reports received by *EudraVigilance*, the European database for ADRs is growing yearly; however, it does not correspond to the number of used medicines. Under-reporting remains a significant issue undermining the effectiveness of spontaneous reports.

Objective. The aim of the current study was to highlight the importance of pharmacists in pharmacovigilance and to identify barriers to ADR reporting in Lithuania.

Methods. A semi-structured interview approach was used in order to reach the aim of this study. Five community pharmacists (CPs), with experience varied between 1.5 and 16 years, were recruited and interviewed through a convenience sampling technique. All interviews were audio-taped, transcribed verbatim, and were then analysed for thematic content analysis.

Results. The analysis of the interviews revealed four major themes: familiarity with the pharmacovigilance system in Lithuania, ADR reporting experience, training on pharmacovigilance and ADRs, and the role of collaboration between patients, healthcare and pharmaceutical professionals. All the interviewed CPs have a general understanding of the pharmacovigilance system and ADR reporting procedure; however, they do not participate in the system actively. Only two CPs had reported ADRs to the competent authority. Current research suggests that the primary barrier to ADR reporting is still remaining significant knowledge gaps with regard to ADR reporting procedure and its importance to medicine safety. It was highlighted by the CPs that the current dissemination of information is not sufficient and can be advanced through continuous professional development programs with integrated theoretical and practical workshops.

Conclusions. All the interviewed pharmacists emphasized a lack of information about ADRs and the pharmacovigilance system in Lithuania, insufficient training and tools to update and amend the knowledge. The information gained from this study disclosed that the current methods used by authorities to promote ADR reporting are insufficient and indicated several key themes that can be used in establishing and continuing efforts to support the pharmacovigilance system in Lithuania.

Acknowledgments. The authors report the absence of conflict of interest in this work. No sources of funding were used to assist in the preparation of this study.

Drug-related problems in Lithuania

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Background. Drug-related problems include medication errors (involving an error in the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not) and adverse drug reactions (any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function). The pharmacist as the final gate keeper is the one who is the last in the chain to detect errors and prevent them.

Objective. The aim of the current study was to investigate the prevalence of drug-related problems among community pharmacy patients in Lithuania

Methods. 620 patients of the random selected community pharmacy were chosen for medication review during the period from April to August of 2017. Altogether, they had 1634 third form ((with national health insurance fund reimbursement) and 1156 first form (without national health insurance fund reimbursement) prescriptions and also 434 non-prescription (self-medication) items (only the items that were bought during the pharmacy visit or declared by the patients themselves were detected). The inclusion criteria – the use of more than 3 medications and agreement to participate in a survey. 1 questionnaire and pharmacist review of their medication were provided for each patient. Lexicomp® Drug Interactions and Micromedex Drug Interactions checkers were used to check drug-drug interaction. Data were entered into SPSS (version 22.0) and analysed using descriptive statistics. Z-score test was used to analyse differences among groups. Results were considered statistically significant, when $p < 0.05$.

Results. It was discovered that 34.2 % ($n = 212$) of the cases have drug-related problems. The main drug-related problems detected in this study were: inappropriate adherence (28.2 %, $n = 175$), unnecessary drug therapy (2.9 %, $n = 18$), dose too high (1.9 %, $n = 12$), adverse drug reaction (0.8 %, $n = 5$), wrong drug (0.3 %, $n = 2$). The result of the study showed that the greatest part of prescriptions had a drug-drug interaction (91 %, $n = 569$). The moderate interactions were the most common (88 %, $n = 504$). The minor interactions were less common (7.6 %, $n = 43$). The level of major interactions was 3.8 %, $n = 22$. 10 cases of these 22 were successfully solved after collaboration with physician. Most respondents (75 %, $n = 434$) who use more than 3 medications do not care about the drug-drug interactions.

Conclusions. Early interventions of the pharmacy and identifying risk factors that contribute to the development of drug-related problems may aid in the prevention of them.

Acknowledgements. Authors declare the absence of conflict of interest.

CYP2C19, CYP2D6 and CYP2C9 genotyping for minimization of therapeutic failure and adverse drug reactions

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Background. CYP2C19, CYP2D6 and CYP2C9 are encoded by genes which are highly polymorphic. Such polymorphisms are influential in occurrence of adverse drug reactions (ADRs) and treatment efficacy.

Objective. To identify patients with abnormal metabolic profiles which are susceptible to developing ADRs or achieving therapeutic failure.

Methods. A total of 54 patients' pharmacogenetic tests were conducted by Autogenomics Infiniti system in Kaunas University Clinics, Department of Genetics and Molecular medicine. Based on the genotype-metabolic phenotypes, patients were classified to: Normal metabolisers (NMs), intermediate metabolisers (IMs), Rapid metabolisers (RMs), Ultrarapid metabolisers (UMs) and poor metabolisers (PMs). Clinically significant alleles were assessed.

Results. Genotype-phenotype distribution of CYP2C19 enzyme: 18 pts (33.33 %) with *1/*1 — NMs; 14 pts (25.93 %) with *1/*2; *2/*17 — IMs; 15 pts (27.78 %) with *1/*17 genotype — RMs; 4 pts (7.4 %) with *17/*17 genotype — UMs; 3 pts (5.56 %) with *2/*2 genotype — PMs. An improved protective effect of clopidogrel after myocardial infarction has been observed in *CYP2C19**17 allele carriers, while *CYP2C19**2 allele carriers are not capable of generating active metabolite of clopidogrel, have lower plasma clearance and longer half-life of diazepam compared to NMs. *CYP2C19* PMs have reduced elimination of proton pump inhibitors (PPIs), consequently eradication of *H. pylori* infection when treated with *CYP2C19* metabolized PPIs is greater among *CYP2C19* PMs. *CYP2C19* PMs are susceptible of ADRs and plasma concentration fluctuations when treated with *CYP2C19* metabolised tricyclic antidepressants. *CYP2D6* results: 26 pts (48.15 %) with *1/*1, *2/*2, *1/*2, *1/*41, *2/*41 genotypes were NMs; 21 pts (38.89 %) with *1/*5, *2/*4, *10/*41, *1/*4, *1/*3, *2/*5, *2/*4, *2/*6 genotypes were IMs; 2 pts (3.7 %) with *2XN genotype were UMs; 5 pts (9.26%) with *4/*5, *4/*10, *4/*9, *4/*41 genotypes were PMs. *CYP2D6* polymorphisms have implications across many drugs, for instance, antidepressants, antipsychotics, antiarrhythmics, opioid analgesics, anticancer drugs. The impact that a *CYP2D6* polymorphism has on therapy is related to the metabolism of prodrugs. *CYP2C9* enzyme: 44 pts (81.48 %) with *1/*1 genotype were NMs; 10 pts (18.52 %) with *1/*2; *1/*3 genotypes were IMs. *CYP2C9**2 and *CYP2C9**3 loss of function allele carriers have low enzyme activity and are at risk of developing an ADR, especially for *CYP2C9* substrates with a narrow therapeutic window, such as S-warfarin, phenytoin, glipizide, and tolbutamide.

Conclusion. Our study showed that rapid, ultrarapid and poor metabolic phenotypes accumulated 53.70 % of patients. This can result in therapeutic failures, ADRs and fluctuations of plasma concentrations when standard dosing is used.

Acknowledgements. Authors of this study declare absence of conflict of interest. No funding for this study was received.

Antioxidant, anti-inflammatory and neuroprotective properties of bog bilberry *Vaccinium uliginosum* L. pomace extract *in vitro*

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Background. Among the extensively studied biological effects of *Vaccinium* spp. berry, the properties of bog bilberry (*V. uliginosum* L.) are less investigated. A number of papers published on the polyphenol content and profile in berries show that *Vaccinium* berries are a rich source of polyphenolic substances, carbohydrates, vitamins, as well as lipids (Grace et al., 2014; Klavins et al., 2015). The bioactive compounds of berries have various health-promoting effects such as preventing and treating many oxidative stress-related diseases, among them cardiovascular diseases, cancer, aging, diabetes mellitus and neurodegenerative diseases. Substances with antioxidant and anti-inflammatory properties possess neuroprotective potential. However, the extracts from the berry juice industry waste, also called berry pomace, are not fully researched.

Objective. The aim of the current study was to evaluate biological properties of bog bilberry pomace extract *in vitro*.

Methods. Broad spectrum of spectrophotometric and fluorescent assays was exploited. Anti-oxidant properties of the extract were assessed by total antioxidant capacity (TAC), antiradical (DPPH) and superoxide dismutase (SOD)-like activity assays. Anti-inflammatory activity was evaluated as inhibition of xanthine oxidase (XO), lipoxygenase 15 (LOX15) and cyclooxygenase (COX) activities. Next, potency of the extract to inhibit acetylcholinesterase (AChE) activity and potentiate effect of known AChE inhibitor neostigmine was assessed.

Results. TAC was found to be 0.397 ± 0.029 µg/mg of ascorbic acid equivalents. The extract showed concentration-dependent DPPH radical scavenging and SOD-like activity with IC₅₀ at 0.25 mg/ml, inhibition of XO with IC₅₀ at 0.125 mg/ml. Bog bilberry extract inhibited COX1 and COX2 activity in similar manner, however, selectivity was not found. Approximately 30 % of COX inhibition was reached at 1 mg/ml concentration. The extract did not inhibit LOX15 activity. Bog bilberry extract inhibited AChE activity with IC₅₀ at 2 mg/ml and potentiated effect of neostigmine.

Conclusion. The bog bilberry pomace extract possesses anti-oxidant and anti-inflammatory, effects, which are closely connected with neuroprotective properties.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, the Faculty of Medicine, University of Latvia.

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Morphofunctional characteristics of hematopoietic progenitor cells in myelodysplastic syndrome in culture *in vitro*

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Background. Myelodysplastic syndrome (MDS) is a group of heterogeneous clonal diseases, which are based on the defection of hematopoietic stem cells, and leads to dysplastic changes in the bone marrow and ineffective haematopoiesis (Gluzman et al., 2017; Shastri et al., 2017). MDS is characterized by a high risk of transformation to acute myeloid leukaemia (AML) (Will et al., 2012). Therefore, the study of the characteristics of hematopoietic progenitor cells in culture is of a paramount importance for understanding the mechanisms of transformation of MDS to AML.

Objective. The aim of the current study was determination of morphofunctional features of hematopoietic progenitor cells in myelodysplastic syndrome *in vitro*.

Methods. Bone marrow samples of 18 patients with myelodysplastic syndrome, namely, refractory anaemia with an excess of blasts I and II were cultured in DMEM medium with 20 % FBS, 1 % of antibiotics (penicillin/streptomycin) and L-glutamine and 50 ng/ml GM-CSF in semisolid agar *in vitro* for 14 days. The obtaining colonies and clusters were examined under an inverted microscope, with further study of their cellular composition.

Results. 18 bone marrow samples of patients with myelodysplastic syndrome were analysed. It has been shown that hematopoietic progenitor cells have a reduced ability to colony (5.0 ± 2.3 per 1×10^5 of explanted cells) and cluster's formation (9.0 ± 2.1 per 1×10^5 of explanted cells) than control (38.5 ± 1.2 and 65.0 ± 3.5 per 1×10^5 of explanted cells, respectively), and they have a whimsy shape. In addition, among other cellular aggregates, colonies of fibroblast-like cells (1.1 ± 0.1 per 1×10^5 of explanted cells) and colonies with adipocytes on their surface (6.6 ± 1.4 per 1×10^5 of explanted cells) were distinguished in some patients (5 patients). Cellular composition of colonies testified to their morphological alterations.

Conclusions. Hematopoietic progenitor cells of patients with myelodysplastic syndrome have a reduced ability to form colonies and clusters. Furthermore, cell aggregates were distinguished by their changes in cellular composition and shape. Colonies with fibroblast-like cells and with adipocytes on their surface were identified.

Acknowledgements. The authors declare the absence of conflict of interest.

Potential biomarkers for early diagnosis of multiple sclerosis

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Background. Multiple sclerosis is a multifactorial disease, its precise cause is not understood yet. Oxidative stress is considered to be one of possible factors triggering development of the disease. Quite a few consequences of oxidative stress have been already explored, but full picture has not yet been acquired. Overexpression of the nitric oxide synthases (NOS) could be involved in the MS pathogenesis leading to the synthesis of harmful peroxynitrite ions that act as extremely potent toxic agents.

Objective. The aim of this study was to quantify levels of nitrates (NO_3^-) and nitrites (NO_2^-) in plasma and serum samples taken from MS patients. In parallel, we have studied specific types of DNA in peripheral blood mononuclear cells (PBMNC) of MS patients.

Methods. Nitrates and nitrites were analysed by chemiluminescence on Sievers NOA 280i in 80 plasma and serum samples taken from MS patients and 80 healthy subjects as a control group ($n = 20$ both for the study group and the control group for plasma and serum samples). Enzymatic alkaline comet assay was performed on PBMNC samples from 20 MS patients and 20 subjects in control group. Currently, the total number of analysed samples for this study is $n = 120$. Some samples for all analyses were taken from the same person, thus, in the future there might be a complete statistical analysis of all factors for each patient from the sample pool.

Results. MS patients had significantly higher levels of nitrates and nitrites both in plasma and serum compared to the control group. MS patients also had higher levels of DNA single-strand breaks induced by potassium bromate (KBrO_3) and hydrogen peroxide (H_2O_2) with and without site-specific enzymes FPG and Endonuclease III.

Conclusions. Statistical analysis of the obtained data has shown a statistical significance between MS group and control group of each assay.

Acknowledgements. This work was supported by European Regional Development Fund project No. 1.1.1.1/16/A/016, and the University of Latvia research project “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”.

Internalizing aptamers for the development of bi-functional aptamer constructs

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Background. Aptamers are short (40–100 nt), single-stranded DNA or RNA oligonucleotides, that can bind specific target due to their 3D structure rather than binding complementary as other therapeutic oligonucleotides (e.g. siRNA, miRNA). Compared to antibodies, aptamers are smaller, more stable, easier to synthesize and easier to develop. Aptamers have been developed to target different signalling pathways and currently are undergoing clinical trials for several oncological diseases – metastatic renal cell carcinoma, leukaemia, metastatic pancreatic cancer and others (1). Aptamers that internalize into cells can be used in multi-component constructs to deliver siRNAs selectively. Modular nanostructures containing aptamer as targeting component and large, functional mRNA as a payload have been described recently (2). Aptamers that are internalized into target cell nucleus provide an opportunity to develop bi-specific constructs that can target nuclei specific cellular processes, e.g. regulation of transcription factors, interaction with promoter or enhancer regions, miRNA inactivation.

Objective. To identify RNA aptamers that internalize into cell nucleus and can be used to deliver functional agents to cell nucleus when incorporated in a multi-component oligonucleotide construct.

Methods. Randomized fluorinated RNA (F-RNA) library that is resistant to nuclease degradation was used for cell-SELEX. After F-RNA library incubation with 769-P (clear cell renal cell carcinoma cell line) cells, nuclei were isolated using Nuclei EZ Preparation kit (Sigma-Aldrich, Product # NUC101-1KT). Internalized F-RNAs were isolated from nuclei using Direct-zol RNA MiniPrep (Zymo Research, Product # R2050). RNAs were reverse transcribed, amplified and used for next selection cycle. After seven selection cycles, RNA library was sequenced using benchtop high-throughput sequencer Illumina MiSeq.

Results. We have performed seven cell-SELEX selection cycles and acquired F-RNA library enriched with nuclei-internalizing aptamers.

Conclusions. The identified aptamers can be further used to develop bi-functional aptamer constructs containing secondary aptamers already reported in scientific literature.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, the Faculty of Medicine, University of Latvia. K. P. work in this study has been supported by PhD research scholarship administered by the University of Latvia Foundation and funded by “Mikrotikls” Ltd.

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Smokeless tobacco associated with periodontal disease and oral malignity, a pilot study

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Background. Smokeless tobacco (snus) is a product that is placed under the upper or lower lip. The nicotine present in this product is absorbed in the body through capillaries in the mucous membrane. Sale of smokeless tobacco is prohibited in the Latvia, nevertheless, in recent years smokeless tobacco is becoming increasingly popular due to young athletes. However, they are not fully informed about possible harmful effects on the oral health due to lack of information.

Objective. The aim of this pilot study was to determine the influence of smokeless tobacco to oral mucosa and periodontal microbiome.

Methods. Using a questionnaire about smokeless tobacco consumption, a survey of a heavy snus group, a light snus group and a control group were made. Oral biopsy samples were collected from heavy and light snus users groups. Samples were immunohistochemically tested for Ki67, PGP 9.5, CAB, IL-1, IL-10. Biofilms from gingival sulcus were collected from all groups and tested with RT-PCR for the presence of pathogenic periodontal bacteria *A. actinomycetemcomitans*, *P. gingivalis*, *T. forsythia*, *T. denticola*, *P. intermedia*. The quantity of bacteria was expressed by the reference interval Lg/equivalents/sample. Statistical analysis was made by Mann-Whitney U test. Statistics SPSS 17.0 to determine differences between results was made. Approved by Rīga Stradiņš University Ethics Committee, permit No. 22/28.01.2016. Written consent was obtained from each research participant.

Results. Biopsy results showed parakeratosis, epithelial disorganization, vacuolization with prevalence of seborrheic keratosis, oral ulcerations. PGP 9.5 marked epitheliocytes, nerve fibres, and fibroblasts. Ki67 basal epitheliocytes were viewed. IL-10 was possessed in the epithelium. IL-1, CAB were absent. Microbiological examination showed presence of periodontal pathogens in heavy and light snus groups ($p < 0.05$). Presence of periodontal pathogens in control group was not statically significant ($p > 0.05$).

Conclusion. Decrease of apoptosis, parakeratosis and cellular disorganization suggest about the decompensation in tissues homeostasis, mainly in the smokeless tobacco raised lesions. Tobacco usage stimulates the persistent proliferation potential in the oral epithelium. PGP 9.5 marked fibroblasts and epithelium might suggest about the phenotype changes in the cells. Smokeless tobacco promotes periodontal diseases regardless of frequency and amount of snus.

Acknowledgements. The authors acknowledge the support of the Department of Morphology, Rīga Stradiņš University.

The *in vitro* study of antimicrobial effect of essential oils on Gram-negative bacteria

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Background. One of the most urgent problems of modern times is the expansion of bacterial resistance against antimicrobials, thus it is necessary to seek and investigate different ways to fight the bacteria by using alternative methods.

In this case, the recent years have shown that polyherbal formulations possess antimicrobial properties, and have a potential to be very useful by themselves or in combination with antibiotics. Unfortunately, most of these formulations are only effective in eliminating Gram-positive bacteria.

Objective. The aim for this study was to test essential oils (cinnamon and oregano) for their antimicrobial efficiency for countering Gram-negative bacteria, especially those found in non-healing chronic infections.

Methods. In this research, the Minimal Inhibitory Concentration (MIC) for essential oils (EO) was determined, and the results were compared with antimicrobials. We chose to work with *S. aureus*, *E. faecalis* (both for testing purposes), *P. aeruginosa*, *E. coli* and *P. mirabilis*. To determine MIC for EO, microplate method was used.

As MIC controls for essential oils, we took gentamicin (0.4 mg/mL) and streptomycin (1 mg/mL).

The presence of bacteria was tested in microplate 24 hours after it had been in the thermostat at the temperature of 37.7 °C. The presence was determined with spread plate method, and after that with resazurin stain. The obtained results were checked by repeated trials.

Results. Based on the obtained results, cinnamon essential oil could be considered more effective for Gram-negative bacteria than oregano essential oil.

The best result for oregano EO was on *E. coli* (the mean MIC = 0.0447; SD ± 0.0281 µg/ml), but results on *P. mirabilis* (the mean MIC = 22.90; SD ± 3.75 µg/ml) and *P. aeruginosa* (the mean MIC = 57.30; SD ± 1.43 µg/ml) were significantly worse. Cinnamon EO showed great results on all three microorganisms – *P. Mirabilis* (the mean MIC = 0.0245; SD ± 0.0155 µg/ml), *P. aeruginosa* (the mean MIC = 0.0982; SD ± 0.0491 µg/ml) and *E. coli* (the mean MIC = 0.0245; SD ± 0.0062 µg/ml).

Cinnamon EO showed great antimicrobial effect on *P. Mirabilis*, which had a lower mean MIC (0.0245; SD ± 0.0155 µg/ml) than both of the antibiotics used (the streptomycin mean MIC = 7.8 µg/ml, the gentamicin mean MIC = 0.0300 µg/ml).

Conclusions. Results show evidence that both (cinnamon and oregano) essential oils have antimicrobial properties. In our research, cinnamon EO shows significantly better results on Gram-negative bacteria than oregano EO. In future, cinnamon EO could be added to polyherbal formulations to improve the antimicrobial efficacy on Gram-negative bacteria.

Natural killer cell activation mechanisms in oncolytic measles virus therapy

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Background. Oncolytic viruses (OV) are rapidly gaining clinical relevance among the currently used cancer immunotherapies. Oncolytic measles viruses (oMV) excel among other OVs with their effective cytotoxic actions, excellent safety record and well-characterized vector platform. Activation of tumour-specific immune response is crucial for the efficacy of oMV and strategies for enhancement of immunotherapeutic properties of oMV are investigated. Natural killer (NK) cells are a type of cytotoxic lymphocytes that are involved in destruction of virus-infected and malignant cells. Mechanisms of NK cell activation during oMV therapy are incompletely understood, limiting the ability to rationally use the NK cell cytotoxic potential to increase the therapeutic efficacy.

Objectives. The aim of the study is to investigate mechanisms of NK cell activation in oMV therapy and to develop novel strategies for modulation of NK cell activity to increase the therapeutic efficacy of oMV.

Methods. Impact of oMV infection on NK cell activity, NK cell cytotoxicity against oMV-infected primary melanoma cell lines and oMV impact on dendritic cell (DC)–NK cell interactions were examined *in vitro*. Untouched NK cells were isolated from blood of healthy donors by magnetic sorting and NK cell–autologous monocyte-derived DCs were used in coculture experiments. Cell surface marker expression was assessed by flow cytometry and cytotoxicity was measured with real-time assays.

Results. Results demonstrate that NK cell phenotype does not change upon infection with oMV and that NK cell cytotoxicity does not differ against oMV-infected and uninfected primary melanoma cell lines. However, NK cells upregulate expression of activation markers CD69 and CD107a in cocultures with autologous oMV-infected DCs. oMV replication is crucial for the NK cell activation, since it is not observed if using UV-inactivated oMV. Also, DCs upregulate expression of maturation markers only after infection with replication-competent oMV. Separation of NK cells from DCs in the cocultures by transwell inserts does not significantly impact the NK cell activation, suggesting that mainly soluble factors are responsible for the effect.

Conclusion. DCs play a role for NK cell activation in the context of oMV infection. Further work will focus on identification of the factors involved in DC–NK cell interactions and assessment of implications for the therapeutic efficacy of oMV.

Acknowledgements. This work was supported by the European Regional Development Fund project No. 1.1.1.2/VIAA/2/18/292 (1.1.1.2/16/I/001). R.V. is listed as an inventor for a patent regarding the use of RNA viruses for cancer immunotherapy owned by Heidelberg University.

A novel approach for quantification of amyloid- β plaques after long-term intracerebral brain infusion using Alzet microosmotic pumps

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Background. Accumulation of amyloid- β (A β) plaques is a hallmark of Alzheimer's disease (AD), a leading cause of dementia, represented by memory deficits and has an immense negative socio-economic impact. To characterize the A β pathology *in vivo* models, a wide range of techniques has been applied over the past decades. One of the most commonly used methods for quantification of A β are high-resolution scans and imaging systems. Various imaging systems offers additional possibility to write scripts – an adjustment of method for quantification. These improvements offer a new analytic tool to quantify A β plaques and can be useful for a several therapeutic approaches, e.g. method for continuous systemic infusion for targeted delivery of test substances into specific sites are Alzet[®] pumps. Until now, no data are available how to examine A β and distribution of test substances in the brain using Alzet[®] pumps.

Objective. To develop an improved methodology to quantify A β plaques (number, size and distance from reference point) and precise distribution of experimental compound infused by Alzet[®] pumps in the brain tissue.

Materials and methods. For this study, we used AxioVision analysing software, by providing additional scripts, to create new analytic tool. C57BL/6J mice, 50 days old, were used, by receiving short sequenced peptide, and loaded into Alzet[®] pumps (model 2006). These pumps were implanted for 42 days into mouse by stereotactic surgery. At the age of 100 days, mice were sacrificed, and brains were collected for immunohistochemistry, with 4G8 antibody. After staining, tissue sections were digitized using a Panoramic MidiII slide scanner and analysed using the AxioVision software.

Results. We generate additional scripts for AxioVision analysing software, to quantify not only number of A β plaques, but also precise size and distance from reference point for A β plaques. After selecting the region of interest 'Alzet[®] pump tool' allows to separate multiple A β plaques, meanwhile alternative imaging software's recognise as one. Our analytic tool provides quantification of A β to analyse plaque numbers, size and coverage, calculating the region of the lost brain tissue, after the removal of Alzet[®] pump cannula.

Conclusions. The results demonstrated that this new analytic tool is beneficial to analyse long-term continuous intracerebral experimental compound infusions using Alzet[®] pumps. This method helps to generate reliable data for A β characterization and distribution of experimental compounds.

Acknowledgements. The study has been supported by Fundamental research grant in Bio-medicine and Pharmacy, University of Latvia, and project No. lzp-2018/1-0275.

Whether the challenge with cigarette smoke can predict lung disease development later in the life?

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Introduction. It is well known that around 20 % of smokers develop chronic obstructive pulmonary disease (COPD), while 15–24 % of smokers develop lung cancer. However, most people are resistant to tobacco smoke. Body's ability to neutralize toxic compounds may vary from person to person and may result in different susceptibility to cancer and COPD.

Objective. The aim of this study was to find out whether the degradation pattern of some of the most common toxic agents present in cigarette smoke could predict the development of lung pathology later in life.

Methods. We analysed the changes in the concentration of 20 volatile organic compounds (VOCs) in the exhaled air of volunteer smokers before and within 2 hours after smoking.

We performed 62 exhaled air analyses on 17 volunteers of different age, gender, smoking history and health status. Smoking subjects abstained from smoking for at least 10 hours prior to the study. Exhaled air samples were taken before, immediately after, 30 minutes, one hour, and two hours after smoking. Air was adsorbed in adsorption tubes and subsequently analysed by gas chromatography/mass spectrometry.

Results. Smokers who had abstained from smoking for at least 10 hours before the test still had significantly elevated levels of toluene, benzene, ethylbenzene and xylene in exhaled air compared to non-smokers. Immediately after smoking, concentrations of both aromatic and aliphatic VOCs increased rapidly. Higher maximum concentrations were found in younger smokers with shorter smoking histories. The clearance patterns of toxic compounds, measured in exhaled air were different for each individual. For some individuals, VOC concentrations declined exponentially to baseline levels. Others were presented with a biphasic model with a transient negative phase. A delayed pattern was also observed when the increase in VOC concentrations peaked one hour after smoking.

The examined persons reproduced their characteristic response patterns in repeated trials.

The rate and pattern of VOC clearance are dependent on a number of factors, including the rate of hepatic metabolism, the deposition of VOCs into body fat, the permeability of certain compounds to the alveolar-capillary membrane, and the interaction of various compounds.

Conclusions. We hypothesize that the individual's body response pattern to the challenge with cigarette smoke reflects the potency of subjects to inactivate certain toxic compounds and thus may be indicative of predisposition to certain smoke-related lung diseases.

As this is a pilot study, further data collection is needed to validate the hypothesis.

Acknowledgements. The study was funded by University of Latvia. No support has been received from tobacco industry.

Label-free characterisation of differentiation and senescence using imaging flow cytometry

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Background. Imaging flow cytometry adds to the power of conventional flow cytometry (FC) by saving images of all acquired objects. Additionally, it accumulates a whole range of signal parameters in brightfield and sidescatter (darkfield) and allows certain analysis without the need to label cells. This approach is already being applied in diagnostics and research on new animal models where no antibodies are available.

Objective. To characterize and distinguish, in a label-free manner, cells exposed to different culture conditions (e.g. differentiated MSCs, senescent cells, cells grown in spheroids).

Methods. Human kidney tumour cell line 769P and adipo-differentiated dermis-derived mesenchymal stromal cells (MSC) were evaluated morphologically and data were analysed using published protocols and various image analysis software (IDEAS, CellProfiler, FCSExpress). Differentiation was carried out using commercial differentiation kit and spheroids were formed by hanging drop method. Cell senescence was induced by doxorubicin (50–500 nM) for a week.

Results. Our preliminary results suggest that adipo-differentiated MSC can be distinguished not only based on their size but also brightfield signal intensity and texture features. Cells grown both adherently on plastic and in 3D spheroids, despite representing seemingly homogeneous population, were segregated by various darkfield channel parameters. Senescent cells could be distinguished from control cells based on texture parameters and displayed differences depending on the doxorubicin concentration used for senescence induction and duration of the exposure.

Conclusions. We conclude that imaging FC offers new opportunities for label-free analysis of cell differentiation and senescence status.

Acknowledgements. Project is funded by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” at the Faculty of Medicine, University of Latvia.

Application of *M. tuberculosis* whole genome sequencing in cluster investigation and verification of infectious sources in children-related tuberculosis outbreak

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Background. Childhood tuberculosis (TB) occurs in the same regions of the world where adult TB is common. Infectious source case tracing, detection of TB outbreaks and determination of possible transmission roots between patients is crucial for TB control strategies. Whole genome sequencing (WGS) is commonly used worldwide in studies of the *M. tuberculosis* (Mtb) strain population structure, exploration of pathogen evolution and public health investigations including confirmation of epidemiological links between patients.

Objective. The aim of this study was to estimate the genetic diversity of Mtb strains involved in one of the largest children-related TB outbreak in Latvia and to assess possible transmission directions in detail.

Methods. In this outbreak investigation, Mtb cultures were isolated from the involved patients in 2005–2016. Mtb DNA samples were provided by the Centre of Tuberculosis and Lung Diseases. WGS analysis of these samples was performed, using IonTorrent technologies. Bioinformatic analysis of raw sequencing data was performed on Galaxy web platform. SNP differences between samples were assessed using web-based tools PhyResSe and CSI Phylogeny v 1.4. A minimum spanning tree was constructed to visualize possible relationships between patients.

Results. In total, WGS analysis was performed for 14 Mtb strains with identical spoligotype obtained from 13 patients involved in the outbreak of TB. The assessment of accumulated SNPs in clinical isolates revealed less than 12 SNP differences between the isolates confirming the genetic relatedness of Mtb strains. The analysis of strain microevolution during the outbreak provided information about the possible timing and direction of the transmission. The results also confirmed epidemiological link between the close relatives. No SNP differences were observed for recurrent case in comparison to the initial episode indicating endogenous disease reactivation in the respective patient.

Conclusions. This study highlighted the opportunities of WGS in outbreak investigation. The use of WGS provided evidence of transmission in addition to classical genotyping and epidemiological methods.

Acknowledgements. We would like to express our gratitude to BMC core facility Genome Centre for the contribution in sequencing. This study was supported by Latvian National Research Programme VPP “BIOMEDICINE” and Riga Stradiņš University grant No. 23030102. We declare the absence of conflict of interest.

Exploring pharmacogenetics aspects of anti-tuberculosis treatment in Latvian tuberculosis patients

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Background. The treatment regimen for tuberculosis (TB) is associated with significant side-effects. Most cases with anti-TB drug-induced liver injury (ATLI) have been attributed to isoniazid. Genetic polymorphisms of several drug-metabolizing enzymes including *NAT2* slow acetylation genotype and *GSTM1* null genotype have been recognized as the risk factors of ATLI.

Objective. The aim of this study was to identify genetic polymorphisms of genes encoding isoniazid-metabolizing enzymes in Latvian TB patients.

Methods. DNA samples and clinical information were obtained from the Centre of Tuberculosis and Lung Diseases, Riga East University Hospital, Riga, Latvia. *NAT2* genotyping was performed by 7-SNP panel identification (G191A, C282T, T341C, C481T, G590A, A803G and G857A) using conventional PCR, cloning and sequencing methods. Obtained sequences were compared to the reference sequence (EC 2.3.1.5) (GenBank: X14672.1) using CodonCode Aligner software. A possible *NAT2* phenotype was assigned based on the obtained genotyping data of alleles showed the presence/absence of a signature mutation, which alone causes a change such that the resultant protein shows reduced activity. *GSTM1* null genotype assay was carried out by a comparative duplex PCR.

Results. In total, 33 TB patients were included in our study, 10/33 (30.3 %) women and 23/33 (69.7 %) men. Before the TB therapy, all individuals had normal ALAT/ASAT biochemical indicators, except 4 patients with an insignificant increase of ALAT (i.e. 40, 49, 62 and 68 U/L; reference for men < 41 U/L, women < 31 U/L). Depending on genotyping results, all individuals were classified in four groups: 1) *NAT2* slow acetylator and *GSTM1* null genotype: 13/33 (39.4 %); hyperfermentemia was detected in 3 cases (23.08 %). 2) *NAT2* slow acetylator and *GSTM1* plus genotype: 10/33 (30.30 %) of patients; hyperfermentemia was detected in 2 cases (20 %). 3) *NAT2* intermediate acetylator and *GSTM1* null genotype: 6/33 (18.18 %) of patients; hyperfermentemia was not present. 4) *NAT2* intermediate acetylator and *GSTM1* plus genotype: 4/33 (12.12 %); hyperfermentemia was not present.

Conclusions. Genotypes that determine the slow rate of *NAT2* acetylation enzyme and *GSTM1* null genotype were predominant among the patients included in our study. Increased ALAT and ASAT values were observed in *NAT2* slow acetylators. More research is needed in larger patient populations to verify the results.

Acknowledgements. This study was supported by VPP “BIOMEDICINE”.

Compact bone analysis after vacuum drying

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Background. Finding more affordable and effective ways of producing bone grafts for transplantation has a significant importance, since these are among the most transplanted tissues used in patient care. One of the production steps is to remove water from the bones. The current method in use is lyophilisation. In lyophilisation, water is removed through sublimation. This process is expensive and can take over 60 hours. Therefore, we investigated whether vacuum drying could be an effective method for extracting water from the bones without affecting their histological integrity.

Objective. The aim of the study was to determine whether vacuum drying can be an effective method to remove water from *substantia compacta* in order to preserve bones for possible future transplantation.

Methods. The bones used in the study were *os tibia* from beef with the mean age of 15 months and 8 months. Firstly, the bones were cleaned, leaving only *substantia compacta*. Afterwards, 6-cm-long samples were cut out of the central parts of the *tibiae*. Then, from the 6 cm pieces 1–4 mm large samples were cut out using a microtome. Before being placed in a vacuum chamber, the samples were weighed and their microhardness was measured. The samples were placed in a vacuum chamber for 24 hours. After this, the samples had all the parameters measured again and they were split into 2 groups. The first group was sent for histological analysis, while the other one was dried in a thermostat for 4 hours at 60 °C to determine the true loss of water. To determine the histopathological integrity, the analysed bone samples were compared to bones that were not processed in a vacuum chamber.

Results. The mass of all samples after 4 hours in a thermostat was almost identical to the mass after vacuum drying.

After vacuum drying processing, all the samples sustained an identical structure to those bones that were not vacuum dried, as attested by evaluating osteocytes, collagen fibres and osteoids.

After vacuum drying, both groups of bones aged 8 months and 15 months had a decrease in microhardness on the Rockwell scale.

Conclusions. The results indicate that vacuum drying might be an effective way to remove water from bones and that vacuum drying is not an aggressive process with regard to bone tissue.

Acknowledgements. The authors would like to express their gratitude to Traumatology and Orthopaedics Hospital and Riga Technical University Institute of Biomedical Engineering and Nanotechnologies in Latvia for their technical support.

The influence of orally administered nanostructural highly activated charcoal on functional activity of hematopoietic progenitor cells in the culture of diffusion chambers *in vivo*

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Background. It has been established that nanostructural highly activated charcoal administered orally for medical purposes removes toxic substances of endogenous and exogenous nature. Peroxidation plays an important role in the pathogenesis of acute irradiation exposure, it seems appropriate to use the sorption properties of the test substance to minimize the damaging effect of irradiation on organism. Hematopoietic system is most sensitive regarding irradiation, consequently, investigation of early stages of haematopoiesis is appropriate and relevant.

Objective. To investigate hematopoietic progenitor cells of healthy and irradiated animals under the influence of charcoal with highly activated carbon.

Methods. 24 Wistar rats were orally fed charcoal (bulk density 0.12 g/cm³) with fodder at the rate of 1.2 g per animal for 3 days before and at the day of the irradiation. Rats' femoral bone marrow cells under sterile conditions were placed in diffusion chambers with semisolid agar at a rate of 1×10^5 cells per chamber and cultured for 8 days in the peritoneal cavity of CBA mice. On the 8th day of cultivation, the number of colonies and their morphological features were analysed under an inverted microscope (Olympus, Japan).

Results. When comparing the results of the bone marrow cultivation of animals irradiated at a sublethal dose, and animals that were fed charcoal for 3 days before irradiation, the differences in the efficiency of colony formation were found, namely, 6.0 ± 0.8 colonies and 5.1 ± 1.1 clusters per 1×10^5 of explanted cells were found for irradiated animals, and 9.1 ± 1.3 colonies and 20.2 ± 2.4 clusters per 1×10^5 of explanted cells were found in animals that were previously fed charcoal.

Conclusions. As a result of the analysis of the obtained data, we came to the conclusion that the test substance improves colony formation in comparison with the group of irradiated animals fed charcoal. This process occurs at the level of stem cells and its nearest progenies.

Acknowledgements. The authors declare the absence of conflict of interest.

Correlation between uric acid and triglycerides levels in normotensive patients in the Ukrainian population

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Background. Hyperuricemia (HU) prevalence is 20 % in females and 20.2 % in males of the general population. HU is a predictor for development of dyslipidaemia. The early detection of HU level may be useful as a preventing method to correct progression of the dyslipidaemia and atherosclerosis.

Objective. To examine the correlation between levels of serum uric acid (SUA) and triglycerides (TG) in normotensive patients.

Methods. The total of the 68 normotensive persons, 32 with SUA < 400 µmol/l (the 1st group) and 36 with SUA > 400 µmol/l (the 2nd group), were included in study. The groups were comparable in sex and age. SUA and triglycerides levels were done according to standard technique. A 24-hour blood pressure monitoring was performed by using the monitor ABMP-50 HEACO.

Results. The baseline TG level was 0.62 ± 0.2 µmol/l in the 1st group and 0.89 ± 0.2 µmol/l in the 2nd group ($p < 0.05$). The average SUA level in the 1st group was 315 ± 22 µmol/l; in the 2nd group – 468 ± 28 µmol/l. The patients with higher levels of SUA had higher levels of triglycerides within reference values. The average blood pressure for the 1st group was: DaySBP 120 ± 5 mmHg, DayDBP 74 ± 4 mmHg, while for the 2nd group – DaySBP 132 ± 6 mmHg ($p < 0.05$), DayDBP 82 ± 4 mmHg ($p < 0.05$), respectively. The Pearson's correlation between the levels of SUA and TG in the 1st group was $r = +0.23$ and in the 2nd group $r = +0.41$ ($p < 0.05$).

Conclusions. The positive correlation between uric acid and triglycerides levels was found in normotensive patients. If uric acid level had rich cut point of 400 µmol/l, the correlation strength between SUA and triglycerides had increased due to significant influence of the SUA excessive amount.

Acknowledgements. The authors declare the absence of conflict of interest.

Medieval dental calculus microbiome in comparison to modern dental plaque and modern dental calculus microbial profiles

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Background. Ancient dental calculus – calcified oral plaque biofilm – is one of the best archaeological materials to provide us with information related to ancient human microbiome and its interaction with its host. A currently widespread hypothesis states that the disruption of the balance and diversity of human microbiota may lead to a range of diseases, and knowledge about our ancestral microbiome would be extremely helpful in exploring of this hypothesis. However, it demands a careful interpretation of differences between the modern and ancient microbiome. The modern oral microbiome research operates mostly with living bacterial biofilm because of the fact that today the dental calculus is not as common as it was historically. Although being related to the same specific body area, dental calculus and dental plaque are exhibiting different forms of dental biofilm, and microbial differences between them are not sufficiently studied.

Objective. To investigate three sample groups – modern dental plaque, modern dental calculus and ancient dental calculus – in order to explore possible differences and evaluate the information retrieved from ancient oral microbiome in the context of human health and disease.

Methods. A set of archaeological dental calculus samples from Latvian medieval cemeteries was collected, pre-processed according to the ancient DNA (aDNA) handling protocols, and aDNA extraction was performed. Modern human oral plaque samples and dental calculus samples were collected and subjected to DNA extraction. All sample groups further underwent shotgun sequencing using Ion Torrent technologies. Data were analysed with a variety of bioinformatic techniques using Galaxy public server and Kraken software. Environmental contamination control was evaluated using R package “decontam”. Microbial functional profiles were assessed via HUMAnN2 metabolic analysis network. Statistical analysis and representation was performed on MicrobiomeAnalyst public server.

Results. Ancient dental calculus was more closely related to the modern dental calculus than to the modern dental plaque both in terms of taxonomic profiling on phylum and genus levels and in terms of metabolic pathways revealed. We found distinct metabolic pathways in all sample groups, which may further expand our perception of microbiome–host interaction. The ancient dental calculus samples had greater diversity of microorganisms, as well as greater diversity of retrieved metabolic pathways in comparison to both modern sample groups.

Conclusions. Overall, our results show that there are noticeable differences between microbial profiles of dental calculus and dental plaque, and it must be considered in ancient oral microbiome research.

Acknowledgements. This work was supported by the ERDF project No. 1.1.1.1/16/A/101.

Analytical method validation for small-scale radiopharmaceutical production laboratory

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Background. Radiopharmaceutical (RP) manufacturing laboratory SIA “Kodolmedicinas klinika” was established in 2015. The goal of our laboratory is to provide Latvian oncology patients with pharmaceutical products, Ga⁶⁸ and / or Lu¹⁷⁷ labelled DOTA-TATE and PSMA compounds.

Objective. The aim of the current study was to interpret and apply analytical method validation processes, in accordance with good manufacturing practice (GMP) and good radiopharmaceutical practice (GRP). Validation process was conducted according to ICH Q2 “Validation methodology” and European pharmacopeia “Guide for the elaboration of monographs on radiopharmaceutical preparations”.

Methods. Validation objectives were set and defined in standard operational procedure. For each objective, data sets were produced via measurements of standard samples (St.), “cold” standard samples (Cld. St.) and product. To determine, whether HPLC method fulfils a validation objective, acceptance criteria were established.

System suitability (SS) test is used to determine whether a method is suitable for evaluation of target analytes. This means determining retention time (R_t) of St. and Cld. St. samples; and calculating theoretical plate count, desired resolution.

Method specificity (MS) is used to prove that the method will be able to identify the target analyte in presence of contaminants.

St. sample undergoes degradation by UV light. Positive spike is added to determine peak corresponding to undamaged analyte.

Specificity for HPLC radiation detector is validated by determining resolution between product and unbound radionuclide.

Detector linearity (DL) proves that method parameters do not interfere with detection. For UV detector, measurement results are plotted against sample concentration.

For radiation detector, the analyst uses sample, with known activity, and repeats measurements, allowing for decay. Peak area is plotted against calculated activity.

Results. SS – resolution 0.69; precision St. and Cld. St. respectively RSD = 0.40 % and RSD = 0.35 %; R_t accuracy for sample mixture 100.00 %

MS – nr. of peaks after degradation = 4; resolution, in product region, 1.8 and 12.6; resolution product / unbound radionuclide 34.62.

$$DL - R^2_{(UV)} = 0.99; LoD < 1 \mu g / 1 mL; signal to noise = 9.6; R^2_{(rad)} = 0.99$$

Conclusion. The discussed method has been successfully validated but a greater degree of certainty can be achieved by setting more validation objectives, and by using more parameters – tailing factor and injection precision.

Acknowledgements. This study was supported by University of Latvia Foundation and “MIKROTĪKLS” Ltd. donation; project No. 2201. I would also like to extend my gratitude to specialists from “Scintomics” Ltd. and “Grindeks” Ltd. for consultation.

GASTROENTEROLOGY & GASTROINTESTINAL ONCOLOGY

Presence and severity of symptom-based gastroesophageal reflux disease associated with levels of pepsinogen

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Background. Levels of pepsinogen indirectly reflect the functional state of the gastric mucosa and can be used for non-invasive diagnosis of gastric atrophy. Studies show controversial results regarding pepsinogen level and type and severity of reflux disease at endoscopy. Large population studies on symptom-based gastroesophageal disease (sbGERD) and levels of biomarkers are lacking.

Objective. The aim of the study was to assess whether pepsinogen levels are associated with the presence and severity of sbGERD.

Methods. 2085 participants (aged 40–64) selected from the general population for the GISTAR study in Latvia completed a detailed questionnaire (supplying sociodemographic, lifestyle, medical data) and were tested for pepsinogens (Pg) by a latex-agglutination test-system (Eiken Chemical, Tokyo). sbGERD was assessed by GerdQ questionnaire score: ≥ 8 (likely) and < 8 (unlikely). PgI, PgII levels, PgI/II ratio and presence of gastric atrophy (cut off value $\text{PgI/PgII} \leq 2$ and $\text{PgI} \leq 30 \text{ ng/mL}$) were compared between participants with and without sbGERD and according to frequency of reflux, retrosternal burn and epigastric pain. Odds ratios (ORs) and 95 % confidence intervals (CIs) were calculated for sbGERD and gastric atrophy, PgI/PgII ratio, as well as for frequency of reflux and retrosternal burn, adjusting for previously identified risk factors for sbGERD (body mass index, proton pump inhibitor use, peptic ulcer disease history, fruit/vegetable consumption, meal frequency) and gender.

Results. Prevalence of sbGERD was 16.5 %. Pg I/II ratio was higher in those with sbGERD (4.43, IQR 2.36 vs 3.84, IQR 2.28, $p < 0.001$). Pg defined gastric atrophy was less common with sbGERD (4.1 % vs 8.2 %, $p < 0.01$). PgI/II ratio increased with increasing frequency of reflux and retrosternal burn ($p < 0.001$). In multivariate analysis, after adjusting for risk factors, sbGERD was associated with increasing PgI/II ratio (OR 1.17; CI 1.10, 1.26) and inversely with Pg defined gastric atrophy (0.51; 0.29, 0.90). PgI/II ratio increased with increasing frequency of retrosternal burn and reflux (1.21; 1.07, 1.38 and 1.17; 1.00, 1.36 for symptoms 4–7 days a week).

Conclusions. In our large population-based cohort study, the inverse association between gastric atrophy and sbGERD could be explained by decreased acid exposure. The relationship between increasing levels of pepsinogen and frequency of sbGERD requires further research, as studies show that pepsinogen levels do not correlate with endoscopically confirmed severity of GERD.

Acknowledgements. The study was supported by Latvian Council of Science, project No. lzp-2018/1-0135 “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions.”

Autoimmune gastritis: determining the level of acid production as one of the criteria for severity of atrophy

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Background. Autoimmune gastritis (AIG) is a silent and slowly progressing immune-mediated disorder with nonspecific clinical manifestations. Due to the blurred manifestations of the disease, the diagnosis is difficult, which leads to a significant delay in the diagnosis. In the existence of anemia and concomitant autoimmune diseases, AIG may be suspected. The first step is to determine the anti-parietal cell antibodies, which is the optimal screening test for AIG.

Objective. The aim of the current study was to assess the pH level in patients with detected antibodies to parietal cells.

Methods. Altogether 32 patients were enrolled in the study. Patients with identified antibodies to parietal cells were assessed for intragastric pH throughout the day. 3 electrodes were inserted in the stomach – cardia, body and antrum.

Results. 84.3 % ($n = 27$) had hypoacid pH values ($\text{pH} > 4$); 6.2 % ($n = 2$) preserved acid production ($\text{pH} < 4$) in one of the stomach sections; 9.3 % ($n = 3$) preserved acid-producing stomach function.

Conclusions. Autoimmune gastritis is a progressive disease that is usually associated with decreased acid-producing function of the stomach. However, according to our research, not all PCA-positive individuals showed a decrease in acid production, which is most likely due to the degree and stage of atrophy.

High-risk colorectal neoplasia detection rate in patients with positive fecal occult blood test undergoing colonoscopy

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Background. Colorectal cancer (CRC) is one of the most common causes of mortality in Latvia. Colonoscopy is the prime diagnostic tool used for persons with positive CRC screening test (fecal occult blood test). Colonoscopy of higher quality (higher high-risk neoplasia detection rate) ensures higher CRC detection rates, especially in early stages.

Objective. The aim of this study was to evaluate high-risk colorectal neoplasia detection rate in patients with positive fecal occult blood test undergoing colonoscopy.

Methods. The study was conducted in Digestive Diseases Centre "GASTRO" from May, 2019 to December, 2019. Data of colonoscopy and histology were collected from persons aged 50 to 75 with a positive fecal occult blood test undergoing colonoscopy. The main outcome measurement – detection of colorectal neoplasia endoscopically and evaluation histologically. Neoplasia were stratified following the current European Society of Gastrointestinal Endoscopy (ESGE) Guidelines as low-risk (1–2 tubular adenomas < 10 mm, serrated polyps < 10 mm) and high-risk (tubular adenoma ≥ 10 mm, 3 or more adenomas, adenoma with villous histology, serrated polyps ≥ 10 mm).

Results. 193 patients were included in this study, 120 (62.2 %) females and 73 males (37.8 %), with the mean age of 61.92 (SD 6.52) years. Based on colonoscopy data, polyps were detected in 28.5 % ($n = 55$) of cases, and in 5.2 % ($n = 10$) of the cases tumours were found. Histologically, 32 (16.6 %) adenomas, 14 (7.3 %) villous adenomas, 2 (1 %) serrated polyps and 8 (4.1 %) adenocarcinomas were found. Adenoma detection rate was 23.83 % ($n = 46$). In 9 (28.13 %) cases with adenomas, 3 or more adenomas were found, in other 4 (12.5 %) cases, adenomas were 10 mm or larger, and in 1 (50 %) case, the serrated polyp was over 10 mm in size. Consequently, in 19.69 % ($n = 38$) of the cases, high-risk neoplasia were found. There was no statistically significant difference in the polyp detection rate or histological findings between sexes.

Conclusions. The detection rate of high-risk colorectal neoplasia was 19.69 %, therefore every fifth person with positive fecal occult blood test undergoing colonoscopy has a high-risk for CRC development.

Peptic ulcer of the stomach and duodenum in Kazakhstan: Epidemiology features of the incidence

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Background. Peptic ulcer is one of the most common diseases of the gastrointestinal tract. Approximately 10% of the world's population is affected by this disease. The duodenal ulcer (DU) is 4–13 times more common than the gastric ulcer (GU). One of the important factors in the occurrence of the peptic ulcer (PU) of the stomach and duodenum is *H. pylori*.

Objective. To study incidence of peptic ulcer of the stomach and duodenum in Kazakhstan.

Methods. The study period was 10 years (2009–2018), the data of the Ministry of Health of the Republic of Kazakhstan on new cases of peptic ulcer (from I2, ICD – K25–K27) in children (under 15 years of age), adolescents (15–17 years of age), adults (18 years old and above) and the entire population. Indicators were calculated using the generally accepted methods of descriptive and analytical epidemiology.

Results. Over the period of study, 174 641 new cases of peptic ulcer were registered, of which 89.9 % were adults (table).

Table. Peptic ulcer in Kazakhstan

Age group	Number (%)	P±m, ⁰ / ₀₀₀₀	95 % CI, ⁰ / ₀₀₀₀	T, %
Children (under 15)	7 706 (4.4)	18.0 ± 2.2	13.6–22.3	–10.8
Adolescent (15–17)	9 897 (5.7)	129.8 ± 12.5	105.3–154.3	–8.5
Adults (18+)	157 038 (89.9)	132.2 ± 2.7	126.8–137.6	–1.2
Total	174 641 (100.0)	102.7 ± 2.9	96.9–108.5	–2.5

The average annual incidence rate was 102.7 cases per 100 000 of the total population, and in the studied groups high rates were found among adolescents and adults – 129.8 ⁰/₀₀₀₀ and 132.2 ⁰/₀₀₀₀, respectively. At the same time, differences in the incidence among these population groups were not statistically significant ($t = 0.19$; $p = 0.85$). In the dynamics, the incidence rates of PU in Kazakhstan tended to decrease, while the most pronounced among the children were, as follows: children under 15 – $T = -10.8$ ($R^2 = 0.5777$) and adolescents – $T = -8.5$ ($R^2 = 0.6284$).

Conclusions. Based on the analysis conducted in the period from 2009 to 2018, it was found that there was a widespread decrease in peptic ulcer of the stomach and duodenum associated with early eradication and prevention therapy of children, adolescents and adults. Thus, according to the calculated data, it can be noted that the diagnostic measures for the prevention and treatment of ulcer have increased significantly.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

On the assessment of lost life from deaths after stomach cancer in Kazakhstan

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Background. Mortality from stomach cancer (SC) significantly affects the average life expectancy of both sexes and has a great socio-economic importance. Life expectancy is the main integral indicator, recommended by WHO, as the health status and living standards criterion of the population within a particular region.

Objective. To assess the years of life lost (YLL) in connection with stomach cancer-caused death rate in Kazakhstan.

Methods. The information about the deaths caused by SC throughout the Republic of Kazakhstan and the survival tables for 2009–2018. The concept of lost life expectancy was used in order to compare the number of deaths from the cancer, YLL was calculated for the age group of 1–69 years.

Results. Over the researched years, 19 332 people in the Republic of Kazakhstan died from SC, 64 % of which were male and 36 % – female (see the table).

Table. Data about SC in Kazakhstan

Indicators	Both sexes	Male	Female
Number of deaths (%)	19 932 (100.0)	12 755 (64.0)	7 177 (36.0)
Age-standardized rate (ASR), $\frac{0}{0000}$ (95 % confidence interval)	13.2 \pm 0.8 (11.7–14.8)	22.7 \pm 1.3 (20.1–25.2)	7.7 \pm 0.5 (6.6–8.7)
YLL	11 526 \pm 535 (10 478–12 574)	7 477 \pm 334 (6 823–8 130)	4 050 \pm 222 (3 614–4 485)

ASR of SC in the total population was 13.2 per 100 000; while in men (22.7 $\frac{0}{0000}$), the incidence rate was 3 times higher than women (7.7 $\frac{0}{0000}$), the difference was significant ($t = 10.77$, $p = 0.000$). ASR trends tended to decrease – $T = -5.8$ % ($R^2 = 0.9763$), $T = -5.5$ % ($R^2 = 0.9468$) and $T = -6.6$ % ($R^2 = 0.9442$) for males and females, respectively. The average annual YLL in the entire population of the republic was 11 526 person-years, while for men it was higher than for women (see the table). Generally, we observed a decrease in this indicator from 12 930 (2009) to 8 703 person-years in 2018, the average annual rate of decrease of the equalized indicator was $T = -4.3$ % ($R^2 = 0.8989$), and the trends decreased in men ($T = -4.3$ %, $R^2 = 0.9631$) and women ($T = -4.4$ %, $R^2 = 0.6523$).

Conclusions. The assessment of YLL allows us to conclude that the socio-economic losses due to mortality from cancer dynamics demonstrate the tendency to decrease over the studied years, which is undoubtedly associated with an improvement in many spheres of diagnostic procedures and targeted anti-cancer measures in Kazakhstan.

Prevalence of gastrointestinal symptoms among young people and their nutrition habits

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Background. Educational process at university is characterized by a high level of psycho-emotional stress and change in the usual lifestyle, compared to the school period. This creates the conditions for the manifestation of functional gastrointestinal disorders.

Objective. Assessment of the gastrointestinal symptoms' prevalence and nutrition habits among young people.

Methods. For accomplishing the aim of the study, an anonymous survey of 3634 students of the medical university was conducted. Students gave an informed consent to participation in the study. All the participants were asked to complete the GSRS questionnaire and the WHO CINDI program questionnaire through online forms. Among the respondents, the majority were female (80.49 %). The participants of the research were aged from 17 to 34 years, while the average age was 23.34 ± 6.48 years.

Results. The analysis of the survey's results revealed the presence of the following gastrointestinal syndromes: dyspepsia in 2703 of respondents (74.38 %), abdominal pain in 2300 of respondents (63.29 %), reflux syndrome in 1690 of respondents (46.5 %), constipation in 1353 of respondents (37.23 %), and diarrhoea in 1215 of respondents (33.43 %).

Most of the respondents eat 2 times (42.5 ± 0.8 %) or 1 time (24.9 ± 0.7 %) a day. 69.9 ± 0.8 % of respondents cannot always eat at the same time, 45.4 ± 0.8 % of respondents have a limited time for eating, and 30.7 ± 0.8 % of respondents often overeat in the evening. 58.2 ± 0.8 % of respondents are addicted to sweet food, 32.8 ± 0.8 % to spicy food, and 27.4 ± 0.7 % to flour-based food. A specific characteristic of the students' daily diet is the low consumption of fruits and vegetables: 107.14 [40.00; 225.00] and 150.00 [66.67; 300.00] grams per day, respectively. Over the past year, 83.3 ± 0.6 % of respondents have tried to change their nutrition habits. Unfortunately, 53.4 ± 0.8 % of respondents, the students of the medical university, obtain the information about healthy diet from the media, and only 33.0 ± 0.8 % from medical specialists.

Conclusions. A high prevalence of gastrointestinal symptoms among young people was revealed, which requires, on the one hand, analysis of the frequency and characteristics of symptoms in relation to nutrition habits and characteristics of mental status, and, on the other hand, the development of measures to increase the health potential of students.

Acknowledgements. The study was supported by the Grants Council of the President of the Russian Federation, No. MK-1679.2020.7.

Prevalence of low and high risk precancerous lesions in gastric mucosa

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Background. Although multiple studies have shown that incomplete intestinal metaplasia (IM) poses a higher risk for developing gastric cancer, the importance of IM subtyping for gastric cancer risk stratification is remaining debated.

Objective. The aim of our research was to analyse the prevalence of precancerous lesions – atrophy, complete and incomplete intestinal metaplasia (IM) and dysplasia in Latvia, by conducting a pilot study.

Methods. The adult patients aged 26–78 years ($n = 1198$) with dyspeptic complaints referred for upper endoscopy from Latvia were prospectively enrolled into the study. Altogether, five biopsy samples were obtained from each patient. The 4 microns-thick sections were stained with haematoxylin and eosin (H&E), Periodic acid–Schiff–Alcian blue (PAS-AB), but staining with high iron diamine–alcian blue (HID-AB) for the subtyping of IM was performed in biopsies positive for IM in other stains.

Results. The prevalence of atrophy was 77.29 %. The OLGA stage I, II, III and IV was observed in 65.94 %, 7.01 %, 2.67 % and 1.58 % of cases, respectively. The prevalence of IM was 44.75 %. Extensive atrophy was found in 2.83 % of cases, whereas extensive IM was found in 2.67 % of cases. The OLGIM stage I, II, III and IV was observed in 32.47 %, 6.67 %, 2.42 % and 1.58 % of cases, respectively. Corpus restricted atrophy was found in 3.42 % of cases, but corpus restricted IM was found in 3.25 % of cases.

The prevalence of complete IM was 61.54 %, whereas the incomplete IM (type II and type III) made up 38.46 % of the study subjects with IM present.

The low grade dysplasia was found in 4.34% of cases, the indefinite for dysplasia was found in 3.67% of cases.

Conclusions. The prevalence of atrophy and intestinal metaplasia was high in our study, however, the high risks lesions (OLGA/OLGIM III/IV; extensive IM and corpus restricted IM) were low. Furthermore, the prevalence of incomplete IM was high, which could contribute to the high incidence of intestinal type gastric cancer.

Acknowledgements. The study was supported by the cooperative grant from UL and AHL and project No. lzp-2018/1-0135. Our acknowledgments to Digestive Diseases Centre "GASTRO" and the Biobank of Institute of Clinical and Preventive Medicine, University of Latvia for the infrastructure support.

Thiopurine monitoring in late-onset inflammatory bowel disease patients

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Background. Thiopurines are widely used immunosuppressants in inflammatory bowel disease (IBD), but in elderly IBD patients they are associated with an increased risk of adverse effects (AE) [Calafat M. et al, 2018]. Elderly patients with IBD are more vulnerable due to a higher rate of comorbidities, polypharmacy and changes in pharmacokinetics, and therefore have an increased risk for treatment related complication [Broekman M., 2017]. Starting thiopurines over 60 years of age should be followed by a closer monitoring. Thiopurine S-methyltransferase (TPMT) deficiency leads to an accumulation of higher levels of cytotoxic thiopurine nucleotides in patients carrying defective *TPMT* alleles [Robert D. Nerenz, 2018].

Objective. The aim of the current study was to evaluate a role of TPMT genotyping in late-onset IBD patients as a part of therapeutic drug monitoring.

Methods. 127 IBD patients over 40 years old (median age 53 years; Q1–Q3 = 47.0–62.0) were obtained from the Genome Database of the Latvian Population. *TPMT* genotyping with a real-time polymerase chain reaction (PCR) (*TaqMan Drug Metabolism Genotyping Assays*) was performed for detection of rs1800462, rs1800460, and rs1142345 single nucleotide polymorphisms (SNPs). The three common non-functional *TPMT* alleles (*TPMT**2, *3B, and *3C) were determined in 57.5 % women and 42.5 % men. Data were collected about demographics, medication intolerance, allergies and comorbidities. Data were analysed in SPSS®23.

Results. 77 % ($n = 98$) of patients with ulcerative colitis were included in our study, the mean age 55 ± 11 years and 23 % ($n = 29$) of patients with Crohn's disease, the mean age 57 ± 13 years, $p = 0.4$. 92.1 % were wild-type homozygous *TPMT**1/*1 genotype, 7.9 % ($n = 10$) were heterozygous. In total, four patients had a history of azathioprine (AZA) adverse events: gastrointestinal intolerance ($n = 2$), hepatotoxicity ($n = 1$), myalgia ($n = 1$). In total, 20.5 % ($n = 26$) of patients marked allergies on different medication groups as antibiotics, analgesics, etc. The most frequent polymorphism was *TPMT**1/*3A genotype in 6.3 %. No patients were homozygous for any mutation. 7.9 % ($n = 10$) of patients with *TPMT**1/*1 genotype take AZA in standard dosage 2–2.5 mg/kg without any adverse drug effects. In total, 75.6 % ($n = 96$) of patients had comorbidities as cardiovascular diseases (arterial hypertension, angina, chronic heart failure) and endocrine diseases (diabetes mellitus, thyroid disorders, adiposity).

Conclusions. We have identified *TPMT**1/3A as the most prevalent polymorphisms in late-onset IBD patients. TPMT genotyping is an effective method of thiopurines toxicity risk evaluation in late-onset IBD patients. Our data shows that AZA still remains effective treatment in late-onset IBD patients, however, detection of TPMT status should be used as a part of therapeutic drug monitoring.

Functional analysis of miR-1246 in colorectal cancer

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Background. Colorectal cancer (CRC) is currently one of the most prevalent cancer types worldwide and is the second leading cause of cancer-related mortality (Bray et al., 2018). Over the last years, CRC detection rates have improved; however, disease-related mortality remains very high (Bray et al., 2018). Despite increasing access to CRC screening programs in Lithuania and other EU countries, more precise methods for early non-invasive disease detection are very much needed (Kalager et al., 2020; Benard et al., 2018).

MicroRNAs are known as post-transcriptional gene expression regulators and potential biomarkers. It has been shown that differential miR expressions allows to discriminate between normal and cancerous tissues, different stages and subtypes of cancer, including CRC (Di Leva et al., 2013; Schetter et al., 2012). Comprehensive miR analysis showed deregulated miR profiles in CRC. However, in order to understand the functional relevance of miR dysregulation, studies analysing their target genes are of a major importance.

Objective. To determine target genes of colorectal cancer associated miR-1246 and its function in colorectal cancer pathogenesis.

Methods. MTT, clonogenic, dual-light luciferase reporter gene, gene and protein expression assays were performed in SW620 and Caco-2 cell lines after cell transfection with hsa-miR-1246 mimic and inhibitor to determine miR-1246 impact in cell function changes and to confirm its target genes.

Results. Reduced cell viability was observed in Caco-2 (28.1 % $p = 0.02$) and SW620 (28.2 % $p = 0.001$) cell lines 72 hours after transfection with miR-1246 inhibitor.

Clonogenic test results demonstrated that inhibition of miR-1246 decreased colony number in Caco-2 (38.3 % $p = 0.005$) cell line, while overexpression of miR-1246 had no significant effect on colony formation in both Caco-2 and SW620 cell lines.

CRC-associated putative target-oncogenes of miR-1246 were retrieved from TargetScan data base, and *CFTR*, *AXIN2* were selected for further investigation. Dual luciferase assay results confirmed *CFTR* and *AXIN2* as miR-1246 target genes.

Overexpression of miR-1246 decreased the expression of *CFTR* (14 % $p = 0.03$) and *AXIN2* (17 % $p = 0.0006$) genes in SW620 cell line 48 hours after transfection. No statistically significant change was determined in Caco-2 cell line.

Tendency of higher *CFTR* and *AXIN2* expression on protein level was observed after inhibition of miR-1246 in Caco-2 and SW620 cell lines.

Conclusion. *AXIN2* and *CFTR* are direct target genes of miR-1246. Overexpression or inhibition of miR-1246 affected cell viability and colony formation in CRC cell lines.

Acknowledgements. The study was supported by “IsomiR in the pathogenesis of colorectal cancer: from miRNome-wide bioinformatic analysis to their functional validation”, grant No. S-MIP-17-22.

SURGERY

Evaluation of the venous system in peripheral artery disease patients after an endovascular PQ bypass system implantation

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Background. PQ bypass endoprosthesis implantation, using the deep venous system of the leg, is a new and innovative method for long segment peripheral arterial occlusive disease treatment. At the moment, there are no long-term investigations of the leg venous system functionality after PQ bypass endoprosthesis implantation.

Objective. The aim of the study is evaluate lower extremities venous system function after PQ endoprosthesis.

Methods. Prospective, single-centre study was done to evaluate functional activity of venous system. Patients with chronic lower limb ischemia defined as *Rutherford* clinical categories 3–5, TASC C and D type lesions, and those with femoral (SFV) and proximal popliteal vein (PV) diameter in Duplex USG is ≥ 10 mm and \pm venous duplication were included in the study with a two-year follow-up. Evaluation was based on 3 parameters: clinically using *Villalta* scale and venous clinical severity score (VCSS), anatomically via Duplex USG and functionally using ELCAT Vasolab 320 system digital (D-PPG) and venous occlusion (SG-VOP) plethysmography measurements: venous pumping capacity (Vo); venous refilling time (To); venous capacity (VC) and venous outflow (VO). Assessment and comparison between the operated and healthy leg, as well as results of the operated leg before and after surgery, was performed using MS Excel and SPSS 20.0 (Wilcoxon Signed Ranks Test with CI 95 %).

Results. 53 patients (49–87 y/o) were included in the study. The mean observation period was 18.5 (1–24) months. The mean SFV and PV diameters were 10.8 (9–17) mm and 10.6 (8–13.2) mm, respectively, while the mean diameter of implanted stents was 6.5 (6–7) mm, filling 62 % of the venous lumen. Venous duplication was observed in 34 % of patients ($n=18$). After obtaining Duplex USG results from the operated leg, clinically asymptomatic deep vein thrombosis (DVT) was found in 8 % of patients ($n=4$). After the 2-year follow-up period, median D-PPG indices were as follow: To– 24s/18s, Vo– 4.7 %/4.4 % in the operated leg and To– 31s/25s, Vo– 6.3 %/6.4% in the healthy leg. Median SG-VOP indices were as follows: VC– 2.5 %/min, VO– 39 % in the operated leg and VC–2.7 %/min, VO–47.9 % in the healthy leg. Statistically significant difference was observed between all indices measured post-operative and two years post-stent implantation ($p > 0.05$).

Conclusions. The results of our study show that PQ bypass endoprosthesis has no influence over the functional activity of the venous system of the leg and PQ bypass endoprosthesis implantation in the venous system of the leg does not increase the risk of DVT at two years follow-up.

Antibacterial prophylaxis vs treatment in patients after major lower limb amputation

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Background. Antibiotic treatment after clean surgery is controversial. Although not indicated, occasionally the patients receive antibacterial treatment after major lower limb amputation.

Objective. The aim of this study is to evaluate surgical site infection (SSI) rate, systemic infection (SI) rate and mortality after major lower limb amputation of patients receiving antibiotic prophylaxis or treatment.

Methods. Prospective randomised study took place in Riga East University Hospital, Riga, Latvia from December 11, 2018 to January 11, 2020. The study was approved by the local ethical committee. Inclusion criteria: atherosclerosis and/or type 2 diabetes, lower limb gangrene or tumour as an indication for major lower limb amputation, no signs of local/systemic infection before amputation. Patients were randomly divided into two groups. The first group received 1 dose of cefazoline 2 g preoperatively. The second group received additional cefazoline 2 g for 7 days. Hospital stay length (days), comorbidities, status of antibiotic use before the study, local/systemic infection occurrence and hospital mortality were assessed. Statistical analysis was done for Chi-squared test, Log Rank test and Kaplan-Meier analysis with SPSS 22 software. The level of statistical significance was set at $p < 0.05$.

Results. 102 patients were enrolled in the study. There was no significant difference in age, gender and comorbidities in both groups. Prophylaxis group ($n = 52$) had 5 SSI, 3 SI, 15 exitus letalis and the mean hospital stay of 20 days. Treatment group ($n = 50$) had 5 SSI, 2 SI, 7 exitus letalis and mean hospital stay of 16 days. Chi-squared test determined statistically insignificant difference of SSI in prophylaxis ($n = 5$) and treatment group ($n = 5$) ($p = 0.57$). Chi-squared test determined a statistically insignificant difference of SI between both groups: prophylaxis ($n = 3$), treatment group ($n = 2$) ($p = 0.46$). Chi-squared test determined a statistically significant mortality in both groups: prophylaxis ($n = 15$), treatment group ($n = 7$) ($p = 0.04$). Kaplan-Meier analysis determined a survival median for prophylaxis group – 35 days (95 % CI = 19.2–50.7), and for treatment group – 43 days (95 % CI = 20.5–65.4). Log Rank Test in Kaplan-Meier analysis determined a statistically significant difference ($p = 0.034$). It is important to note that only 5 of 22 deaths were brought about by infectious causes (pneumonia, sepsis) and 17 were originated in non-infectious causes (cancer intoxication, thrombosis, acute heart and vascular failure, acute pulmonary and cerebral edema).

Conclusions. From the perspective of infectious complications and mortality, antibiotic prevention alone is not inferior to antibiotic treatment of the patients with major lower limb amputations.

Benefits and limitations in FLACS surgery vs. traditional manual phacoemulsification procedure

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Background. Cataracts are the leading cause of blindness, and cataract surgery is the most common ocular surgery performed worldwide with more than 20 million surgeries annually. Phacoemulsification probe was invented by Dr. Charles Kelman in 1967. In the following decades, foldable intraocular lens (IOL) was invented, allowing to insert an implant through a smaller incision, as well as multifocal and toric IOLs. Femtosecond laser-assisted cataract surgery (FLACS) is the latest development in the history of cataract surgery. In 2010, FDA approved the use of the femtosecond laser for cataract surgery. The femtosecond laser can be used to create tissue planes for arcuate keratotomies, anterior capsulotomies and nuclear fragmentation. The first Femto-LASIK operation in the Baltic region was performed in 2009. The first corneal segment implantation procedure and the first corneal graft with the help of femto laser platform in Baltic states was carried out in 2013.

Objective. The aim of the current study was to compare benefits and limitations that is offered by femto laser platforms with traditional phacoemulsification method.

Methods. The retrospective study was performed in Dr. Solomatin Eye Center. 50 eyes were treated using FLACS surgery, whereas 50 eyes were treated using traditional manual phacoemulsification procedure. Age range was 26–83 years. The mean patient age was 65 years. Used equipment: *Alcon, LenSx; Valeant, Bausch & Lomb Victus; Alcon, Infiniti* phacoemulsification system. FLACS were performed on two different platforms. This study does not claim superiority of any commercial product or service.

Results. The mean visual aberration (VA) was similar in both groups ($p = 0.35$) (SD was wider in phacoemulsification group). Nearly no high-order aberration changes in FLACS group ($p = 0.10$). Significant difference in high-order aberration in phacoemulsification group ($p = 0.010$). Approximately 12 % of manual capsulorhexis achieved ± 0.25 mm accuracy of the femto platform. Mean endothelial cell loss was 133.8 cell/mm² in the FLACS group ($p = 0.001$). The mean endothelial cell loss in the phacoemulsification group, 277.7 cell/mm² ($p = 0.001$). One posterior capsule rupture (in both groups). 100 % of the cases had a complete capsulotomy in FLACS group. No “bridges” observed during femtocapsulorhexis.

Conclusions. FLACS surgery is safe. Results in lowering effective phacoemulsification time. Precise capsulorhexis make FLACS suitable for premium IOL use. FLACS results in a greater procedure efficiency. FLACS results in a decreased post-operative complications.

Long-term outcomes of microvascular decompression for trigeminal, glossopharyngeal neuralgia and hemifacial spasm

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Background. Microvascular Decompression (MVD) is a surgical treatment for facial pain or facial spasm. In specific circumstances, small arteries and/or veins can irritate cranial nerves by compressing them. This microsurgical technique involves protecting these nerves with small Teflon sponges. This anatomical relationship is often referred to as a “neurovascular conflict” (NC).

Objective. To investigate the long-term outcomes of MVD for Trigeminal neuralgia (TN), glossopharyngeal neuralgia (GPN), hemifacial spasm (HFS) and to identify any prognostic factors.

Methods. The total of 498 patients underwent MVD by one surgeon since 1985. Out of all the patients, 116 who were operated since 2005, had undergone a short-term follow-up within one week and a long-term follow-up within 1–4 years after the surgery. Out of these, 106 had TN, 3 had GPN and 7 – HFS. The age of onset was in a range of 42 to 84 years. The main indications for MVD surgery were clinical symptoms of TN, GPN and HFS with finding of a possible NC in MRI; ineffective pharmacological therapy and/or previous unsuccessful destructive procedures. MVD via retro-sigmoid approach to the pontocerebellar region was sufficient in cases when NC was visible during surgery.

Results. Short-term follow-up after MVD of TN revealed that patients were pain free in 94.3 % of the cases, in GN – in 100% of the cases, while HFS showed a cure rate of 85.7 % of all cases. In patients with TN 6 (5.7 %), atypical pain remained with a loss of sensation (after previous destructive procedure). No complications and lethal outcomes occurred. In TN, the NC did not manifest on MRI in 7.5 % of the operated cases. The long-term results showed that 88.7 % of the patients with TN and GN were pain free, and 71.4 % with HFS had completely recovered. Recurrence of TN after MVD was observed in 12 (11.3 %) patients, 6 of whom were successfully treated with Carbamazepinum, whereas 6 patients, who had undergone a previous ablative procedure did not see a decrease in burning and aching facial pain.

Conclusions. MVD may be a safe and effective therapy for patients with TN, GN and HS to achieve relatively higher cure rates and lower complication risks. MVD preserves functionality of cranial nerves and it is recommended as the first surgical method of choice.

Acknowledgements. The authors declare that there is no conflict of interest regarding the publication of this article.

Nuss procedure: how the equipment and anaesthetics impact the results

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Background. Pectus excavatum (PE) is the most common chest wall deformity. PE is corrected by using Nuss procedure. During the procedure, a Nuss bar is implanted and stabilizers can be used. Epidural analgesia is used to control postoperative pain.

Objective. The aim of the current study was to retrospectively analyse the records of those patients of Children's Clinical University Hospital (CCUH) who had undergone Nuss procedure due to PE, to analyse the technique of the surgery, use of stabilizers, postoperative anaesthetics, complications, hospital stay.

Methods. The research includes retrospective data of 216 patients' records with PE who were hospitalized in CCUH from 2006 till 2019. Patients were divided into two groups to analyse epidural anaesthesia – epidural anaesthesia was implemented in everyday practice from 2013, group 1 – patients from 2006 to 2012, group 2 – from 2013 to 2018.

Results. 216 patients were included, male/female ratio 3.3:1. The mean age was 16.5 (SD = 3.1) years. In surgery thoracoscopy on both sides was used in 87.5 %. Stabilizers were used in 63.9 % ($n = 138$), for 82 patients – on both sides. 38 (17.6 %) patients had complications after the surgery. The most common complication was migration of the stabilizers in 5.1 % ($n = 11$) of the cases. Wound infection due to stabilizers was observed in 2.3 % ($n = 5$). With stabilizers on both sides, the complications occurred more often ($p = 0.043$).

The average length of antibiotic therapy was 3.5 days (SD = 1.69), for patients without stabilizers – 2.9 days, with 1 or 2 stabilizers – 4.3 days ($p < 0.001$). The average hospital stay – 8.6 days (SD = 3.15), for patients without stabilizers – 7.4 days, with 1 or 2 stabilizers – 9.4 days ($p < 0.001$). The patients with wound infection spent a longer time in hospital – 12.4 days ($p = 0.005$).

Postoperative epidural anaesthesia was used in 51 cases (23.6 %). The length of hospital stay decreased to 7.41 days ($p < 0.001$). In group 1, the mean duration of the hospital stay was longer (9.5 days) than in group 2 (8 days) ($p < 0.001$) with the longest decrease in 2013 ($p < 0.001$).

Conclusions. Most commonly, thoracoscopy on both sides is used, with stabilizers on both sides. The use of stabilizers leads to more complications. The most common complication is migration of the stabilizers. Stabilizer use increases the length of antibiotic therapy and hospitalization. Introduction of postoperative epidural anaesthesia significantly decreases the length of hospital stay.

Acknowledgements. Study did not receive funding.

Correlation of patients' age with operation time, blood loss and hospitalization time in patients with primary osteoarthritis undergoing cemented hip arthroplasty

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Introduction. World's population is aging and elderly patients comprise a large share of population that is more likely to need surgical treatment. Osteoarthritis is strongly linked to aging but the mechanisms is still not fully understood. Aging causes changes in the musculoskeletal system, which increase the risk of developing osteoarthritis. Osteoarthritis is primarily treated with medication and physical therapy. When conventional therapy no longer can provide satisfactory results, arthroplasty is the next option for treatment.

Objective. The main objective of this study was to analyse the impact of patient age on operation time, hospitalization time and blood loss during surgery in patients with primary osteoarthritis undergoing cemented hip arthroplasty.

Methods. A single-centre retrospective cohort case-review study was carried out. The study population included all patients aged 60 to 80 years with primary osteoarthritis, who have undergone a cemented hip arthroplasty between January 1, 2018 and December 31, 2018. 361 patient cases were included in the study and reviewed. Data were analysed using software SPSS statistics and Microsoft Excel. Nonparametric Spearman's correlations were used to determine correlation coefficient between patient age and operation time, blood loss and hospitalization time. The value of $p < 0.05$ was chosen for the statistical significance.

Results. The analysed population consisted of 269 females (74.5 %) and 92 males (25.5 %) with the mean age of ~72 (71.55) years. The patients' age correlates with hospitalization time Sig. 0,000; correlation coefficient 0.216 (moderate correlation strength). Patients' age does not correlate with operation time Sig. 0,142; correlation coefficient – 0.088, while blood loss during surgery correlates with age Sig. 0,042; correlation coefficient –0,122 (weak correlation strength).

Conclusions. Patients' age correlated with hospitalization time. The mean age of analysed population is ~72 years and population as a whole is ageing – it is important to take into consideration that if the operation is carried out on an elderly patient then it is more likely that a longer stay in hospital will be required. Patients' age had no significant correlation with operation time, which means that the age does not change the operation length. However, patients' age did have a weak correlation with blood loss during surgery. The older the patient was, the less blood they lost during surgery. That means that there are more important factors than age, which were not identified in this study, that have a stronger association with blood loss during surgery.

Acknowledgements. The authors declare the absence of conflict of interest. The study received no funding.

Postural asymmetry analysis using muscle sparing technique thoracotomy in esophageal atresia patients – long term follow-up

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Background. Right-sided posterolateral thoracotomy approach in esophageal atresia patients may result in a long-term postural asymmetry.

Objective. Evaluate frequency of possible long-term postural asymmetry (PA) and complaints after (EA) repair using muscle sparing technique thoracotomy (MSTT).

Methods. 24 patients, 2 – 14 years old (average age – 5.1) (female to male ratio – 15:9) with EA operated in MSTT from 2003 to 2015 were included in the study. Visual assessments of shoulder, scapular, and pelvic alignments were performed. In asymmetric patients, biplane x-rays (Cobb angle) were performed.

Parent questionnaire evaluated visual changes in posture, pain at rest or during physical exercises, and child's exercise habits. The approval of Ethics Committee was received (26/21.12.2017).

Results. In 22 patients, MSTT was the only operation – 16 patients did not have vertebral anomalies (NVA): 9 – symmetrical, 6 – scapular asymmetry (± 2 cm), 1 – scoliosis. Six patients had congenital vertebral anomalies (CVA): 1 – symmetrical, 2 – scapular asymmetry (± 2 cm), 3 – scoliosis.

Additionally, two NVA patients had repeated MSTT. No. 1, MSTT included tracheoesophageal fistula (TEF) closure, gastrostomy; the second patient had gastric replacement of the esophagus (GRO) – scoliosis. No. 2 – operated four times: MSTT with TEF closure and primary anastomosis; MSTT – TEF and esophageal anastomosis insufficiency; TEF ligation, esophagostomy; GRO – symmetrical.

Questionnaire was completed by 20 parents. NVA group – 17 children: 4 – changes in posture; 0 – pain in spine/or thorax; 1 – pain during physical examinations; 8 – pain during exercise. CVA group – 2 noted changes in posture; 2 – pain in spine/or thorax; 1 – pain during physical examinations; 2 – during exercise.

Conclusions. MSTT cannot completely avoid postural asymmetry. Patients after MSTT should be monitored regarding a possible posture asymmetry.

Acknowledgements. The authors declare the absence of conflict of interest.

The role of radiological examinations in ankle fracture management

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Background. Ankle fractures are among the most common fractures observed in trauma surgery. Although these are considered to be easy-to-treat fractures, it does not refer to all cases of ankle fractures, especially those accompanied with distal posterior aspect of tibia in combination with lateral and medial malleolus. According to AO/OTA classification, these cases are— 44B3.1, 44B3.2, 44B3.3, 44C1.3, 44C2.3, 44C3.3. Precise diagnostics and appropriate postoperative result evaluation are of an utmost importance on preoperative planning and outcome. For the last five years in Hospital of Traumatology and Orthopaedics (HTO), computed tomography (CT) is increasingly used to assess pre- and postoperative fracture alignment for fractures with distal posterior aspect of tibia.

Objective. The aim of the current study was to evaluate the role of radiological examination methods in perioperative ankle fracture management for ankle fractures with distal posterior aspect of tibia.

Methods. In Hospital of Traumatology and Orthopaedics, all hospitalised patients with ankle fractures were analysed in 2016, 2017, 2018, 2019. The number of all ankle fracture patients grew from 215 in 2016 to 377 in 2019. We analysed these patients for fracture type, use of CT examination and surgical method of fixation for distal posterior aspect of tibia.

Results. Results are provided in the following table.

	Ankle fractures with distal posterior aspect of tibia	CT preop	Posterior fracture of tibia fixed, total	Posterior fracture of tibia fixed from posterior approaches
2016	113	1	28	15
2017	126	14	41	29
2018	133	28	54	37
2019	193	48	74	63

Conclusions.

1. The number of ankle fractures treated in HTO increases significantly, both in total and in number of fractures with distal posterior aspect of tibia.
2. Use of CT as diagnostic tool can be related to higher surgical activity according to fixation of distal posterior fracture of tibia.
3. In our opinion, CT examination provides better diagnostics and more careful preoperative planning, and that explains the increase of using posterior approaches in fracture fixation.

Surgeons' experience of hidradenitis suppurativa in Latvia

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Background. Hidradenitis suppurativa (HS) is a chronic, recurrent, and debilitating skin condition. HS manifests itself with painful, deep-seated, inflamed lesions in the apocrine gland-bearing body areas. The inflammatory nodules can progress to abscesses and mucopurulent discharge, with hypertrophic scarring and sinus tract formation in the late stages of the disease. Little is known about HS recognition in the medical community, but the present consent suggests differential diagnosis and interdisciplinary treatment.

Objective. The aim of the study is a comparison of surgeons' exposure to HS cases in Riga and country regions with regard to frequency, pre-emptive examination, and subjective competence.

Methods. A survey of surgeons based on a questionnaire consisting of 17 questions about frequency of HS patients, pre-emptive examination, treatment, subjective competence, and willingness to learn. The data were subjected to statistical analysis, using Mann-Whitney-U, Pearson-Chi-Square and Fisher's Exact Test.

Results. In total, 56 surgeons were surveyed, out of these, 33 were working in Riga and 23 in country regions. Factually, 77 % of respondents occasionally encounter HS cases: 70 % in Riga and 87 % for country regions with an average of 8 cases per treating specialist (Dev. 1–32). HS-susceptible areas would be pre-emptively examined by 73 % respondents in Riga and 96 % in regions ($p = 0.039$). Confidence level is 55 % in Riga and 70 % in regions. A willingness to supervise the treatment is present in 63 % of respondents in Riga and 87 % in regions. Interest in additional training was expressed by 75% of the surveyed in Riga and 96 % in regions ($p = 0.05$).

Conclusions. The study revealed a higher number of HS patients in country regions, where check-ups of susceptible areas were more frequent. Furthermore, surgeons in Riga felt less competent about HS and less inclined to supervise treatment in contrast to other cities, but nearly every specialist would like to improve their skills.

Prevention of hospital-acquired pressure ulcers by usage of wearable sensors

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Background. In the United Kingdom, hospital-acquired pressure injuries occur in approximately 2.2 % of the patients per year or 330 000 patients, if we take into account that NHS reported more than 15 million hospitalizations. The average costs in the United Kingdom to heal the 1st grade pressure ulcer are £ 1214 per patient, healing the 4th grade ulcer costs £ 14 108 per patient, while osteomyelitis adds expenditure in the region of £ 30 000 per case. The estimated average treatment time of pressure ulcers is 28 days for the 1st grade, 94 days for the 2nd grade, 127 days for the 3rd grade, and 155 days for the 4th grade.

Objective. The aim of the current study was to decrease health care costs, to shorten the length of hospital stay, to reduce depression and pain relief medication usage and associated addiction, to curb the rate of injury complications (fasciitis, Osteomyelitis, SEPSIS), and to increase patient survival rate, as well as the perceived well-being and comfort.

Methods. The authors conducted a literature analysis, proposed a vision of technical solution and described a prototype version built, consisting of a combination of wireless sensor nodes (for the purposes of the preliminary study, sensor nodes manufactured by “Movesense” were used), and a custom-built mobile Android application was used for sensor data acquisition, patient check-up and user administration.

Results. The authors constructed an application that is currently being tested in Riga East University Hospital Clinical Centre “Bīķernieki”. The application user role table consists of 3 user groups – administrator, doctor and patient. The first group of users are system administrators, who will be able to add and manage all the system users. Doctors will be able to register the check-ups of patients, log of monitor movements and get notified via the “priority list” of patients to be visited by period of patient repositioning. The third group of users consists of patients. This part of the application is designed for the patient’s device that communicates with a motion sensor attached to the patient, obtaining data on his movements. The app provides the ability to keep track on position changes by sending the physician data on movements performed. The purpose of the developed system is facilitating patient care by providing a quick and easy way to understand your patients’ status based on the in-app data.

Conclusions. Proposed solution allows to enhance the classical prevention protocol in hospitals by tracking the patients’ movements in real time and decrease pressure ulcer rate, as well as a workload of medical personnel.

Similar clinical results after total hip arthroplasty and hemiarthroplasty due to femoral neck fracture

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Background. Studies comparing total hip arthroplasty and hemiarthroplasty due to femoral neck fracture report different results.

Objective. The aim was to obtain our own result in local setting.

Methods. The patients operated by one surgeon due to femoral neck fracture from September 2013 to December 2017 were included in the study. Exclusion criterion – a missed visit 8 to 26 weeks after the operation. Data were extracted from the institutional arthroplasty register. Data analysed: age, sex, ASA grade, type of operation, visit time after the operation, Harris Hip Score (HHS) before the operation and after it (during the visit), factors influencing HHS after the operation (local, neurological, systemic). Additionally, the difference between HHS after the operation and before the operation was calculated as dHHS. Mann-Whitney U test and T-test were used to compare differences between groups.

Results. In total, 210 patients met the inclusion criteria, 147 were excluded. As a result, 54 women and 9 men were analysed; 36 in total and 27, who had hemiarthroplasties.

The mean age in hemiarthroplasty group was 80.3 years (SD = 7.4), in total – 72.8 (SD = 10.0), $p = 0.001$. The mean ASA grade in hemiarthroplasty group – 3 (range = 2–4, IR = 3–3), in total – 3 (range = 2–3, IR = 2–3). The mean time of the visit after the operation in hemiarthroplasty – 103 days (range = 85–170, IR = 96.0–127.5), in total – 104 (range = 82–174, IR = 95.5–113.0), $p = 0.749$. On average, 1 factor influenced HHS (in hemiarthroplasty range = 0–3, IR = 1–2; in total – range = 0–3, IR = 0.5–1), $p = 0.221$. The mean HHS before the operation in hemiarthroplasty – 4 (range = 0–9, IR = 4–4), in total – 4 (range = 4–24, IR = 4–4), $p = 0.018$. The mean HHS after the operation in hemiarthroplasty – 83 (range = 57–99, IR = 78.0–88.5), in total – 91 (range = 64–100, IR = 80.5–97.0), $p = 0.010$. The mean dHHS in hemiarthroplasty – 78.7 (range = 53–95, SD = 9.3), in total – 81.9 (range = 60–96, SD = 8.6), $p = 0.162$.

After excluding cases with a local factor, analysis was performed on 34 women and 5 men, 23 in total and 16 hemiarthroplasties. The mean HHS before the operation in hemiarthroplasty was 4 (range = 0–9, IR = 4–4), in total – 4 (range = 4–24, IR = 4–4), $p = 0.263$. The mean HHS after the operation in hemiarthroplasty – 85.5 (range = 72–99, IR = 79–92), in total – 89 (range = 64–100, IR = 82–97), $p = 0.121$. The mean dHHS in hemiarthroplasty – 80.9 (range = 66–95, SD = 8.3), in total – 82.1 (range = 60–96, SD = 8.7), $p = 0.670$.

Older patients with higher ASA grade had hemiarthroplasty, their HHS after the operation on average was 8 points lower than in total, but the mean dHHS difference of 3.2 between the groups was not statistically significant. After excluding the cases with a local factor, no statistically significant difference in HHS was observed between the groups.

Conclusions. Clinical results after total hip and hemiarthroplasty due to femoral neck fracture are similar.

Acknowledgements. The authors declare the absence of conflict of interest.

CARDIOVASCULAR MEDICINE

Comparison of culture positive and negative infectious endocarditis patients undergoing cardiac surgery

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Background. Infective endocarditis (IE) is a disease affecting endocardial surface of the heart. It is associated with high morbidity and mortality. Diagnosis of IE together with clinical presentation is based on echocardiography and positive blood culture. However, the data in literature indicates that in up to 30 % of IE cases the blood cultures are negative.

Objective. The aim of this study was to analyse findings between culture-positive and culture-negative patients with infectious endocarditis.

Methods. In this retrospective study, we analysed 169 medical histories of patients undergoing cardiac surgery due to heart valve IE in Pauls Stradiņš Clinical University Hospital in the time period from 2015 to 2019. The study was implemented with the approval of hospital's committee of ethics. Patient data, clinical course, laboratory analyses, imaging before and after surgery, operation and intensive care unit records were studied. Data were analysed using IBM SPSS Statistics 20.

Results. Within the period of 5 years, we analysed 169 medical histories of patients with IE who underwent cardiac surgery. The mean age of the patients was 56 (the youngest patient was 20, the oldest – 80) years. 24.9 % (42) were female and 75.1 % (127) – male.

Operation due to left side of heart IE was performed in 158 patients, while in 11 patients due to right side of heart IE. Native valve endocarditis was observed in 76.9 % of the cases, whereas prosthetic valve endocarditis was found in 23.1 %. Pathogen was detected only in 59.2 % of cases. In culture-positive IE, the most common pathogens were *Staphylococcus aureus* in 28 % of the cases, followed by *Streptococcus sp.* 26 %, *Enterococcus faecalis* – 24 %, *Streptococcus sp.* 26 % and others in 22 % of the cases. The mean Euroscore II risk in culture-positive IE was 7.82 %, and in culture-negative – 6.68 %. The overall intrahospital mortality was 8.88 %. In culture-positive patients, the mortality was 10.0 % and in culture-negative patients – 7.25 %, however, no statistically significant difference was found among the groups ($p > 0.05$).

Conclusions.

1. In this study, microorganisms causing infective endocarditis were detected less frequently in comparison with the data provided in literature.
2. The most commonly detected microorganisms in culture-positive infectious endocarditis were *S. aureus*, *E. faecalis* and *Streptococcus sp.*
3. In culture-positive endocarditis, we observed a higher mortality, however, it did not reach statistical significance ($p > 0.05$).

Patient-Prosthesis Mismatch after aortic valve replacement: experience of a centre

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Background. A Patient-Prosthesis Mismatch (PPM) is a condition caused by too small effective orifice area (EOA) of prosthetic valve relatively to body surface area (BSA). According to the literature, various grades of PPM after aortic valve replacement was reported in case of 20 % to 70 % of patients. A PPM is defined when indexed EOA is $0.85 \text{ cm}^2/\text{m}^2$ or less. Although data is controversial, some authors found it as an independent predictor of mortality in both early and late postoperative period. A correlation between the severity of PPM and the postoperative mortality was noticed.

Objective. The aim of the study was to evaluate incidence, severity and outcomes of PPM in our centre.

Methods. In total, 140 patients were included in the study. Preoperative clinical and demographic data was examined (age, gender, left ventricle ejection fraction (LVEF), EOA). Transvalvular gradients and velocity were evaluated preoperatively and postoperatively. We compared the outcomes of patients with and without PPM, including postoperative stay, cardiac echocardiography at rest and during exercise – 6 minute walking test (6MWT) results.

Results. The average age of the patients was 67.2 ± 10.4 years. 60 % of the group were male. The average LVEF was $49.4 \pm 10.2\%$. The mean indexed EOA of aortic valve preoperatively was $0.49 \pm 0.21 \text{ cm}^2/\text{m}^2$. The mean preoperative and postoperative transvalvular gradients at rest were $45.9 \pm 21.4 \text{ mmHg}$ and $16 \pm 8 \text{ mmHg}$. The maximal velocity at rest was $4.1 \pm 1.2 \text{ m/s}$ and $1.9 \pm 0.5 \text{ m/s}$, respectively. PPM was observed in 8 cases (5.71 %). The compared data of PPM and non-PPM patients is shown in Table.

Table. Characteristics of PPM and non-PPM patients

Variable	Non-PPM group (n = 132)	PPM group (n = 8)	p-value
6MWT distance (m)	274 ± 113	265 ± 122	0.83
Mean transvalvular gradient at rest, mmHg	10.3 ± 5.2	11.7 ± 7.3	0.44
Mean transvalvular gradient during exercise, mmHg	8.25 ± 4.86	8.94 ± 4.85	0.7
Hospital stay, days	17.5 ± 10.8	14.1 ± 6.8	0.38

Conclusions. We observed a low incidence of PPM in our centre. There was no difference between PPM and non-PPM patients according to 6MWT performance, transvalvular pressure gradients and hospital stay.

Acknowledgements. This study was approved by local committee of bioethics. Authors have no conflicts of interest.

The effectiveness of thrombolytic therapy in patients with acute cerebral infarction and a NIHSS score of 0–5 points at Riga East Clinical University Hospital “Gaiļezers”

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Background. Cerebrovascular diseases are the primary cause of disability and the second most common cause of death in the world. In Latvia, acute cerebral infarction (CI) occurs in around 7000 people a year, with a 30 % mortality rate. CI is an acute development and thrombolytic therapy can either provide a complete recovery or lessen symptoms, reducing disability and improving quality of life.

Objective. Selected patient records with acute CI diagnosis and a National Institute of Health Stroke scale (NIHSS) score of 0–5 points at Hospital “Gaiļezers” were compiled and analysed, defining the effectiveness and clinical profile of thrombolytic therapy.

Methods. The research was implemented as a retrospective cross-section study. Data was analysed using information on acute CI entered in the Hospital “Gaiļezers” stroke registry during the period from 03.10.2016 to 31.12.2019 to assess thrombolytic therapy effectiveness in patients with CI and a NIHSS score of 0–5 points. Results were processed with MS Excel and IBM SPSS 22 statistics.

Results. During the study period, Hospital “Gaiļezers” had registered 4836 patients with acute CI. 1258 patients with a NIHSS score of 0–5 points were selected, of which 14.4 % ($n = 181$) received thrombolytic therapy and 85.6 % ($n = 1077$) did not. The severity of CI in patients who had thrombolysis decreased on average from 3.6 to 1.5 points ($p < 0.05$) and in patients without thrombolysis treatment it decreased from 3.1 to 2.2 points ($p < 0.05$). In patients with thrombolysis, the NIHSS score decreased by 2.1 points on average, without thrombolysis it decreased by 0.9 points. In patients with thrombolysis, clinically positive dynamics were observed in 86 %, negative dynamics in 6 %, and no clinically relevant dynamics in 8 % of cases ($p < 0.05$). In patients without thrombolysis, clinically positive dynamics were observed in 64 %, negative dynamics in 7 %, and no dynamics in 28 % of all cases ($p < 0.05$). The clinical outcome in different age groups (< 45 years, 45 to 65 years, > 65 years) was generally not significantly different ($p > 0.05$).

Conclusions. The clinical outcome in patients with thrombolytic therapy and a NIHSS score of 0–5 points is better than without it. The results of the study provide an understanding of the dynamics of CI development depending on the type of treatment, as well as an opportunity to analyse the effectiveness of thrombolytic therapy in patients with mild/moderate CI.

Acknowledgements. This study has received no financial support and the absence of any conflicts of interest is declared.

Sudden death from post-traumatic complication: pulmonary artery fat embolism and pulmonary artery thromboembolism. Retrospective study

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Background. Pulmonary artery fat embolism and pulmonary thromboembolism are two different types of potentially fatal embolism that may occur as a complication of a trauma with the same clinical presentation. The only indisputable method to diagnose a cause of death remains an autopsy with histological investigation. Therefore, it is a reliable source of information for forecasting of more accurate possible post-traumatic outcomes.

Objective. The aim of the study is to identify fatal pulmonary fat embolism and pulmonary thromboembolism demographics, pathomorphological findings and to assess the Abbreviated Injury Scale and Injury Severity Score respectively.

Methods. Retrospective analysis of Lithuanian State Forensic Service 2013–2019 autopsy data. Out of 6132 autopsies, 32 histologically confirmed post-traumatic cases with pulmonary artery fat embolism and pulmonary artery thromboembolism were selected. The following data were collected: date, location (indoors, outdoors, hospital), age, sex, thickness of subcutaneous adipose tissue, bone fractures, hospitalization time, injury mechanism, the main cause of death, Abbreviated Injury Scale and Injury Severity Score. Statistical analysis was performed using SPSS v. 25.0. Data was tested for normality using a Kolmogorov-Smirnov Test, a Student's T-Test was used for analysis of normally distributed continuous data, while in cases of not normally distributed data, Mann-Whitney Test was applied. Categorical variables were compared using χ^2 or Fisher's exact test, where the expected frequencies were below 10. *P*-value below 0.05 was considered statistically significant.

Results. Fatal pulmonary artery fat embolism was found in 18 (56.3 %), and pulmonary artery thromboembolism – in 14 (43.8%) of the cases. The mean age in all cases was 63.59 ± 17.82 years. Post-traumatic survival was significantly longer in cases of pulmonary thromboembolism (the mean 11.66 days) than in fat embolism (the mean 2.25 days) ($p = 0.021$). Injury Severity Score was significantly greater in cases of pulmonary fat embolism (the mean 25.89) than in those of thromboembolism (the mean 14.71) ($p = 0.008$).

Conclusions. Injury Severity Score is significantly higher in cases of the pulmonary artery fat embolism and occurs more rapidly after the injury in comparison with the pulmonary artery thromboembolism.

Acknowledgements. The study has not received any funding.

Why is it important to follow up cardiovascular and physical health status of student volleyball athletes?

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Background. The most frequent causes preventing athletes from participation in regular sport activities are musculoskeletal trauma and diagnosis of cardiac diseases. The athletes of the Riga Stradiņš University (RSU) volleyball teams have limited access to a sports medicine specialist who would be able to assess the health status of athletes and perform cardiovascular screening. Therefore, the current situation calls for highlighting the importance of accessibility of sports medicine specialists to university athletes.

Objective. To perform a screening of RSU male and female volleyball teams and clarify their cardiovascular and physical health status.

Methods. A prospective study involved volleyball athletes participating in cardiovascular screening using the AHA 14-point evaluation test with specific questions about trauma and medication history and a resting 12-lead ECG interpreted according to international criteria for electrocardiographic interpretation in athletes during November 2019. SPSS 23 was used for statistical analysis.

Results. 56 athletes participated in this research: 36 of these were women, the average age – 20.09 years (SD 4.34), body mass index – 22.13 (SD 2.09), and 20 were men, the average age – 26.80 years (SD 6.60), body mass index – 24.73 (SD 2.15). There were 31/56 (55.4 %) athletes who had had limitations of physical activities due to musculoskeletal trauma in last 6 month period. According to AHA 14-point evaluation survey, there were 37/56 (66.1 %) athletes who arrived at positive test results indicating an increased cardiovascular disease risk. In case of 6/56 (10.7 %) athletes, there were observable abnormal changes in their resting 12-lead ECG, which are associated with increased sudden cardiac death risk. 9/32 (28.1 %) The athletes who have suffered from any musculoskeletal trauma in the past 6 months responded that they had experienced at least 1 syncope episode during their physical activities, in comparison, there were no respondents (0/24) who had experienced it in the group who had not suffered from musculoskeletal trauma ($p = 0.003$; 95 %).

Conclusions. It is important that the sports medicine specialist is readily available for RSU volleyball team athletes and that the injuries are treated according to scientifically proven methods. An excellent examples, if accurately done, are cardiovascular screening and AHA 14-point evaluation survey, which can reduce the risk of sudden cardiac death events.

Acknowledgements. To perform the current study, the authors used the electrocardiograph provided by RSU Medical Education Technology Centre and the RSU Sports Club premises.

Variability of low-density lipoprotein cholesterol reduction: statin monotherapy vs combination of statin and ezetimibe

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Background. The primary aim of atherosclerosis prevention is aggressive low-density lipoprotein cholesterol (LDL-C) lowering. Individuals with familial hypercholesterolemia (FH) have extremely high LDL-C levels from birth and, as a consequence, develop significant atherosclerotic disease with major complications early in their life. Statin monotherapy is frequently not potent enough to reach LDL-C goals in this population, so dual therapy approach with addition of ezetimibe is frequently used. Moreover, it has a very high interindividual variability. Combined lipid-lowering therapy (LLT) with statin and ezetimibe achieves a less variable LDL-C lowering effect.

Objective. To investigate, whether addition of ezetimibe to statin monotherapy results in a less variation in LDL-C reduction.

Methods. Patient data was taken from Latvian Registry of Familial Hypercholesterolemia (LRFH). Only the patients with clinical and possible FH, who were not using any LLT at the time of the highest documented lipid levels and had not used LLT during the last visit, were selected for this study. Coefficient of variation (CV) of LDL-C percentage reduction was used as a tool for assessment of variation within LLT groups.

Results. By January 2020, 313 patients with clinical FH and 285 patients with possible FH were included in LRFH, and met criteria for the analysis. The mean LDL-C reduction in treated patients was 51.2 % (3.6 mmol/l) from baseline. Patients who were treated with combined maximal LLT, achieved better LDL-C reduction with less variability in lipid lowering effect than patients on maximal statin dose monotherapy. Coefficient of variation ranged from 19.8 % to 28.0 %, and from 27.5 % to 36.9 % among the patients treated with atorvastatin and rosuvastatin monotherapy, respectively, while it was less than 19.0 % for combined LLT (Fig.).

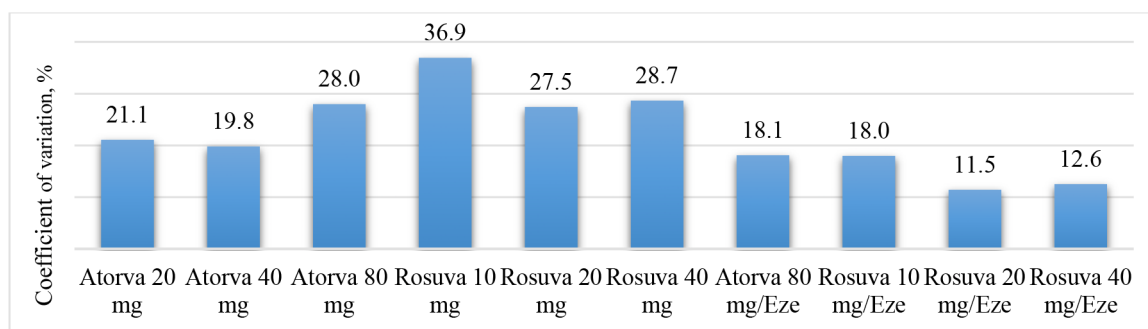


Fig. Coefficient of variation LDL-C percentage reduction in different LLT groups.

Conclusions. Combined lipid-lowering therapy results in more predictable LDL-C reduction, when compared with statin monotherapy.

Angiotensin converting enzyme inhibitor and thiazide use is associated with higher plasma trimethylamine-N-oxide levels in patients with type 2 diabetes

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Background. Elevated blood level of trimethylamine-N-oxide (TMAO) is a cardiovascular risk marker. Our study group has previously reported that age, body mass index and diabetes are associated with higher TMAO levels in selected patients. We have also found that loop diuretics increase plasma TMAO levels in non-diabetic patients.

Objective. To evaluate a potential effect of cardiovascular medications on plasma levels of TMAO in patients with type 2 diabetes.

Methods. A cross-sectional study including patients with high or very high cardiovascular risk undergoing coronary angiography at the Latvian Centre of Cardiology. Two subgroups of patients were distinguished and TMAO levels were compared in patients with and without diabetes. All the diabetic patients used metformin. Information on cardiovascular medications, doses and duration of use was recorded, and TMAO plasma levels were measured in fasting state. All the patients were requested to abstain from any intake of fish, fish products and omega-3 supplements for one day before and on the day of sampling. For the purpose of data normalization, TMAO values were logarithmically transformed.

Results. The patients with diabetes ($n = 31$) had higher TMAO levels compared with the patients without diabetes ($n = 300$): $3.650 \mu\text{mol/l}$ [IQR 3.150–4.490] vs $2.144 \mu\text{mol/l}$ [IQR 1.570–3.104] and the same with log-TMAO levels: 0.564 ± 0.183 vs 0.347 ± 0.277 , respectively ($p < 0.001$). In diabetics, univariate analysis showed that TMAO levels significantly correlated with ACEI ($r_s = -0.388$; $p = 0.031$), thiazides ($r_s = -0.373$; $p = 0.039$), age ($r_s = 0.377$, $p = 0.037$) and GFR ($r_s = -0.585$, $p = 0.001$). In multivariate backward linear regression analysis only GFR remained significantly associated with log-TMAO levels ($p = 0.001$), while use of ACEI had a trend to higher log-TMAO ($p = 0.076$).

Conclusions. Our observational data suggest that use of ACEI is associated with increased plasma TMAO levels in patients with type 2 diabetes using metformin. Further large prospective clinical studies are required to clarify whether this association is causative.

Acknowledgements. The study was funded by the Latvian National Research Programme “Biomedicine for Public Health” (BIOMEDICINE) 2014–2017 and the Latvian Council of Science, project “Trimethylamine-N-oxide as a link between unhealthy diet and cardiometabolic risks”, project No. Izp-2018/1-0081.

Use of stenting techniques for treatment of coronary bifurcation lesions

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Background. Coronary bifurcation lesions are frequent and continue to be among the most complex lesions in interventional cardiology. Percutaneous coronary intervention (PCI) for bifurcation lesions is associated with increased rates of in-hospital complications and long-term major adverse cardiac events. Treatment of coronary artery bifurcation lesions is still a controversial subject due to bifurcation morphology and necessity to choose the most appropriate stenting strategy for each type of lesion.

Objective. The study evaluates in-hospital and long-term outcomes of PCI with various techniques for the treatment of coronary bifurcation lesions.

Material and methods. A 3-year retrospective study of the Latvian Centre of Cardiology Coronary Bifurcation Treatment Registry and a 1-year follow-up. A total of 407 patients with coronary bifurcation lesions were included in the study. PCI were performed between January 11, 2017 and December 23, 2019. The 1-year follow-up included all the patients treated in 2017–2018. The patients were divided into provisional one-stent group and systematic two-stent group. Patients with ST segment elevation myocardial infarction (STEMI) in the last 24 hours and left main coronary artery stenosis were excluded. In-hospital and long-term complication rates were compared between both groups. Creatine kinase MB measurements were performed after the procedure.

Results. 340 (84 %) patients underwent PCI using provisional one-stent technique and 67 (16 %) – with systematic two-stent technique. In-hospital complications were vessel perforation (1-stent 0 % ($n = 0$) vs 2-stent 1.5 % ($n = 1$), $p = 0.165$), side branch occlusion (1-stent 2 % ($n = 7$) vs 2-stent 1.5 % ($n = 1$), $p = 1$), cardiogenic shock (1-stent 0 % ($n = 0$) vs 2-stent 1.5 % ($n = 1$), $p = 0.165$), stent thrombosis (1-stent 0.3 % ($n = 1$) vs 2-stent 0 % ($n = 0$), $p = 1$), and periprocedural myocardial infarction (1-stent 4.1 % ($n = 14$) vs 2-stent 5.9 % ($n = 4$), $p = 0.514$). No cases of main branch occlusion, in-hospital death, stroke and transient ischemic attack were detected in either of the groups. In-hospital BARC bleeding type 2 and type 3b were observed in 3 and 1 cases, respectively. 64.4 % of the patients completed the 1-year follow-up (1-stent – 223 patients, 2-stent – 39 patients). Long-term complications were death from cardiovascular disease (1-stent 0.45 % ($n = 1$) vs 2-stent 0 % ($n = 0$), $p = 0.06$), myocardial infarction (1-stent 0.9 % ($n = 2$) vs 2-stent 0 % ($n = 0$), $p = 1$), target lesion restenosis (TLR) (1-stent 1.3 % ($n = 3$) vs 2-stent 0 % ($n = 0$), $p = 1$) and target vessel restenosis (TVR) (1-stent 2.2 % ($n = 5$) vs 2-stent 2.5 % ($n = 1$), $p = 1$).

Conclusions. This study demonstrates that there was no significant difference in in-hospital and long-term complication rates between both groups undergoing PCI for the treatment of coronary bifurcation lesions.

Thirty-day mortality and safety of transcatheter aortic valve implantation procedure in Latvian Centre of Cardiology during 2017–2019

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Background. Due to demographic changes in Latvia and other developed countries, the burden of aortic stenosis is gradually increasing, and the same situation is observed worldwide. Aortic stenosis is a debilitating disease causing progression of heart failure, which leads to increasing hospitalization rate. TAVI (transcatheter aortic valve implantation) procedure is established as a gold standard for aortic valve replacement in patients with very high surgical risk.

Objective. To analyse 30-day mortality rate and early major adverse cardiac events (MACE) in all performed TAVI procedures during 2017–2019 in Latvia all performed at Latvian Centre of Cardiology (LCC).

Methods. Data on all TAVI procedures performed at the Latvian Centre of Cardiology from January 2017 to December 2019 was collected using LCC registry of TAVI procedures.

Results. During analysed period of time 204 TAVI procedures were performed at LCC. The mean age was 81 ± 6 years ($n = 119$), and 58 % of patients were female. 86.8 % ($n = 177$) of the implanted bioprosthetic valves were Edwards Sapien[®] (balloon-expandable), and 12.3 % ($n = 25$) were Acurate Neo[®] (self-expandable). The most frequently used approach was transfemoral – applied in 93.6 % ($n = 191$) of the cases. Transapical approach was used in 2.5 % ($n = 5$), whereas direct aortic approach in 2.9 % ($n = 6$). The all adverse event rate was 6.5 % ($n = 13$). The stroke rate was 0.5 % ($n = 1$), there was no myocardial infarction in early setting of procedure. The 30-day mortality rate was 1.5 % ($n = 3$), of which none occurred in 2019. Permanent pacemaker implantation after the procedure was required in 5.4 % ($n = 11$) of the cases. Conversion to conventional surgery due to implantation complications was observed in 1.5 % ($n = 3$), and valve embolization occurred in 1.5 % ($n = 3$) of the cases. Vascular complications requiring stent implantation or vascular surgery were found in 4.4 % ($n = 9$), and major bleeding requiring blood transfusions was registered in 0.5 % ($n = 1$) of the cases.

Conclusions. TAVI procedure for patients over the age of 75 years and with high surgical risk is safe. The adverse event rate in this study is low. Compared to other studies, experience in Latvia concerning MACE at LCC is lower. With 0.5 % rate of stroke, no myocardial infarction and 1.5 % of 30-day mortality in patients with high surgical risk during 2017–2019 were found.

Acknowledgements. There is no conflict of interest to declare.

PEDIATRICS

A six-month progress in psychomotor function of children with autistic spectrum disorder

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Background. In the last 10 years, the frequency of Autism spectrum disorders (ASD) symptoms in Europe has more than doubled. As of yet, no effective treatment of ASD exists. The efficacy of different kinds of therapies in the case of ASD have been proposed but not fully proven, and the current body of scientific evidence is controversial, therefore requiring further investigation.

Objective. The aim of this study was to investigate progress in psychomotor function of 2–5 years old children who participated in different types of therapies for ASD.

Methods. The study sample consisted of children within the age range of 2–5 years, who attended the Children's Clinical University Hospital and the Social Paediatrics' Centre of the University of Latvia over the span of 2013 to 2015. We used the Munich Denver functional scale to assess children's psychomotor abilities after two years of therapy. After the initial assessment of psychomotor function by each child's physician, children participated in different kinds of therapies or did not participate in any therapy, according to the decision of their parents. The second assessment was performed 6–8 months after the baseline examination. Multiple logistic regression models were adjusted to age, compliance of development to age norms and initial diagnosis of a child, were built for the association between attendance of therapies and improvement of psychomotor functions.

Results. Of 100 children enrolled in the study (median age 4.0), 28 were considered as healthy, and most of others (N = 62) received various therapies: Montessori therapy (N = 26), attendance of special pedagogue (N = 21), or others. The children with atypical autisms and those with other diffused development disorders typically attended special pedagogue (68.8 % and 55.6 %, respectively), while the children with infant autisms mostly received a Montessori therapy (67.9 %). We observed no difference between the preferable type of a therapy regarding ages of children and the compliance of their development to age norms (Chi-square test $p = 0.55$, and Kruskal-Wallis test $p = 0.26$, respectively). In the fully adjusted multiple logistic regression models, participation in any kind of therapy was significantly associated with an improvement of some or all psychomotor functions. Montessori therapy was especially effective for improvement of hearing and fine motor skills (odds ratio OR = 19.3 [95 % confidence interval, CI 1.7; 221.1], and OR = 3.8 [2.81; 757.0], respectively).

Conclusions: Attendance of therapy is essential for children with ASD, but the specific type of therapy should be individually matched with the needs of each particular child.

Acknowledgments: None declared.

Differences in quality of life of 9th grade adolescents at the beginning and at the end of the final school year

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Background. During the final – 9th – school year, teachers, parents and general practitioners notice a decreased quality of life (QOL) of adolescents due to stress related to the final examinations.

Objective. The aim of the current study was to assess differences in eight domains of self-reported QOL in the 9th grade adolescents of Riga's schools at the beginning and at the end of the final school year.

Methods. We assessed eight QOL domains using SF-36 survey at two time-points: at the beginning and at the end of the last study year. The maximal value in each particular question was 100 and the minimal was 0. The mean scores were calculated from two to ten questions of the survey according to questionnaire recommendations: physical functioning (10 questions), role limitations due to physical health (4 questions), role limitations due to emotional problems (3 questions), energy/fatigue (4 questions), emotional well-being (5 questions), social functioning (2 questions), pain (2 questions), and general health (5 questions). The differences between points of follow up were calculated using Wilcoxon test. The differences between high-rated and regular schools, as well as between genders were examined using Mann-Whitney test. Statistical difference of $p < 0.05$ was considered as significant.

Results. Altogether 286 adolescents (mean age 15.0, Standard deviation (SD) 0.34 years; 50.5% boys) were enrolled in the longitudinal prospective study performed in seven Riga's schools. We observed significant differences between two time-points in following domains of QOL: mean energy (55.8, SD 20.5 and 54.2, SD 20.0, respectively; $p < 0.01$), mean emotional well-being (63.5, SD 18.0 and 60.8, SD 19.9, respectively; $p < 0.01$), and mean general health (59.7, SD 13.0 and 58.5, SD 13, respectively; $p = 0.02$), but not in other QOL domains. In all three domains we did not observe statistically significant differences between high-rated and regular schools. At both points, girls displayed lower QOL at all investigated domains (from $p < 0.01$ to $p = 0.02$, according to domain). We did not observe differences between genders in both time-points in all QOL domains.

Conclusion. Three QOL domains were statistically significantly decreased in girls' population: mean energy, emotional well-being and general health.

Acknowledgements. Authors declare no conflicts of interests.

Opinion of children with motor disability diseases and their parents about their quality of life according to Kidscreen-52 questionnaire

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Background. The child is a physically and intellectually immature person who needs specific protection. Particular attention should be paid to children whose quality of life is affected by diseases such as motor disability syndromes. The epidemiology of children with cerebral palsy today is on the increase.

Objective. The objective of the study is to analyse the quality of life in children with motor disability syndromes. The aim of this study is to find out the opinions of children about their health, physical and emotional well-being in comparison with their parents' opinions.

Materials and methods. In this study, children aged 8 to 18 years and their parents were surveyed at the Children's Clinical University Hospital and at the Association for Latvian Children with Functional Disabilities. The participants voluntarily filled out KIDSCREEN-52 questionnaire. Survey includes 10 Health-Related Quality of Life (HRQoL) dimensions, including physical, emotional and social life. Participants were divided into two groups – children's and parents' group. Statistical analysis was performed with SPSS statistics 22 by using Mann-Whitney test. The level of statistical significance was set at $p < 0.05$.

Results. Overall, 100 participants were surveyed – 50 children and 50 parents of these children. The mean of children's age was 13.56 ± 2.9 (8–17) years. 60 % ($n = 30$) of children had cerebral palsy, 14 % ($n = 7$) of children had unspecified myositis, 26 % ($n = 13$) had congenital musculoskeletal diseases. 62 % of children thought that his/her health was more than good. 8 % felt sad and 38 % felt happy at school. Using Mann-Whitney test, a statistically significant difference ($p < 0.05$) was found between children's and parents' views regarding the following questions: if the child was physically active, if the child felt that everything in life is going wrong, if the child felt lonely, if the child felt under pressure, if the child felt jealous of the way other girls and boys look, if the child had fun with his friends. In answers to other questions no statistically significant differences ($p > 0.05$) were found.

Conclusions. Opinion of children and their parents about quality of life did not differ significantly, except six questions from the section "Physical activities and health", "General mood", "About yourself", "Friends". A further research about quality of life of children with musculoskeletal diseases is needed with an increased sample size of patients.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment", the University of Latvia, Faculty of Medicine.

Relations between use of electronic devices and psychomotor development of 6–36 months old children

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Background. Scientific reports show a vast increase of screen-time among children, even at a very early age. As the first five years of life are crucial for a child's physical development, American Academy of Paediatrics recommends to limit screen-based media use assuming its cognitive-behavioural risks, especially for those under 2 years of age.

Objective. To assess relationships between use of electronic devices and psychomotor development of 6–36 months old children.

Methods. A cross-sectional study was conducted in Latvia between November 2018 and January 2019. We used an electronic survey of parents of 6 to 36 months old children to assess parental socio-demographic data, screen time of their children, and skills related to use of electronic devices (search, unblock, swipe, recognise, and pick an app). Munich Functional Developmental Diagnostic test was used to estimate the psychomotor development. Answers were divided according to children's age into groups of 6–12 months, 13–18 months, 19–24 months, and 25–36 months. We used Kruskal-Wallis test, ANOVA and Chi-square test to investigate univariate relationships between use of electronic devices, skills related to use of electronic devices, and psychomotor development of children. Statistical significance was considered as $p < 0.05$.

Results. The study included 4123 respondents: 21.6 %, 20.9 %, 18.9 %, and 38.5 % according to age groups 6–12 months, 13–18 months, 19–24 months and 25–36 months of their children, respectively. 63.1 % of parents had higher education; 51.5 % of children were boys. Most of the parents (25.3 %) responded positively to one out of five skills related to electronic devices. Statistically significant relationships were found between skills related to use of electronic devices and parental age ($p < 0.02$). The most prominent skills related to use of electronic devices were observed in children of parents with higher/doctoral education. Statistically significant relationships were observed between skills related to use of electronic devices and children's development in all groups: 6–12 months ($p < 0.01$); 13–18 months ($p = 0.04$); 18–24 months ($p < 0.01$); and 2–3 years ($p = 0.03$). Adverse relationships were observed between screen time and child development in the age groups of 6–12 months ($p = 0.01$) and 19–24 months ($p = 0.05$).

Conclusions. Increased use of electronic devices might leave a negative effect on the development of children. However, a positive impact might be assumed in cases when children use an electronic device together with their caregivers.

Acknowledgements. None declared.

Self-rated health among adolescents: What matters more – emotional or physical factors?

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Background. Self-rated health is an important indicator reflecting person's general health. Previous research indicates that self-rated health may predict certain somatic health outcomes and mortality similarly or in addition to the objective clinical measures. As somatic disease is a relatively rare condition in young age, adolescent's emotional state may play an important role in self-rated health similarly to somatic health perceptions.

Objective. The aim of the current study is to evaluate, what is more important for adolescent self-rated health – somatic complaints or emotional state?

Methods. The study was conducted in April–June of 2018 during the Health Behaviour in School-aged Children (HBSC) survey in Lithuania. In total, 4191 schoolchildren from 5th, 7th and 9th grades were enrolled to the study (response rate – 80.7 %). By gender, 50.9 % were boys, 49.1 % – girls, the mean age of sample was 13.9 ± 1.69 years. Self-rated health was assessed using a question “Would you say your health is...” with choices from “poor” to “excellent”. Health and emotional complaints were assessed by asking about frequency of psychosomatic complaints (headache, stomach-ache, backache, feeling low, irritability or bad temper, feeling nervous) in the last 6 months. The associations of psychosomatic complaints and self-rated health were estimated by using logistic regression method, adjusting each factor by gender, grade, and family affluence.

Results. The study showed that poorer self-rated health was among girls, older schoolchildren (7th and 9th grades) and the children from families with lower socioeconomic status ($p < 0.05$). The frequent presence of at least one somatic complaint more than once a week was related to 3.87 times higher risk for poor self-rated health ($p < 0.001$). A similar situation was observed when assessing the psycho-emotional adolescent state – at least one frequent emotional complaint was related to 3.91 times higher risk for poor self-rated health ($p < 0.001$). Additionally, the total sum of psychosomatic complaints was assessed: the increase by one psychosomatic complaint was associated with 1.53 times higher risk of poor self-rated health ($p < 0.001$). Consequently, a frequent presence of (for instance) three symptoms gives $OR = 3.59$ for poor health compared to the absence of such symptoms.

Conclusions. The regular presence of at least one somatic or one emotional complaint brings 3.9 times higher odds for poor self-rated health, suggesting comparable effect of mental and physical factors on adolescent health perception.

Acknowledgements. The authors declare that no conflicts of interest have been present in the study. The study was financed from the internal institutional sources.

Use of ultrasound examinations in pregnancy by region

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Background. Ultrasound (US) can help monitor normal foetal development and screen for any potential problems. Three ultrasound screening examinations during pregnancy are recommended.

Objective. The aim was to analyse US examination frequency comparing urban and rural areas.

Methods. Data source – Health Care Monitoring Datalink (HCMD). We used two data sources: Medical Birth Register and ambulatory care data provided by public and private health care providers about US. US screening was detected by two manipulation codes: 50694 – routine US screening in the 1st trimester of pregnancy and 50695 – US examination in obstetrics. All singleton births in 2018 (n = 18759) were included in the data analysis. The places of residence were categorized in three groups: Riga, other biggest cities and rural areas (including regional cities).

Results. A total of 40.7 % (n = 7634) birth data in Riga, 38.8 % (n = 7279) in other cities and 20.5 % (n = 3846) in rural regions were analysed. The average mother's age in Riga was higher – 31.4 years (SD 5.3) than in other cities (30.1 (SD 5.5)) and rural areas (29.7 (SD 5.5)) ($p < 0.01$). 69.1 % (n = 12955) of births were routinely screened in the 1st trimester and 83.3 % (n = 15633) had US examinations through other trimesters. The median number of scans received during pregnancy was 3 (IQR 2) in Riga and other cities, and 4 (IQR 2) in rural regions. A higher proportion of US scan once in the 1st trimester was observed in rural regions ($p < 0.01$) 61.6 % (n = 2369), by 3 percent points higher than in Riga and other cities (57.8 % to 58.7 %). A higher proportion of US scan 2 times ($p < 0.001$) was observed in rural regions – 10.1 % (n = 390) than in Riga and other cities. Regarding US scan 3 times and more in the 1st trimester, an average was 1.6 % (n = 301). The higher proportion by 5 to 8 percent points ($p < 0.001$) of US scan 3 times and more in other trimesters was observed in rural regions 45.2 % to 39.9 % in other cities, whereas 36.8 % in Riga. Congenital anomalies at birth were registered 2.9 %. 4.4 % in Riga, 1.5 % in other cities, 2.4 % in rural regions.

Conclusions. A higher average number of US examinations per pregnancy and more than 3 scans were observed in rural regions. There is a need for more studies to analyse the efficiency of US examinations for prenatal detection of congenital anomalies.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, the University of Latvia, Faculty of Medicine.

Congenital cytomegalovirus infection – effectiveness of diagnostics and treatment in Latvia

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Introduction. Congenital cytomegalovirus (cCMV) is the most common congenital infection in neonates and is the leading cause for sensorineural hearing loss. It occurs in 0.2–2.4 % of all live births. Despite its clinical significance, cCMV infection often goes undiagnosed, since up to 90 % of infected infants are asymptomatic at the birth. Multiple studies present evidence that early diagnostics and treatment may improve the neurological outcome. Until now, there is no data on the diagnostics, clinical outcome and treatment possibilities for cCMV infection in Latvia.

Objective. The aim of this study was to evaluate epidemiological, clinical, diagnostic and therapeutic data on cases of cCMV infection in Children's Clinical University Hospital (Riga, Latvia) from 2009 to 2019.

Materials and methods. A retrospective descriptive study included 21 patients with a confirmed diagnosis of cCMV infection. The data was collected and analysed in Microsoft Office Excel 2013.

Results. In the time period between 2009 and 2019, 16 % ($n = 3$) of patients were diagnosed prenatally with cCMV infection, 58 % ($n = 11$) were diagnosed during the neonatal period, and 26 % ($n = 5$) were diagnosed after reaching one month of age. To confirm the diagnosis, CMV DNA in urine (positive 53 %; $n = 10$), CMV DNA in blood (positive 32 %; $n = 6$), CMV IgM (positive 32 %; $n = 6$) and IgG (positive 47 %; $n = 9$) were taken. Clinical manifestations (e.g., convulsions, encephalopathy) and changes in imaging diagnostic examinations (e.g., ventriculomegaly, lenticulostriate vasculopathy, periventricular calcifications) involving the central nervous system were observed in 63 % ($n = 12$) of the patients. Of all the patients included in this study, 56 % ($n = 10$) received appropriate treatment with ganciclovir or valganciclovir. Only two pregnant women received antenatal therapy. About half ($n = 9$) of the patients experienced long-term complications of cCMV infection, including retardation of psychomotor development ($n = 3$), and sensorineural hearing loss ($n = 3$).

Conclusions. The implementation of evidence-based recommendations for the diagnosis and treatment of congenital CMV infection in clinical practice in Latvia is very important. Less than a half of the patients enrolled in the study received appropriate antiviral therapy, which in the future may affect the development of late complications. New strategies developed by multidisciplinary team (including gynaecologists-obstetricians, midwives, neonatologists) are necessary to improve the early diagnostics and treatment of cCMV infection, and further clinical studies are needed.

Acknowledgements. The authors declare that the research was conducted in the absence of any commercial or financial relationships and without conflict of interest.

The role of factor V Leiden (F5L) mutation in stillbirth at term

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Background. In 1994, Dahlback and Hildebrand reported an association between a mutation in the factor V gene and increased thrombotic risk, and named the factor V Leiden (FVL) mutation. Several studies have found strong associations between FVL and second or third trimester foetal loss but not with the early first trimester losses.

Objective. 1. Identification of mutations in factor V Leiden genes – the most prevalent genetic thrombophilia in people of European descent (G1691A polymorphism).

2. Determination of the need for screening for hereditary thrombophilia mutation factor V Leiden (G1691A polymorphism) in a group of patients whose history is aggravated by intrauterine death of mature foetus.

Methods. To achieve the objective of the research, a prospective study was carried out, which included all the cases of intrauterine demise of mature foetus in Institute of Mother and Child from January 2016 to July 2018. All pregnant women were interviewed according to the special questionnaire. Biological samples (2 ml of peripheral venous blood) were taken to analyse thrombophilia profile (with informed consent of the patients). The main research group L1 consisted of a total of 44 pregnant women whose pregnancy was terminated with term stillbirth (from these, ADN extracted in 33 cases). The control group L0 included 132 pregnant women whose pregnancy ended with the birth of a live foetus (from these, ADN extracted in 86 cases).

Results. At this stage of the study, samples for hereditary thrombophilia in the basic and control group were processed. From these samples, in basic group normal homozygous alleles or 1691GG genotype was determined in 97.0 % cases (n = 32), allele in the heterozygous state – 3.0 % (n = 1) (genotype 1691GA), homozygous for the mutation (genotype 1691AA) – 0.0 % (none). In the control group – 1691GG genotype was determined in 93.0 % cases (n = 80), allele in the heterozygous state – 7.0% (n = 6) (genotype 1691GA), homozygous for the mutation (genotype 1691AA) – 0.0 % (none). Thus, OR = 0.42, CI 95 % = 0.05–3.6. If so, a congenital form of thrombophilia (Leiden factor polymorphism) is not a significant risk factor for intrauterine death of a mature foetus.

Conclusions.

1. Literature data on the role of the factor V Leiden mutation in foetal death of the foetus is ambiguous.
2. At this stage of the study, we did not find a statistically confirmed need for screening for a Leiden mutation among women with a history of stillbirth at term.

Acknowledgements. None declared.

Characteristics of paediatric acute hematogenous osteomyelitis – our approach

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Background. About 30 children with acute hematogenous osteomyelitis (AHO) are admitted to the Children's University Hospital every year. AHO is caused by bacteraemia and can progress into sepsis and even lead to lethal outcome if left untreated or misdiagnosed. Diagnosis of AHO can be quite challenging. Early radiographic imaging may show no pathological changes. Therapy of AHO in children has improved recently, mainly in terms of reduced need for surgical intervention and shorter intravenous antibiotic usage.

Objective. The aim of the study was analysis of epidemiological parameters, diagnosis and treatment outcomes of paediatric population admitted to University Children's Hospital due to AHO.

Methods. This retrospective descriptive study included patients under 18 years of age admitted at the University Children's Hospital from 2014 to 2018 due to AHO (diagnosis code M 86.1 according to ICD-10). Duration of hospitalization, patient gender and age, affected bone and causative agent, imaging findings and treatment outcomes were analysed. Statistical analysis was performed with SPSS 23.0.

Results. 125 patients were enrolled, 16 % of them were infants, 34% – girls. The average time from the onset of symptoms until the hospitalization was 4 days. Causative microbiological agent remained undiscovered in 26 % of cases, while 43 % of blood cultures were positive. *Staphylococcus aureus* was identified in 82 % of positive cultures. Femur (25 %), tibia (17 %) were the most commonly affected sites. X-ray was performed in 65 % of cases – only 16 % suspected AHO, MRI was performed in 60 % of cases, most of them positive (91 %). The average time between the onset of symptoms and positive x-ray finding was 12 days. Surgical intervention was used as part of the treatment in 74 % of cases. The mean hospitalization time for surgically treated patients was 18 days, in conservatively treated patients – 13 days. The mean duration of total antimicrobial therapy was 30 days (from 15 to 63 days). Intravenous antimicrobial therapy was administered for the mean period of 14 days. Monotherapy with Oxacillin (66 %) as parenteral agent was used, followed by Cefuroxime (39 %) or Clindamycin (38 %) *per os*. Chronic osteomyelitis developed in 7 cases.

Conclusions. MRI showed high specificity and sensitivity in AHO patients and remains the golden standard for early diagnosis. Treatment of AHO is still based on prolonged antibacterial therapy. Surgical treatment predicts a longer hospitalization time. Chronic osteomyelitis is the most common late complication of AHO.

ETHICAL, SOCIAL & LEGAL ASPECTS OF MEDICINE

Public attitudes towards research biobanks in Latvia

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Background. Public awareness and engagement are among the main prerequisites for successful functioning of research biobanks. Thus, analysis of public opinion is very important for development of national regulations for biobanks. The 2010 Eurobarometer study indicated a low level of public knowledge of biobanks in Latvia. We decided to repeat the survey in 2019 to explore public attitudes, concerns, and trust in biobanking.

Objective. The aim of the study was to analyse public attitudes towards research biobanks in Latvia and to compare the results with the results of 2010 Eurobarometer study.

Methods. Conducted in March 2019, the survey included a sample ($n = 1017$) representing the general population of Latvia aged 18 to 75. The questionnaire included questions on biobanks from the 2010 Eurobarometer study and several additional questions.

Results. In 2019, 260 (25.6 %) out of 1017 respondents had ever heard about research biobanks, and 196 (19.2 %) of respondents had heard about the Genome Database of Latvian Population. 462 (45.4 %) respondents stated that they would agree to donate their blood samples to a biobank; 409 (40.2 %) – to provide their surplus surgical material, 430 (42.2 %) to donate urine samples, and 411 (40.4 %) – samples of their faeces. There was a relationship between awareness on biobanks and engagement and willingness to participate ($p < 0.01$). Those who were actively engaged in searching for information, showed a higher willingness to participate.

There were statistically significant differences between the results of 2010 and 2019 surveys regarding awareness of biobanks, willingness to participate, type of consent, and sharing samples among EU member states. In 2019, more participants had not heard about biobanks, there were more participants who were willing to participate, preferred broad consent, and were positive about sharing data and samples among EU member states.

Conclusions. The general public in Latvia is still poorly informed about research biobanks, the number of those who have heard about research biobanks is smaller than in 2010. At the same time, the number of respondents who are willing to donate samples and data to a biobank has slightly increased. Overall, the concerns about the donation of different types of samples and data to a biobank have decreased.

Acknowledgements. This research is funded by the Latvian Council of Science, project “Ethically and socially responsible governance of research biobanks in Latvia: analysis of opinions of public, donors and researchers”, project No. lzp-2018/2-0171.

Patient organizations in Latvia

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Background. Among more than 23 thousand non-government organizations registered in Latvia in 2019, only several organizations represent interests of patients. There is no definition of a patient organization in Latvia, causing various biases regarding their purpose, governance and management. According to European Medicines Agency's definition and criteria from European Patients' Forum, only few nonprofits are true patient organizations: they represent interests of people with a specific disease or group of diseases, are led by patients and/or their relatives, and their main tasks involve patient advocacy, education and awareness building about disease and health, as well as ensuring peer-to-peer contacts for experience sharing; it can also be an umbrella organization, which unites several disease-related patient groups nationally or internationally. In 2018, almost 30 patient organizations organized themselves in a network to improve patient advocacy efforts.

Objective. The aim of this survey was to evaluate compliance of patient organizations in Latvia to internationally accepted patient organization definitions, identify their main tasks and resources.

Methods. A structured online survey with 32 open-ended and closed questions was carried out in July 2019. The data gathered from 21 patient organization in Latvia were analysed mathematically by using MS Excel in July 2019.

Results. Nearly all the organizations are led by patients or their relatives, they represent interests of target patient group, as well as carry out various activities to raise awareness of disease and/or health, organize patient education campaigns, organize and participate in conferences and trainings, advocate for access to healthcare and various services, and cooperate with other patient organizations locally, nationally and internationally. The majority of organizations have no paid staff and most tasks are carried out as voluntary work. A half of organizations operate with less than 10,000 EUR in annual budgets, in fact, one third of organizations operate with 1,000 EUR or less annually. All the organizations are diversifying their annual income to ensure transparency according to national legislation and international policies.

Conclusions. Nearly all patient organizations in the network comply with internationally accepted definition of a patient organization. Further research is needed upon expansion of the network. Public awareness campaigns to build reputation are needed.

Acknowledgements. No funding was received for conducting this study nor establishing or running patient organization network. Special thanks to all the patient organizations in Latvia for their continuous efforts to improve patients' lives.

Donors' perspective on research biobanking in Latvia: practical implications for involved professionals

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Background. Donor involvement is crucial for functioning and development of research biobanks. Thus, donors' perspective must be taken into account in the biobank governance process.

Objective. The aim of the presentation is to provide practical implications for biobanking professionals arising from qualitative research of donors' perspective on participation in research biobanks in Latvia.

Methods. Twenty qualitative semi-structured interviews with 21 donors of two research biobanks based in Latvia (Genome Database of Latvian population and biobank of the Institute of Clinical and Preventive Medicine, University of Latvia) were analysed.

Results. Analysis of interviews showed that the most important aspect for successful collaboration with donors is trust built during informed consent process and viewed in two ways. Firstly, trust means trustful relationship based on transparency of informed consent practice. Secondly, trust can be based on relationship with a particular person (doctor, researcher, staff member), and this relationship might be more important than a content of informed consent. Trust level developed during an informed consent process affects further collaboration with a biobank: willingness to donate certain type of samples, amount of information given about oneself and relatives, etc. The feedback on research results is another major aspect affecting collaboration with biobank donors. Analysis showed specific interest in feedback on planned and incidental individual research results, also as a benefit for relatives. Lack of understanding the nature of the possible research results produces false expectations regarding the content of feedback. Disappointment due to these false expectations impacts the chances of further collaboration, once more emphasizing the importance of the process of informed consent.

Conclusions. Trustworthiness of research biobanks is an important precondition for building short- and long-term collaboration with donors. A transparent informed consent covering all the crucial aspects of research biobanking is an important prerequisite for successful functioning of biobanks. Especially important is clear and understandable information on feedback of research results to avoid false expectations. Donors prefer dynamic informed consent to be able to retain control over the usage of their samples and data as a part of trustful collaboration.

Acknowledgements. This research is funded by the Latvian Council of Science, project "Ethically and socially responsible governance of research biobanks in Latvia: analysis of opinions of public, donors and researchers", project No. LZP-2018/20171.

Negotiating the meaning of hospital-acquired infection control: ethnographic insights from Latvia

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Background. Despite infection control being a quintessential element of biomedicine, the problem of hospital-acquired infections (HAIs) is the most common patient safety problem worldwide. The insufficient progress in providing safe healthcare, free from these infections, is widely recognized worldwide and demands more in-depth studies into daily HAI control practices.

Objective. The aim of the study is to understand how HAI control is negotiated and navigated within and between different settings and people in Latvia.

Methods. The presentation is based on ethnographic PhD research project, using interviewing and observation to generate detailed accounts of daily HAI control practices. The study, based in Latvia, comprised interviews with hospital infection control specialists, medical personnel, support and administrative staff and patients. Observations were carried out in both hospital and social settings.

Results. Study reveals how hospital staff understands and engages with the key aspects of HAI control. Ethnographic insights demonstrate that HAI-causing microbes, infection control specialists and hospital hygiene plan have unstable and ambivalent status within the hospital.

On the one hand, HAI-causing microbial presence is perceived as inherent in the hospital landscape and relationships through ‘domestication’ of their presence in the hospital. On the other hand, microbes at the same time are imagined operating as outsiders and ‘invaders’, interrupting healthcare in hospitals.

The status of infection control specialists in the hospital structure is ambivalent, as they are simultaneously navigating their status of both belonging and not belonging to the fabric of a hospital. Specialists rely on their social relationships with other people in the hospital as ‘infrastructure’ to build up their status and HAI control as an ‘insider issue’.

Hospital staff also positioned the hospital hygiene plan in contradictory ways. Personnel engaged with the main HAI control policy instrument as (1) burden and unnecessary ‘luxury’ for already fragile healthcare; (2) part of maintaining cleanness of hospital environment; (3) part of hospital bureaucratic apparatus; (4) part of hospital quality management.

Conclusions. Examining how medical personnel understands the very phenomena of HAI control reveals deeper factors determining HAI control practices. Diverse understanding and engagement with the key elements of HAI control lead to a diverse understanding of how HAI control should be implemented (if at all) and different, contesting expectations, practices and results. This study shows that ethnographic insights can provide an important source of evidence to be considered when planning and implementing HAI control practices.

Acknowledgements. PhD research project was funded by University of Leeds, UK.

Legal framework of patient's decisional capacity and patient's legal competence (capacity) in Latvia

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Background. Self-determination of a patient is exercised by free and informed decision making on various health care matters. In order to take health care decisions and give informed consent/refusal, a patient has to have capability to understand, retain, use and weight the information, as well as communicate a decision. A patient who does not have the decisional and/or legal competence to consent to an intervention because of a mental disability, a disease or for similar reasons should be particularly protected due to his vulnerable state. Research data published by UK researchers suggest that prevalence of mental incapacity in medical in-patients is at least 40 % of patients, where 24 % of patients are severely cognitively impaired (Raymont V. et al, 2004). No studies have been conducted in Latvia to provide data on the number and needs of adult patients with limited capacity. To improve protection of such patients in Latvia, it is crucial to develop legal and clinical approaches suitable for protection. To start such research journey, two legal notions, namely, the patient's decisional capacity and the patient's legal competence should be analysed. It has to be explored how these two notions should be applied in legal and clinical practice.

Objective. The overall aim of the current study was to reveal how two legally and clinically significant notions, first, a patient's decisional capacity, and second, a patient's legal competence should be interpreted and applied within the framework of Latvian patients' rights.

Methods. The national and international legal regulations, relevant case law and research papers regarding protection of the patients' rights with limited capacity have been analysed.

Results. The notion of patient's decisional capacity in health care matters differs from the notion of patient's legal competence. Patient's ability to make health care decisions in general and give informed consent or refusal to interventions in particular is determined by his/her decisional capacity (Latv. *lemtspēja*). Consequently, a patient without or with limited decisional capacity lacks the ability to take health care decisions autonomously. Therefore, patient's decisional capacity is a crucial prerequisite in medical settings, both clinically and legally. Additionally, there are patients whose legal competence (capacity, Latv. *rīcībspēja*) has been restricted by a court, stating that a person lacks legal competence to decide as to listed tasks.

Conclusions. If a patient has a limited decisional and/or legal capacity, a health care institution is required to provide scientifically appropriate evaluation of capacity and suitable legal protection of such patient.

MENTAL HEALTH

Mood disorders among Lyme disease patients in Latvia

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Background. Lyme disease or Borreliosis is tick-borne disease widespread all around the world. Latvia as a part of North Europe is located in the main endemic area.

Objective. The aim is to evaluate mental health of patients during an onset of Borreliosis symptoms.

Materials and methods. Cross-sectional study was conducted in Lyme disease support group in Facebook. 127 respondents filled out the questionnaire. The answers were collected using google survey functionality and data was statistically analysed in IBM SPSS Statistics 22. The questionnaire has been adapted from M.D. Robert Bransfield's "The Neuropsychiatric Assessment of Lyme Disease" assessment form [1]. Respondents filled 6-point (0 – no symptoms, 5 – max symptoms) or 2-point (yes, no) Likert scale of ordinal data.

Results. The questionnaire has been filled by 109 women (85.8 %) and 18 men (14.2 %). Age = 43.65; SD = 11.98; Min = 21; Max = 72 years. There is serious tendency among responders to gravitate towards positive answer in depression scale (Median = 3.00, $n = 30$, 23.6 %) and the same tendency is explorative for bipolar disorder (Median = 3.00, $n = 27$, 21.3 %). There was a statistically significant ($p = 0.01$) non-parametric Spearman's rho correlation between both diseases – depression and bipolar disorder ($r = 0.677$). Conducting Mann-Whitney U two independent samples tests between depression and gender groups, no statistically significant difference was found ($p = 0.667$, mean rank for men = 67.39, mean rank for women = 63.44), the same characteristics were observed between depression and diagnosis status – whether patient received diagnosis from clinician ($n = 99$, mean rank = 63.5) or was self-diagnosed ($n = 28$, mean rank = 65.77) ($p = 0.769$). A pretty similar result was found for depression and the fact whether patient has noticed the erythema migrans before ($n = 58$, mean rank = 62.07) or not ($n = 69$, mean rank = 65.62) ($p = 0.581$), a statistically significant difference was found between depression and the status whether patient knew precise infection time ($n = 81$, mean rank = 58.06) or not ($n = 46$, mean rank = 74.46) ($p = 0.014$).

Conclusions. Both depression and bipolar disorder highly prevail in the sample group of Lyme disease patients in Latvia. The same pattern with a high correlation is noticeable for depression and bipolar disorder symptoms among Lyme disease patients. A psychiatrist's or medical psychotherapist's consultation would improve the treatment of Borreliosis in Latvia, because untreated depression and bipolar disorder negatively influence chronic diseases.

Acknowledgements. The authors would like to express their gratitude to the founder of Lyme disease support group Elīna Prikule. The study has received no funding.

References.

<https://www.mentalhealthandillness.com/tnaold.html>

Subjective barriers when (not) seeking mental health services: a patient-oriented internet forum content analysis

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Background. The most common environment for gathering health-related information is the Internet. People suffering from mental disorders do not get treated timely; subjective experience forms a crucial part when seeking mental health services (MHS). Individuals' messages from an internet forum could provide the perceived obstacles to seeking MHS by any other feasible means.

Objective. The aim of the study was to evaluate the subjective perceived obstacles of the Internet users with complaints about psychological disturbances to seeking MHS via primary care doctor or any other form of counsel.

Methods. Individuals' anonymous and voluntary inquiries (n = 68) addressed to certified psychotherapists about mental health related questions were selected from a patient-oriented internet forum on the Latvian Doctors Association of Psychotherapists website (www.arstipsihoterapeiti.lv). All the data from 2019 were included in the qualitative content analysis.

Three independent researchers classified the inquiries using grounded theory coding and independent unstructured mode of coding. Keywords from all the questions were freely and separately identified. Then, the main obstacles to seeking MHS via the traditional route were established. The results were grouped into 2 categories adopting the psychodynamic concept and the cognitive beliefs. Finally, individual analyses were condensed.

Results. The majority of the inquiries were self-reported complaints (n = 40). Out of 68 patient inquiries, Researcher 1 (R1) identified 41 keywords or phrases, Researcher 2 (R2) – 8, Researcher 3 (R3) – 25. The most common obstacles identified were negative transference (7 %) by R1, inability to make a decision (38 %) by R2 and a lack of information (49 %) by R3. Lack of information and inability to make a decision were excluded from further analysis as confounding bias due to the fact that the individuals might be in the process of making progress towards seeking MHS after receiving a satisfactory feedback from a psychotherapist on the given forum. After the exclusion, the most common obstacles identified by Researcher 2 were uncertainty/hesitation (18 %), while Researcher 3 most frequently identified confusion/ignorance (26 %).

Similar keywords by at least 2 researchers were found in almost 60 % (n = 39). Identical keywords were found in almost 10 %.

The most common repeated keywords were confusion/ignorance (26 %), uncertainty about further action (25 %) and uncertainty about seeking MHS (21 %).

Conclusions. Intrapsychic obstacles such as fear and confusion, as well as interpersonal reasons were identified. This coincides with the published research findings, suggesting that there is a population not accessing MHS, and seeking help traditionally may still be heavily stigmatized.

Acknowledgements. No conflict of interest or funding to disclose.

Symptomatic remission in patients with schizophrenia and its correlating factors

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Background. Schizophrenia is a mental disorder with a lifetime prevalence of approximately 1 % worldwide. Schizophrenia occurs 1.4 times more often in males than females. Schizophrenia is one of the top 15 leading causes of disability worldwide. The main goal of treatment is to achieve remission and increase quality of life (Vos T. et al., Lancet 2017).

Objective. To determine the symptomatic remission in schizophrenia inpatients at discharge from two mental hospitals according to proposed remission criteria by N. Andreasen in 2005 (Andreasen et al. 2005) and to describe its correlating factors.

Methods. The patients were interviewed 3 days before discharge using the positive and negative syndrome scale (PANSS). Data was also gathered from patient medical charts and sociodemographic data gathered from the patient using a form made by the authors. The data were analysed using SPSS 23 and windows excel. Information about the patient behaviour from the medical staff was also taken in consideration

Results. 111 patients were interviewed within the study period from 01.01.2018 to 01.01.2019. 57 (51.4 %) of the patients were male and 54 (48.6 %) were female. The mean age of participants was 44.7 years. Out of 43 (38.7 %) patients, which met the criteria, 16 (37.2 %) were female. Out of the 111 patients, 14 (12.6 %) had paid jobs, 10 (71.4 %) had achieved symptomatic remission, 81 (73.0 %) had a disability group, of which 27 (33.3 %) achieved remission ($p = 0.048$). 14 (12.6 %) patients were unemployed and had no disability group, of which 5 (35.7 %) achieved remission ($p = 0.048$). For 44 (39.6 %) patients' criterion G16 (active social avoidance) was graded with 1 (absent), out of these 26 (59.1 %) achieved remission, 33 (29.7 %) patients were graded with 3 (mild), of which 8 (24.2 %) achieved remission ($p = 0.002$). There was a statistical significance between symptomatic remission and 12 other PANSS scores.

Conclusions. Less than 50 % of the study participants reached symptomatic remission. The patients with paid jobs had a higher prevalence of achieving remission than the patients with a disability group. Evaluating the correlation between symptomatic remission and PANSS criterion that showed statistical significance with the exception disorientation (G10) and lack of judgement and insight had a rate of achieving remission above 50 % only when valued 1 (absent) and 2 (minimal).

Psychoemotional characteristics of patients with genital endometriosis

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Background. The “chronic pelvic pain” due to genital endometriosis is of outstanding importance, since it significantly disrupts the quality of life and psychoemotional state of patient. This necessitates a complex treatment of severe pain syndrome

Objective. The aim of the current research was to study the psychoemotional state of patients with genital endometriosis.

Methods. Altogether 40 patients with endometriosis were enrolled in the study. Subjective assessment of pain was assessed using a 10-point analogue visual scale; to determine the level of anxiety, we used a personal Taylor Manifest Anxiety Scale; the severity of depression was determined on a Hamilton scale.

Results. All the patients of the main group (40 patients) complained of constant pain in the lower abdomen and lower back in the duration of more than 5 years. 21 (52.5 %) patients noted constant pain in the lower abdomen with irradiation in the lumbosacral region, in 13 (32.5 %), the pain attacks were provoked by primary dysmenorrhea, in 4 (10.0 %) – secondary dysmenorrhea, 8 (20.0 %) had noted dyspareunia, 6 (15.0 %) – pain in the middle of the menstrual cycle. 7 (17.5 %) women had operations of the uterus and ovaries, 5 (12.5 %) of them had adhesions of the pelvic organs.

Medical and psychological testing and a psychological interview showed that 29 (72.5 %) patients noted weakness, fatigue, inability to work, anxiety, loss of appetite, sleep disturbance.

The patients with genital endometriosis had more pronounced emotional disorders of the depressive-hypochondriac type, a high level of personal anxiety, sleep disturbances, decreased physical activity and performance, sexual dysfunction, social maladaptation. Similar disorders associated with pelvic pain amounted to 52.5 %. Only 5 (12.5 %) patients rated pain as mild, while 9 (47.5 %) – as severe, and 18 (45.0%) – as moderate.

This data revealed a heredity of occurrence of psychoemotional disorders, the formation of a perverse pain reaction, low pain tolerance. The formation of a characteristic psychoemotional portrait in chronic pelvic pain syndrome could also be affected by the trauma in 5 (12.5 %) patients. An analysis of the peculiarities of emotional disorders of patients showed that 15 (37.5 %) had disorders of a mixed anxiety-depressive nature. The dominance of depressive disorders in genital endometriosis is probably associated with dysfunctions of pelvic organs.

Conclusions. Clinical studies have shown that genital endometriosis contributes to the risk of chronic pelvic pain syndrome. There is a need for joint approach of gynaecologist and psychotherapist in the treatment.

Acknowledgements. The authors declare the absence of conflict of interest.

INTERNAL MEDICINE, INFECTIOUS DISEASES & PULMONOLOGY

Impact of alcohol consumption habits and other risk factors in development of alcoholic hepatitis

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Background. Acute alcoholic hepatitis is a common, progressive liver disease both in Latvia and all over the world. It is the primary cause of death for individuals consuming excessive amount of alcohol. It is known that progression of the disease is dose-dependent. Alcoholic hepatitis patients have a high risk of death – 30–50 % die within three months. It is important to study the risk factors of acute alcoholic hepatitis as the development of this disease is fully preventable.

Objective. The aim of this study was to find out what alcohol consumption patterns and other risk factors, like increased body mass index, other liver diseases, long-term (more than one year) use of medication or nutritional supplements affect the development of alcoholic hepatitis.

Methods. Data were collected prospectively during the period of 15.01.2019–15.02.2020. Patients with acute alcoholic hepatitis were interviewed in Riga East University Hospital, Latvian Centre of Infectious Diseases. The control group were patients in Riga Psychiatry and Narcology Centre who were not affected by disease. Both groups completed the same questionnaire with questions about alcohol habits, risk factors and the Alcohol Use Disorders Identification Test (AUDIT). Statistical analysis was performed using IBM SPSS Statistics Version 21.

Results. 201 patients were included in 2 groups; hepatitis group comprises 100 patients, while and control group – 101. In the hepatitis group, the frequency of alcohol use was, as follows: every day for 75 % of patients, in the control group 23 % ($p = 0.05$), actual length of such habits of use in hepatitis group was more than 15 years – 60 %, the most common result in the control group was 5–10 years – 34.7 % ($p = 0.05$). In both groups, the most consumed alcohol was vodka ($p = 0.134$). Audit test results in the hepatitis group mean result was 25.98 (SD = 7.785), whereas in the control group 23.07 (SD = 6.540) ($p = 0.05$).

Conclusions. Patients suffering from acute alcoholic hepatitis drink alcohol regularly each day for more than 15 years. The quantity of alcohol doses taken by patients of acute alcoholic hepatitis per day is higher than by the patients of the control group. In both groups, the most consumed alcohol was vodka, the patients of acute alcoholic hepatitis consumed considerably more bottles of cocktails. Results of Alcohol Use Disorders Identification tests are higher for patients suffering from alcoholic hepatitis. Risk factors, including elevated body mass index, use of drugs, medications or food supplements, other liver diseases, were not considered as relevant.

Investigation of local and systemic biomarkers in allergic airway diseases caused by house dust mite

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Background. Prevalence of allergic rhinitis and allergic asthma is increasing worldwide. Recently, a hypothesis of united airway disease was proposed. It means that upper and lower airway diseases are the manifestation of a single inflammatory process. House dust mite is one of the most common allergens that cause allergic airway diseases. The etiopathogenesis of these diseases is not yet fully investigated.

Objective. The aim of this study was to investigate local and systemic biomarkers of allergic airway diseases caused by house dust mite.

Methods. Patients with a diagnosed allergic asthma (according to GINA) and/or persistent allergic rhinitis (according to ARIA and duration of symptoms ≥ 2 years) were involved in the study. Allergy was assessed using a skin prick test. Peripheral blood cell count, eosinophil count in nasal smear, serum total immunoglobulin (Ig) E and vitamin D (25(OH)D) level were measured. IL-22 level was measured in serum and nasal lavage using commercial ELISA kit.

Results. The study comprised 40 subjects – 22 with allergic rhinitis (AR), 9 with allergic rhinitis and allergic asthma (ARA) and 9 healthy individuals. IL-22 levels did not differ significantly between patients with AR, ARA and healthy individuals (in nasal lavage: 8.14 ± 1.63 pg/ml vs 3.77 ± 1.22 pg/ml vs 4.45 ± 1.02 pg/ml; in serum: 22.25 ± 6.44 pg/ml vs 24.35 ± 6.22 pg/ml vs 13.11 ± 2.52 pg/ml). However, the tendency was observed that serum IL-22 was higher in ARA and AR patients than in healthy individuals. Serum vitamin D level was similar in studied groups (53.14 ± 5.06 nmol/l vs 50.81 ± 7.29 nmol/l vs 48.08 ± 4.00 nmol/l, respectively). Blood eosinophil count was significantly higher in patients with ARA and AR than in healthy individuals ($0.29 \pm 0.04 \times 10^9/l$ vs $0.23 \pm 0.04 \times 10^9/l$ vs $0.13 \pm 0.04 \times 10^9/l$, $p < 0.05$); whereas lymphocyte and neutrophil count did not differ between groups. Serum IgE level was significantly higher in ARA and AR patients compared with healthy individuals (328.24 ± 91.80 kU/l vs 243.98 ± 61.25 kU/l vs 34.83 ± 20.26 kU/l, $p < 0.01$). Eosinophil count ≥ 10 % in nasal smear was found more frequently among patients with ARA than AR (62.5 % vs 31.6 %, $p < 0.05$).

Conclusions. An increase of IL-22 and IgE in systemic and eosinophils in local and systemic compartments during any allergic airway disease caused by house dust mite was observed, however, the increase of these biomarkers was more remarkable when allergic rhinitis was accompanied by allergic asthma, indicating that inflammation is more enhanced in “united airway disease”.

Acknowledgements. The authors declare the absence of conflict of interest. Research was partly funded by Research Fund of Lithuanian University of Health Sciences.

Efficacy of allergen-specific immunotherapy in patients with allergic asthma and allergic rhinitis: a single-centre experience

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Background. Allergic asthma is one of the most frequent allergic diseases, whose prevalence is increasing worldwide. There is an evidence that allergen-specific immunotherapy (ASIT) can have positive effect on the course of this disease. The main indication for ASIT is moderate to severe allergic rhinitis. About 80 % of the patients have allergic rhinitis along with allergic asthma.

Objective. The aim of this study was to evaluate efficacy and safety of ASIT in patients having both allergic rhinitis and allergic asthma.

Methods. Retrospective study was performed in the Department of Immunology and Allergology, Hospital of Lithuanian University of Health Sciences (HLUHS) Kauno Klinikos. Demographic and clinical data of patients treated with ASIT in 2018–2019 was taken from the Medical Statistics Department of the HLUHS. Case histories were revised, and patients' data was collected: type of ASIT, skin prick test or allergen-specific immunoglobulin E test results, asthma control test (ACT) results and the total daily dose of inhaled steroids before ASIT and after one year of treatment.

Results. 15 patients were diagnosed with allergic asthma and allergic rhinitis, and had been treated with ASIT during the studied period. Nine patients were treated with house dust mite ASIT, six patients were treated with mugwort, dog or cat ASIT. Fourteen patients received subcutaneous ASIT and one patient received sublingual ASIT. ACT results did not differ significantly before and one year after the beginning of treatment with ASIT (18.50 ± 1.94 vs 20.25 ± 2.21). The daily dose of inhaled steroids also did not differ significantly between studied groups (400.00 ± 136.63 µg vs 353.33 ± 95.45 µg). No adverse events were observed.

Conclusions. One-year treatment with ASIT of patients with allergic rhinitis and allergic asthma showed a positive tendency in the improvement of asthma control and decrease of inhaled steroid dose, however, additional evaluation after a prolonged ASIT would be more informative.

Acknowledgements. The authors declare the absence of conflict of interest and funding.

iOS 12 measure application in assessment of low leg discrepancy in patients with diabetes mellitus

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Background. Every 30 seconds in the world one amputation is performed in a patient with diabetes mellitus (DM). Unilateral foot ulcer may be formed in DM patients due to asymmetrical overload of the longer extremities. Prevention of these events should include an analysis of the length of the legs (LL). The measurement method should give an accurate assessment of the possible differences between the LL as a risk factor for the development of DF.

Objective. The aim of the study is to evaluate usability of electronic devices in the measurement of low leg discrepancy in patients with diabetes mellitus.

Methods. The total of 190 adults (the 1st group – 101 healthy volunteers and the 2nd group – 90 patients with DM) were tested, measuring of LL by two different methods: typical anthropometric and automatically measurement using mobile devices. The iOS 12 Measure application was used to automatically measure LL in patients with DM. To take a measurement, we proposed patients to stand sideways to the iPhone camera without shoes with feet close together to provide the same position after turning to the other side. We used the Person's Height tool in metric system, indicating centimetres. After calibrating, denoted by a white dot in a circle, we created an anchor point on the top of the iliac crest and lined the white dot down to the underside of the foot. All the measurements were repeated thrice and averaged. The obtained data were compared with the results of anthropometric measurements of leg length (cm) with metal stadiometer.

Results. After checking data normality, the non-parametric Mann-Whitney *U* test was selected to determine whether or not there were differences between the initial measurement data in the two groups. We demonstrated that there was no statistically significant difference in the obtained results between the two methods in both groups ($p = 0.246$ in the 1st group; $p = 0.133$ in the 2nd group).

To automatically evaluate the measurement methods, we tested over time the reliability at the baseline and a month apart in both healthy and diabetic cohort. Test-retest correlation between the two data sets was calculated as Pearson's $r = +0.85$. These indicate a good reliability.

Conclusions. Estimation of the leg length with iOS 12 Measure application for automatically gauging the size of objects in the real world is a reliable tool and easy to use both for DM patients, and healthy volunteers.

Acknowledgements. The authors declare the absence of conflict of interest.

DNA breakage is enhanced in type 1 diabetes

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Background. It is known that chronic hyperglycaemia leads to DNA damage in diabetes and might be associated with nitrosative stress. However, there are few studies addressing single-stranded DNA breaks and their association with diabetes-related parameters and nitric oxide metabolism markers in patients with type 1 diabetes.

Objective. The aim of the current study was to assess the level of single-stranded DNA breaks in patients with type 1 diabetes and healthy controls.

Methods. We analysed single-stranded DNA breaks in 128 subjects: 71 patients with type 1 diabetes and 57 healthy controls. Single-stranded DNA breaks were analysed by single-cell gel electrophoresis in alkaline conditions and break level was scored with arbitrary units (AU). Prevalence of diabetic complications was retrieved from medical files. Progression of complications was analysed after a follow-up time of 3–5 years and analysed in association with AU at baseline.

Results. We observed a higher level of DNA breakage in patients with type 1 diabetes, compared to healthy subjects (type 1 diabetes 56.8 ± 40.04 ; control -35.94 ± 17.78 , $p < 0.001$). The difference remained significant also after adjustment for age, which was performed because of the difference in age between both groups (type 1 diabetes 36.63 ± 13.04 years; control 29.60 ± 13.64 years, $p < 0.001$). Within the group of type 1 diabetes, AU correlated positively with total cholesterol $R = 0.262$, $p = 0.028$; and negatively with serum glucose level $R = -0.284$; $p = 0.018$ and serum nitrite concentration $R = -0.335$; $p = 0.008$. In addition, when patients with diabetes were divided into three groups according to the tertiles of AU (group 1: AU 0 – 39.2; group 2: AU 39.3 – 63.69, group 3: AU > 63.69), we observed statistically significantly higher serum glucose and nitrite concentration and lower total cholesterol levels in the group of lowest AU tertile.

Conclusions. Our results demonstrate that type 1 diabetes is associated with a higher level of single-stranded DNA breaks. Due to our results, AU levels in diabetes is dependent on serum glucose, cholesterol and serum nitrite levels. Further studies are needed to understand the mechanisms of DNA breakage and repair in diabetes.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” by the Faculty of Medicine, University of Latvia and Genome Database of the Latvian population.

Impact of interval walking training managed through smart mobile devices on leptin/adiponectin ratio and cardiovascular risk in patients with type 2 diabetes mellitus

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Background. Interval walking training has been shown to be superior to continuous walking in the effects on the level of cardiovascular risk factors such as cytokines, adiponectin and leptin in type 2 diabetes in fully supervised training programmes or highly controlled real-life settings. Taking into account the effect of physical activity on weight reduction and insulin sensitivity, adipocytokines might be among the effectors of physical activity on vasculature. In individuals with type 2 diabetes, adiponectin levels are decreased and leptin levels are increased due to its resistance. Increased leptin/adiponectin ratio in these conditions might predispose affected individuals to vascular inflammation and therefore progression of micro- and macrovascular complications of diabetes.

Objective. The aim of this study was to determine whether the interval training program affects the level of cytokines associated with risk of cardiovascular disease development in type 2 diabetes mellitus patients.

Methods. The study randomized patients with type 2 diabetes aged 35–75 into control ($n = 26$) and interval training (IT, $n = 14$) groups. Patients in IT group had to perform three 60-minute-interval walking sessions (3-minute intervals of slow and fast walking with the intensity of 40 % and 70 % of the peak energy expenditure) per week delivered by smartphone application for four months. The adherence to training protocol was monitored remotely. Variables measured were leptin/adiponectin ratio, albuminuria, glycaemic control, lipid profile, anthropometric measures. Leptin and adiponectin concentration was measured in serum samples by Luminex technology. Repeated measures ANOVA, repeated measures ANCOVA, Pearson correlation coefficient were performed to analyse the impact of intervention on variables of interest.

Results. Interval walking training did not cause statistically significant changes in leptin and adiponectin level, however, a statistically significant reduction in leptin/adiponectin ratio in IT group in the course of intervention (pre-median (IQR) = 1.6 (0.6–2.3), post- median (IQR) = 1.3 (0.8–1.9); $p = 0.01$, interaction effect) was observed. In IT group, Δ leptin/adiponectin correlated significantly with changes in hip circumference ($R = 0.62$, $p = 0.024$), and Δ adiponectin ($R = -0.713$, $p = 0.006$). A statistically significant decrease in albuminuria ($p = 0.002$, interaction effect) in IT group was also observed.

Conclusions. As leptin/adiponectin ratio has been associated with progression of vascular complications of diabetes, our results indicate that interval walking training is effective for improvement of vascular health in diabetes.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” at the Faculty of Medicine, University of Latvia.

Dyslipidaemia as a risk factor for renal function decline in type I diabetes mellitus patients

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Background. Diabetic nephropathy – a significant and frequently observed life-threatening microvascular complication of diabetes. In diabetic nephropathy patients, dyslipidaemia is a common finding. However, the results of the studies about the association of serum lipid and apolipoprotein concentration with diabetic kidney disease differ.

Objective. The current study aimed to investigate the association between lipid and lipoprotein levels and renal function indicators (estimated annual glomerular filtration rate (eGFR) decline and albuminuria) in type 1 diabetes patients.

Methods. In this cross-sectional study, we used biological samples and clinical data of 104 type 1 diabetes patients from a longitudinal study “LatDiane: Latvian diabetic nephropathy study”, that were collected from recruitment visits and follow-up visits with a mean follow-up time of 4.37 years (SD \pm 1.00). Rapid eGFR decline was defined as more than -2.5 ml/min/1.73m²/yearly. Nephropathy progression was defined as a state of albuminuria progress (albuminuria progression was defined as an elevation in albuminuria level to a higher category) and/or rapid eGFR decline. Linear and logistic regression models were performed to evaluate the impact of lipid profile on eGFR decline, changes in albuminuria and nephropathy progression between the two visits. The regression models were adjusted for age, diabetes duration and statin usage at the time of recruitment and follow-up visits, GFR rate, HbA1c and albuminuria levels at the time of recruitment visit.

Results. The mean age of study population (of 104 patients) at both visits was 38.14 years (SD \pm 13.37) and 42.52 years (SD \pm 13.35), respectively, the majority of patients were female (51.9 %). The mean diabetes duration at the time of recruitment was 18.03 years (SD \pm 11.87). Linear regression analysis showed that increased LDL-C and HDL-C levels are associated with a more rapid eGFR annual decline ($\beta = 2.14$; $p = 0.036$, $\beta = 2.83$; $p = 0.006$, respectively). In our multiple logistic regression models, rapid eGFR decline was statistically significantly affected by apoB levels (OR = 1.39; $p = 0.02$).

Conclusions. This study implies the importance of early intervention by correcting serum lipid levels in type I diabetes patients, as it affects eGFR decline and over-all diabetic nephropathy progression.

Acknowledgments. We thank Leonora Pahirko (University of Latvia) for counselling and Sanita Kalva-Vaivode for the recruitment of patients. This study was supported by Roche Academy of Latvia, State Genome database project, the fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases diagnostics and personalized treatment” at the Faculty of Medicine, University of Latvia.

Patch testing for patients with and without atopic disease

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Background. Atopic dermatitis is inflammatory long-term skin disease with a tendency to recur, and most often it affects people in childhood. Atopic disease includes symptoms like allergic conjunctivitis, allergic rhinitis and asthma. Allergic contact dermatitis (ACD) and irritant responses were carefully defined, as was the presence or absence of atopy obtained by history. Patch testing is a method of testing haptens to see if it will work for patient's unique skin.

Objective. The aim of this research was to establish whether the patient with atopic disease is most likely to have positive patch test.

Methods. The retrospective study was performed in Ventspils poliklīnika. This study included 182 patients aged 7 to 83 years. 66.5 % ($n = 121$) women and 33.5 % ($n = 61$) men. For this study, patch tests were used. The patients were included in the study for allergic contact dermatitis using the standard application test kit S-1000 – European Baseline Series, made in Sweden by Chemo-technique containing 30 allergens. Before patch test application, patients determined whether they were suffering from atopic dermatitis. The materials collected from 2013 to 2016 were analysed.

Results. Of 182 patients studied, 73 % ($n = 133$) had no history of atopic disease and 27 % ($n = 49$) were classed as definitely atopic. 133 patients were without atopic dermatitis and out of these, 61.7 % ($n = 82$) had a positive patch test. Additionally, 42 of these patients had a positive test for more than one hapten. 49 patients were suffering from atopic disease and out of these, 42 % ($n = 21$) had a positive patch test. 56.6 % ($n = 103$) tested positive at least to one patch test, and 11.5 % ($n = 21$) were suffering from atopic disease. Patients were divided by age into two groups. The first one was a younger group (Y) aged 7 to 40 years, while the older group (E) was aged 41 to 83. 61.2 % ($n = 30$) patients from Y group were suffering from atopic dermatitis, while in group E only 38.8 % ($n = 19$) had this diagnosis. 36.8 % ($n = 49$) of those who denied atopy were in group Y, but 63.1 % ($n = 84$) – in group E.

Conclusions. Among the atopic disease patients there were fewer positive patch tests. Young atopy patients more often performed patch tests seeking causes of disease without results. Older patients without atopy performed patch testing to find out ACD more frequently. We recommend performing less patch testing for atopic disease patients. However, the older patients without atopic disease should take patch tests more often.

Acknowledgements. The authors declare the absence of conflict of interest.

Low-level laser therapy in treatment of hepatobiliary disorders in patient with acne vulgaris

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Background. Low-level laser therapy (LLLT) includes intravenous laser therapy (IVL), and percutaneous low-level laser (PLLL) can be used in many different areas of medicine. Many functional disturbances, including acne vulgaris and functional disorders of the hepatobiliary system, have a persistent character and can be treated not only with medications, but also using physiotherapy.

Objective. The aim of the current study was to evaluate the effects of low-level laser therapy in hepatobiliary disorder treatment in acne vulgaris patients.

Methods. The total of 92 patients with moderate acne vulgaris combined with functional disorders (gallbladder ejection fraction less than 40 % according to the Rome III), matched by sex and age, were divided into two groups due to the therapy of hepatobiliary disorders (HBD): in the 1st group ($n = 42$), the patients were advised to follow a light normal diet, in the 2nd group ($n = 50$), the patients were prescribed a course of LLLT. For the correction of the gallbladder hypo function, all patients had a course of 10 procedures. Daily intravenous laser therapy was performed according to the following modes: radiation head ($\lambda - 635$ nm), continuous mode, radiation power of 1.5 mW at the end of sterile optic fibre. Ultrasound examination of the abdomen with fatty meal testing were performed twice – at the baseline and after 28 days.

Results. The average gallbladder ejection fraction value at the baseline was by 36 % (± 3.1) in the 1st group, by 34 % (± 4.6) in the 2nd group. The average ejection fraction in the 1st group on the 28th day was 37 % (± 2.2); in the 2nd group – 48 % (± 7.9). Finally, ejection fraction in the 2nd group increased by 30 % after 10 procedures.

Conclusions. The study demonstrates the ability of the low-level laser therapy to influence the gallbladder functional activity in the patients with hepatobiliary system dysfunction comorbid with acne vulgaris. Normalizing of ejection fraction was achieved in all the patients of the 2nd group compared with a mild improvement in the 1st group.

Acknowledgements. The authors declare the absence of conflict of interest.

Predictive factors of obstructive sleep apnoea

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Background. Obstructive sleep apnoea (OSA) is common amongst Latvian population, nevertheless, there is a poor diagnostic coverage. Improved physician's knowledge about risk factors and screening methods could help to diagnose OSA.

Objective. The primary aim of this study is to define the most important and independent risk factors when predicting OSA. The secondary aim is to compare the predictive capabilities of the factors included in STOP BANG Questionnaire (SBQ) with alternative factors using multiple logistic regression.

Methods. Retrospective study includes 634 patients who from 2014 to 2018 underwent polygraph tests in the Sleep Disorders Centre in Riga. Spearman's correlation coefficient was used to explore relationships between OSA and predictive factors of the SBQ, as well as Mallampati score, palate type, distance from posterior wall of pharynx and others. Significant variables were entered into a multiple logistic regression model to identify statistically significant predictors for OSA. ROC curve was used for evaluating logistic regression models.

Results. Multiple logistic regression for SBQ included factors showed that features such as BMI ($\geq 35 \text{ kg/m}^2$) (adj. OR 4.79, $p = 0.005$), age (≥ 50 years) (adj. OR 3.70, $p < 0.001$), neck circumference ($< 40 \text{ cm}$) (adj. OR 2.64, $p = 0.003$) loud snoring (adj. OR 2.64, $p = 0.013$) and male gender (adj. OR 2.11, $p = 0.044$) are independent factors for predicting OSA. Alternative multiple logistic regressions models (M1, M2) were created for the purpose of better determining independent factors on which OSA depends. M2 showed, that a narrow palate type is an independent factor for OSA (adj. OR 3.618, $p < 0.001$). Two alternative multiple logistic regression models (M1, M2), which includes factors like Mallampati class IV, small distance from posterior wall of pharynx, a narrow palate showed higher AUC in ROC curve when compared to SBQ model (M2 – AUC 0.853; M1 – AUC 0.832 vs. SBQ – AUC 0.825, $p < 0.001$). These models also showed a better specificity, PPV, NPV, when compared with the model with all the SBQ features included.

Conclusions. The most important and independent risk factors for predicting OSAS are BMI ($\geq 35 \text{ kg/m}^2$), neck circumference ($> 40 \text{ cm}$), age (≥ 50 years), systolic arterial pressure ($\geq 140 \text{ mm Hg}$), male gender and narrow palate type. Narrow palate, small distance of posterior wall of pharynx and Mallampati class IV proved to have higher predictive capabilities when compared to SBQ factors such as fatigue, sleepiness or observed apnoea episodes. Future research should be dedicated to validating these factors in the screening questionnaires.

A case-control study of the association between genetic polymorphisms and the exudative age-related macular degeneration in Latvian population

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Background. Age-related macular degeneration (ARMD) is a complex, multifactorial disease associated with age, environmental and genetic factors. It is the most common cause of blindness in the Western populations.

Objective. The purpose of this study was to determine whether the genetic polymorphisms in genes CFH (rs1061170), HTRA1 (rs11200638), ARMS2 (rs10490924), C3 (rs2230199), IL-8 (rs4073), VEGF (rs833061), VEGF (rs3025000) are associated with exudative ARMD in the Latvian population.

Methods. This case-control study included 73 exudative ARMD patients admitted to Riga East University Hospital, Department of Ophthalmology for intravitreal injections (age: 78 ± 7.7 ; females: 65.8 %) and 50 controls (females: 66.0 %; 22 cataract patients (age: 74.68 ± 9.46) and 28 primary open angle glaucoma patients (age: 70.29 ± 7.68)). Genomic DNA was extracted from peripheral blood leukocytes by phenol-chloroform method. Genotyping was performed by qPCR reaction using TaqMan SNP Genotyping assays. Statistical analysis was performed using Plink version 1.9, covariate-age was used in the calculations.

Results. No deviation from Hardy-Weinberg equilibrium was detected in control and patient groups in all seven SNPs ($p > 0.05$). Allelic frequencies of five SNPs were found to be significantly different between cases and controls in our cohort. SNPs CFH rs1061170 (minor allele C: $p < 0.001$, OR = 4.33, 95%CI: 2.12–8.83), HTRA1 rs11200638 (minor allele A: $p = 0.0024$, OR = 2.32, 95 % CI: 1.35–4.00), ARMS2 rs10490924 (minor allele T: $p = 0.0012$, OR = 2.50, 95 % CI: 1.435–4.35) increases risk, whereas VEGF rs3025000 (minor allele T: $p = 0.0013$, OR = 0.32, 95 % CI: 0.16–0.64) and VEGF rs833061 (minor allele T: $p = 0.0103$, OR = 0.47, 95 % CI: 0.26–0.83) are protective of exudative ARMD. No statistically significant association was found between the IL-8 rs4073 ($p = 0.432$) and C3 rs2230199 ($p = 0.124$). The minor allele frequency (MAF) for all SNPs in control group were similar with previous reports of allele frequencies in European populations.

Conclusions. Overall, the results replicated the previously reported associations between risk alleles and ARMD. There was a significant association between five SNPs in CFH, ARMS2, HTRA1 and VEGF genes with exudative ARMD in Latvian population. These findings may advance the potential for preclinical prediction for ARMD in future genetic tests.

H. PYLORI, MICROBIOTA & NUTRITION

Comparison of effectiveness of standard triple therapy and high-dose amoxicillin/ bismuth therapy in eradication of *H. pylori*

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Background. Antibiotics are the standard treatment for *Helicobacter pylori* infection. A standard triple therapy including Clarithromycin leads to persistent macrolide resistance in the normal microbiota, and tends to cause a wide spectrum of side effects.

Objective. to compare effectiveness of standard triple therapy (Amoxicillin 1g x 2, Clarithromycin 0.5g x 2 and Esomeprazole 0.04g x 2 – 10 or 14 days) and non-macrolide high-dose amoxicillin/bismuth therapy (Amoxicillin 1g x 3, Esomeprazole 0.04g x 2 and Bismuth subcitrate 0.24g x 2 – 14 days), as well as to evaluate patients' compliance with regimens.

Methods. Clinical trial participants were healthy individuals aged 40–64. Eradication subgroup underwent urea breath test (UBT); positive patients were randomly divided into eradication subgroups. Control group included patients with unknown *H. pylori* status. Patients were called in 21–28 days after therapy; side effects and patients' compliance were registered. Control UBT was performed after six months. Participants also provided stool samples before and six months after therapy for microbiome analysis.

Results. Overall, 2341 patients participated. By now, follow-up UBT was undergone by 777 patients (33.2 %). Standard 10-day therapy was effective in 87.8 % (115/139), standard 14-day – in 88.8 % (143/161) and alternative therapy – in 78.5 % (117/149). There was no significant difference of effectiveness between therapy regimens ($p = 0.169$, $\chi^2 = 6.4$). Moreover, the full usage of alternative therapy was higher due to fewer side effects: 84.2 % vs 78.3 % in 14-day-triple therapy (89.4 % in 10-day-triple). Compliance was associated with effectiveness of the therapy ($p = 0.002$).

Conclusions. Reduction of antibiotic use may avoid resistance growth, have a positive effect on patients' compliance and a foreseeably lower impact on microbiota with similar effectiveness.

Acknowledgements. The authors declare the absence of conflict of interests. The work was supported by ERDF (European Regional Development Fund) in Latvia, project No. 1.1.1.1/18/A/184 "Optimisation of *H. pylori* eradication therapy for population-based gastric cancer prevention".

The comparison of side effects of standard triple therapy and high-dose amoxicillin / bismuth therapy in eradication of *H. pylori*

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Background. Antibiotics are the standard treatment for *H. pylori* infection. A standard triple therapy including two antibiotics tends to cause a wide spectrum of side effects, which may lead to therapy discontinuations and decrease of eradication rates.

Objective. To compare side effects of standard triple therapy and high-dose amoxicillin/bismuth therapy in eradication of *H. pylori*.

Methods. Clinical trial participants were healthy individuals aged 40–64. Eradication subgroup underwent urea breath test (UBT); positive patients were randomly divided into eradication subgroups – standard triple therapy (Amoxicillin 1g x 2, Clarythromycin 0.5g x 2 and Esomeprazole 0.04g x 2 – 14 days) and high-dose amoxicillin/bismuth therapy (Amoxicillin 1g x 3, Esomeprazole 0.04g x 2 and Bismuth subcitrate 0.24g x 2 – 14 days). Patients were called in 21–28 days after therapy; side effects and patients' compliance were registered. Control UBT was performed after six months. Participants also provided stool samples before and six months after treatment for microbiome analysis.

Results. By now, we acquired data from 157 patients with triple and 149 patients with bismuth therapy. Side effects were reported by 63.1 % ($n = 99$) and 51.7 % ($n = 77$) respectively. The mean number of side effects in triple therapy was higher ($p = 0.03$): in standard triple therapy – 2.1 (median 2.0, deviation 1.3), while in bismuth therapy – the mean 1.8 (1.0; 1.10).

Table. Side effects in different eradication regimens (*significant difference)

	Standard triple 14 days (n, %)		High-dose amoxicillin/ bismuth, 14 days (n, %)	
Bitter taste*	72	72.7 %	8	10.4 %
Diarrhoea*	36	36.4 %	16	20.8 %
Nausea	15	15.2 %	9	11.7 %
Fatigue*	14	14.1 %	5	6.5 %
Stool colour change*	7	7.1 %	51	66.2 %
Vomiting*	6	6.1 %	0	0.0 %
Other	3	3.0 %	5	6.5 %

Moreover, the compliance due to fewer side effects was higher: 96.3 % vs 93.2 % ($\chi^2=4.1$).

Conclusions. Lower frequency of side effects provides better compliance and therefore increases a chance of positive outcome.

Acknowledgements. The work was supported by ERDF (European Regional Development Fund) in Latvia, project No. 1.1.1.1/18/A/184 "Optimisation of *H. pylori* eradication therapy for population-based gastric cancer prevention". Conflicts of interests: none.

Correlation of lactulose and glucose breath test results in diagnosing small intestinal bacterial overgrowth (SIBO)

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Background. Lactulose and glucose breath testing is the generally accepted standard for diagnosing SIBO. The North American and the Italian (European) guidelines are available for standardizing the diagnostic approach.

Objective. The aim of the current study was to compare the results of lactulose and glucose tests in SIBO detection and to address the differences for test-positivity in our cohort.

Methods. Retrospective analysis of patients who underwent both glucose and lactulose breath testing in Digestive Diseases Centre "Gastro" from 2015 to 2019 was performed. 60 patients with abdominal symptoms (bloating, diarrhoea, and malabsorption) were enrolled in the study. Standard breath testing protocols were applied. All the patients performed lactulose and glucose breath tests on separate days.

Hydrogen (H₂) and methane (CH₄) concentrations were measured in each of the breath samples with carbon dioxide correction factor applied. *QuinTron* breath analyser was used for all measurements.

We used the criteria set out in the North American guidelines for defining SIBO positive subjects. The criteria listed in the European guidelines were used for comparative purpose.

Patients were also asked to report any symptoms throughout the breath testing period.

Results. The study cohort was 60 patients (50 % male) with median age of 42 years.

41.6 % ($n = 25$) and 13.3 % ($n = 8$) of patients were diagnosed SIBO positive with lactulose and glucose test, respectively. If the criteria of the European guidelines were applied for the glucose test, one subject would have turned positive.

Out of 21 discrepant cases (positive lactulose, negative glucose test) elevated (≥ 16) H₂ and (≥ 10 ppm) CH₄ concentrations were detected during the entire testing period (in lactulose test 8 (38.0 %) and 7 (33.3 %) subjects, respectively; in glucose test 1 (4.8 %) subject with elevated H₂ concentration). 2 subjects (9.5 %) had elevated (≥ 16 ppm) basal H₂ concentration in glucose test.

12 subjects (5 males, 7 females) reported symptoms during lactulose test, and 16 subjects (6 males, 10 females) during glucose test, while 7 subjects (11.7 % of all patients) reported symptoms in both tests.

Conclusions. There was a relatively poor correlation between the glucose and lactulose test results. One possible explanation is failure of glucose test to detect SIBO in the distal part of ileum.

Discrepancies between the North American and European guidelines were identified suggesting the necessity to update the European guidelines (currently in process).

Acknowledgements. The authors acknowledge the support extended by Digestive Diseases centre "GASTRO", which enabled retrospective data collection of patients included in analysis.

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***Helicobacter pylori* and peptic ulcer disease**

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Background. Peptic ulcer is a recurrent disease characterized by the formation of an ulcer in the stomach or duodenum lining. The highest annual rate of peptic ulcer was recorded at 141.8 per 100 000 people in Spain, and the lowest in the UK at 23.9 per 100 000 people.

Objective. The purpose of this study is to evaluate the dynamics of peptic ulcer disease and *H. pylori* incidences over a long period of time based on the results of our own research.

Methods. One group of 252 patients with peptic ulcer disease was examined in 1997, another selection of 130 patients – in 2006, and 30 patients – in 2018.

Results. The study showed that in comparison with data from 1997 and 2006, the structure of *H. pylori*-associated diseases changed in 2018. In general, incidences of *H. pylori* in the group of patients with chronic gastritis and peptic ulcer decreased from 85 % in 1997 to 40 % in 2018. As a result of these developments, the gastric dyspepsia now prevails and peptic ulcer occurrences are radically less common than before (7 % vs 93 %).

At the same time, internal structure of the ulcer disease among patients did not change, duodenum ulcer was a prevailing form. In 1997 and 2006, *H. pylori* rate in the group of patients with peptic ulcer was the same – 76.2 %. In 2018, the presence of *H. pylori* in patients with peptic ulcer disease increased to 85 %.

In a group of patients with peptic ulcer disease infected with Cag A. positive strains of *H. pylori*, proliferation processes were morphologically predominant (50 %), and apoptosis processes were suppressed (20 %), which determined the morphogenesis of chronic gastritis and peptic ulcer disease.

Conclusions. During the period of observation, the structure of *H. pylori*-associated diseases changed – gastric dyspepsia prevailed over peptic ulcer diseases. Peptic ulcer disease occurs less frequently than before (7 % vs 93 %), and this is due to the results of successful *H. pylori* eradication therapy, improved sanitary conditions and good disinfection processes of endoscopic equipment. *H. pylori* incidences also decreased, the share of peptic and duodenum ulcers in gastric diseases became smaller, but the presence of *H. pylori* and structure of ulcer diseases has not changed.

***H. pylori* clarithromycin resistance: experience in Kazakhstan**

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Background. The current Maastricht V/Florence consensus report guidelines recommend *Helicobacter pylori* (*H. pylori*) eradication in all *H. pylori*-positive patients with an eradication regimen based on the local *H. pylori* resistance pattern. In patients or areas of well-documented low clarithromycin resistance (< 15 %), it is recommended to use a standard first-line triple eradication therapy consisting of two antibiotics, usually – clarithromycin with either amoxicillin or metronidazole, and a proton pump inhibitor. The steadily increasing rate of clarithromycin resistance is one of the major factors affecting *H. pylori* eradication rates, therefore in areas of high clarithromycin resistance (> 15 %), quadruple therapy regimens are strongly recommended.

Objective. The aim of this study was to evaluate the susceptibility of *H. pylori* to clarithromycin in an asymptomatic adult population in Kazakhstan.

Methods. Upper endoscopy was performed on healthy individuals, aged 40–64 and residing in Kazakhstan (GISTAR regional pilot study). Biopsies were obtained and evaluated according to the updated Sydney system. Histologically confirmed *H. pylori* positive biopsies were used for testing with molecular methods described in Oleastro et al., 2003. This involved DNA extraction directly from gastric biopsies, amplification of 23S RNA gene with *H. pylori* specific primers and subsequent real-time PCR evaluation to determine the most frequent clarithromycin resistance conferring point mutations.

Results. Altogether, 66 strains were tested. 60 out of 66 (90.6 %) were *H. pylori* positive and clarithromycin resistance was detected in 11 out of 60 cases (18.3 %) with five being homozygous mutants and six – heterozygous with both mutant and wild type variants.

Conclusions. The frequency of *H. pylori* resistance to clarithromycin in the tested group was higher than 15 %, which indicates a need to abstain from using empiric clarithromycin containing first line triple therapy, and to switch to bismuth-containing quadruple therapies or introduce routine *H. pylori* susceptibility testing.

Acknowledgements. The work was supported by the Fundamental and Applied Research Projects Program in Latvia, project No. lzp-2018/1-0135, “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions”, and conducted as part of the regional pilot study of GISTAR (Gastric Cancer Prevention Study in collaboration with the project “Decreasing the burden of gastric cancer in Kazakhstan: evaluation of the existing situation and search for improvement possibilities”), project No. AP05133849.

Single nucleotide variants in long non-coding RNAs *ANRIL* and *H19* are associated with gastric cancer type and *Helicobacter pylori*

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Background. Long non-coding RNAs (> 200nt; lncRNA) are important in regulation of various genomic functions, epigenetic and biological processes. Various alterations in lncRNA expression and polymorphisms have been associated with many human diseases, including cancer. Gastric cancer (GC) is one of the most common and lethal cancer cases worldwide. Known risk factors of GC include *Helicobacter pylori* infection, environmental factors, genetics (CNVs, SNPs), epigenetics (methylation, miRNA). To improve the diagnosis of GC, the research of new biomarkers is needed.

Objective. The aim of this study was to assess association between single nucleotide polymorphisms in long non-coding RNA genes and gastric cancer.

Methods. In total, 990 individuals (control group ($n = 484$), GC group ($n = 506$)) were included in this study. Study group was recruited during 2005–2013 years at the Dept. of Gastroenterology, Lithuanian University of Health Sciences Hospital Kaunas Clinic (Lithuania) and Digestive Disease Centre GASTRO (Riga, Latvia). Genomic DNA was extracted using salting-out method. Genotyping was performed using TaqMan assays and real-time PCR. SNPs ($n=10$) in *H19*, *MALAT1*, *HOTAIR*, *MEG3*, *ANRIL* lncRNAs were selected. Statistical analysis of the results was performed using PLINK (v1.9). P-values were corrected using Bonferroni correction ($P<0.05$).

Results. Three SNPs (*H19* rs2067051; *MEG3* rs11160608 and rs3742396) were not in Hardy Weinberg's Equilibrium in control group ($P_{HWE} > 0.05$) and were therefore excluded from further analysis. A combined genetic analysis of Lithuanian and Latvian GC individuals' data revealed nominal association between *ANRIL* gene rs17694493 and GC, but after Bonferroni correction this result did not remain significant ($P_{corr} > 0.05$). Genotype-phenotype analysis in Lithuanian population revealed significant associations between: (1) *H. pylori* infection and *H19* rs217727 A allele ($P_{corr} = 2.83 \times 10^{-6}$) and AA genotype ($P_{corr} = 9.8 \times 10^{-6}$); (2) intestinal GC type and *ANRIL* rs1011970 T allele and TC genotype ($P < 0.05$). In Lithuanian population, there was no correlation between explored SNPs and tumour stage (TNM). No significant associations with phenotype of GC were found in Latvian study group.

Conclusions. Association between rs1011970 (T allele, TC genotype) of the *ANRIL* gene and the intestinal gastric cancer has been identified in the Lithuanian population. Association of *H. pylori* infection and rs217727 (A allele and the AA genotype) polymorphism of *H19* gene was identified in the Lithuanian population.

Acknowledgements. The authors declare the absence of conflict of interest. Study was funded by Lithuanian University of Health Sciences, Faculty of Medicine and EU structural funds, grant No. 09.3.3-LMT-K-712-01-0130.

Adherence to the Nordic and Mediterranean diets in Latvian population 40–64 years of age

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Background. WHO Health Evidence Network Synthesis Report in 2018 stated that there was an evidence of clear health benefits for both the Mediterranean diet (MD) and the Nordic diet (ND); European Region States are to consider the existing MD and ND based dietary guidelines for either adoption or enhancement of the existing nutrition policies. The last time the Republic of Latvia Ministry of Health approved dietary guidelines was in 2008.

Objective. To evaluate adherence to MD and ND in average 40–64 years old Latvian population.

Methods. Study was carried out as a sub-study of the “Multicentric randomised study of *H. pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (the GISTAR study)”. Participants aged 40 to 64 years were enrolled in the study centre located in Jēkabpils from October 2019 to January 2020. Individuals were invited to participate in the study by using patient lists of general practitioners in the area of local recruitment centre and contacted through telephone and/or mail. Participants signed an informed consent form and were examined by a study physician upon enrolment. Participants completed 22 item self-administered questionnaire in Latvian or Russian. The questionnaire included translated and adapted MEDAS (14-item Mediterranean Diet Adherence Screener) and the New Nordic Diet score questionnaires. One score point was assigned for each match according to the published references. Adherence to MD was evaluated as low (score 0–5), medium (score 6–9) or high (score 10–14). Adherence to ND – as low (score 0–3), medium (score 4–5) or high (score 6–10).

Results. 391 participants completed the questionnaire, 27 had not answered all the questions and were excluded from the ND analysis. Low adherence to the MD was revealed in 267 responders (68.3 %), medium – in 116 (29.7 %), high – in 8 (2.0 %). Adherence to the ND was evaluated as low in 111 (30.4 %), medium – in 145 (39.7 %) and high – in 109 (29.9 %) of the cases. In both diets, there was a statistically significant difference in adherence between genders (Chi-squared test, $p < 0.001$), but no significant effect of age was observed. On average, respondents received 34.1 % of the maximal MD score, but 45.2 % of the ND maximal score ($p < 0.001$).

Conclusions. Adherence to the MD in Latvia is low; there is a significantly higher adherence to the ND pattern. Local food preferences should be taken into account during the development of new dietary guidelines.

Acknowledgements. The study was supported by Latvian Council of Science, project No. lzp-2018/1-0135 “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions.”

Assessment of dietary intake in Latvian adults in relation to their mental wellbeing

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Background. Diet has an impact on subjects' mood and vice versa. When assessing subjects' food choices, the emphasis is more often placed on mental disorders. In this study, we focus on positive mental health and mental wellbeing and the way it affects subjects' food choices and dietary intake.

Objective. The aim of the current study was to evaluate whether the subjects with a higher wellbeing score make healthier food choices and consume more adequate amount of energy than those with lower wellbeing score.

Methods. A stratified sample of Latvian adults aged 19–64 ($n = 140$) was drawn. The dietary data was collected using food propensity questionnaire, one 24-h dietary recall and a three-day food diary. The data on mental wellbeing was collected using an adapted version of the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS).

Results. The preliminary data suggests that the subjects with a higher wellbeing score tend to have healthier food choices in terms of consuming more food products considered healthy and beneficial for health (e. g., vegetable and fruit) and less food products that are considered less healthy (e. g., processed meat products, savoury snacks and sweets). The preliminary data also suggests that subjects with a higher wellbeing score tend to consume less energy than the subjects with a lower score.

Conclusions. A higher wellbeing score contributes to healthier food choices and consumption of lower amount of energy by individuals in comparison to those with a lower wellbeing score.

Acknowledgements. The results are obtained within the project No. lzp-2018/2-0266 "Gut microbiome composition and diversity among health and lifestyle induced dietary regimen" which is funded by the Administration of Studies and Science.

PUBLIC HEALTH & SOCIAL MEDICINE

Low birth weight temporary trends in the Baltic states, and in the European Union over 25-year period

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Background. Low birth weight (LBW) is an important indicator of population's health, and reflects the living conditions, health and health behaviour of pregnant women. Information about trends of LBW in the Eastern Europe is scarce.

Objective. We assessed the changes in patterns of LBW in the Baltic states over 25-year period. In addition, we analysed the associations between changes in macroeconomic factors and LBW in the European Union (EU-28).

Methods. Data on LBW below 2500 g and Gross Domestic Product per capita were extracted from the World Health Organization's database. Joinpoint regression analysis was performed to analyse trajectories over the years 1990–2014. We also investigated how changes in well-being influenced the changes in LBW.

Results. In the Baltic countries, the average value of LBW did not exceed 5 % during 25 years, and it was distinctly lower compared to EU-28. Over 1990–2014, the significant increase in LBW rate was observed in Lithuania (by 0.6 %/year); a similar trend was shown in the EU-28 (0.7 %/year). In Latvia, in the 1990s the rate of LBW was on the increase (by 1.3 %/year), but later on a decreasing trend was observed (by –1.3 %/year). In Estonia, no significant changes in trend were found. Despite this, a gap in LBW between all Baltic States and the EU-28 has increased, especially in Latvia. The strongest effect of reduction in LBW was associated with the annual increase in Gross Domestic Product.

Conclusions. Among the Baltic states, only Lithuania demonstrated an increase in LBW trends. Therefore, the need for further observation and interventions addressed to women's health in reproductive age is of importance. The study revealed that decrease in LBW may have been influenced by the increased Gross Domestic Product and improved well-being: better living conditions of families, availability for counselling, accessibility of obstetric care, and access to prenatal examinations.

Acknowledgements. The authors declare the absence of conflict of interests.

The present study was supported by the Medical University of Bialystok, Poland (Grant No. N/ST/ZB/18/002/3303).

Adherence to prescribed medications – administrative data study of discharged acute myocardial infarction patients

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Background. The problem of suboptimal adherence to prescribed medications is widely known. Linking personalised administrative data of hospital discharges to state-reimbursed medication data and causes-of-death registry data gives a real-life insight into this problem.

Objective. The aim of the study was to estimate levels of adherence to specific medications within the study population by using individual-level adherence estimates.

Methods. 9832 patients from acute myocardial infarction (AMI) dataset for years 2014–2018 were selected corresponding to the following eligibility criteria: (1) discharged alive after AMI hospitalization; (2) spending no more than 2 weeks in hospital during a 360-day follow-up period; (3) at least one post-discharge prescription of any medication of interest during the follow-up period. For each patient, the amount of purchased medication was calculated using state-reimbursed medication dataset. The defined daily dose (DDD) for substances contained in each medication was used to obtain individual-level adherence estimate. Adherence was measured at time periods of 30 and 360 days. At each time period, adherence was measured for patients that have not had predefined endpoints (death from any cause, myocardial infarction, stroke) during the time period of interest. When calculating adherence for the period of 30 days, the patients whose next post-discharge hospitalization during this time period exceeded 3 days were also excluded.

Results. From the total number of selected AMI discharge cases (including the patients for whom a full follow-up period was not observed), the number of patients with at least one post-discharge prescription of specific medication group were, as follows: 8734 (89 %) for β -blockers, 7876 (80 %) for angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB), 8926 (91 %) for statins, 8916 (91 %) for antiplatelet therapy. Among the discharged patients without any endpoint event and where a full corresponding follow-up period was observed, 80 % adherence threshold at time periods of 30 and 360 days was reached for the following numbers of users of each group of medicine: 1591 (29 %) and 498 (9 %) – β -blockers, 3749 (74 %) and 3014 (60 %) – ACEi/ARB, 4810 (86 %) and 4313 (77 %) – statins, and 4600 (83 %) and 1649 (30 %) – antiplatelet therapy.

Conclusions. The approach used to estimate medication adherence requires several data processing and interpretation issues to be addressed in order to investigate the effect of adherence on specific outcomes. The main issue could be an accurate estimation of prescribed amount of medication at individual level, as the mismatch between the daily defined dose and the prescribed daily dose can significantly bias the estimated adherence.

Acknowledgements. The study was a part of the University of Latvia and the Centre for Disease Prevention and Control joint-project “Transparency and healthcare data – towards public monitoring for quality and efficiency”.

Common background, different pathways: primary healthcare system in Latvia and the Republic of Moldova after twenty-five years

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Background. Before regaining their independence, former Soviet Republics shared a common health system, the so-called Semashko model, which is highly specialized and hospital-oriented. A goal was established to achieve universal coverage and equal medical services for urban and rural populations. The restored states had to decide on the future development of their health systems after 1991. Following the Alma-Ata Declaration, both Latvian and Moldovan governments decided to introduce family medicine as the basis for their health systems, which showed better health indicators and higher efficiency of the entire healthcare system.

Objective. This study observes the pathways of primary healthcare in Latvia and Moldova and compares the progress made after twenty-five years.

Methods. Analysis of the official legislative and health regulation documents, reports and statistic data, country health profiles and WHO Observatory Reports and a comparison of the results.

Results. The number of family physicians in Latvia and Moldova is currently similar at around 1 500; however, the population in Moldova is larger by one third. Family physicians see 5.9 million patients a year in Latvia and 10.3 million in Moldova, an average of 3 visits per registered patient. Life expectancy remains six years below the European Union (EU) average in Latvia and it is more than three years below the Latvian level in Moldova. Circulatory system disorders accounted for 56 % of all deaths in Latvia in 2016 and 58 % of the deaths in Moldova in 2017, in comparison with slightly more than one third across the EU. Despite a 45 % increase since 2010, health expenditure per capita in Latvia remained the second lowest in the EU at € 1 213 in 2017. According to the World Bank, per capita health expenditure in Moldova in 2016 was five times lower than in Latvia.

Conclusions. Latvia and Moldova have had a common influence on the pathways and health outcomes since 1991. The initial approach to primary care reform was based on political power, but there was a lack of a stable long-term strategy for primary healthcare in both countries. Nevertheless, Latvia has focused on a step-by-step implementation of the family medicine model. The focus of the reform process in Moldova is on the completion of current objectives. In addition, the low income and socio-economic situation of both countries are the factors that keep health indicators at the lowest in the EU.

Acknowledgements. The authors declare the absence of conflict of interests.

Perception of patient safety climate in Latvian health care organizations: differences in personal opinions

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Background. Hospital-based studies from different countries show that medical errors occur in approximately 10 % of hospitalizations. The fundamental source of errors is weak safety culture. Studies suggest possible relationships between safety culture, climate and outcomes, including medical errors. The first Latvian concept for patients' safety was accepted in 2017, however, in Latvia there are only few measurable safety indicators, lack of research on patient harm and safety culture, and assurance that the proposed concept fits the actual needs of hospitals. Differences in personal evaluation of patient safety climate are not fully investigated yet.

Objective. The aim of the current study was to investigate differences between nurses in comparison with other healthcare professionals in assessment of domains of safety climate.

Methods. Altogether, 744 healthcare professionals were enrolled in the study. We assessed patient safety climate using a previously validated Staff Survey for Measuring of Patient Safety (SSMPS) questionnaire. In addition, information on socio-demographic and work-related conditions was assessed. The reliability of observed answers was investigated by using α -Cronbach reliability measure. The differences between nurses and other healthcare professionals in their assessment of domains of SSMPS were evaluated by using Kruskal-Wallis test.

Results. Most of the study participants were women (92.1 %) aged 45–54 (36.4 %) and working full time (91.5 %). 390 (52.4 %) of the participants had never attended a patient safety training or had attended only one lecture about it. Four out of six domains of SSMPS displayed medial reliability: Safety Climate (α Cronbach = 0.729), Teamwork Climate (α Cronbach = 0.635), Job Satisfaction (α Cronbach = 0.717), and Stress Recognition (α Cronbach = 0.735), however, two of them displayed a low reliability and were excluded from the analysis (Work Conditions (α Cronbach = 0.465), Perception of Management (α Cronbach = 0.395)). We observed significant differences between assessment of patient safety climate by nurses in comparison with other healthcare professions two of four investigated SSMPS domains (Safety Climate $p = 0.02$ and Teamwork Climate $p < 0.01$). Nurses perceive the safety climate more critically than other healthcare professionals: the mean \pm Standard deviation for Safety Climate 3.37 ± 0.45 and 3.49 ± 0.49 , and for Teamwork Climate 3.62 ± 0.48 and 3.81 ± 0.66 , as indicated by nurses and other professionals, respectively.

Conclusions. Nurses can understand the teamwork and safety climate more completely than other healthcare professionals. Specific training programmes with joint participation of nurses and physicians should be devised to increase the capacity of healthcare professionals, and to profit from the advantages of including nurses in the team.

Muscle fatigue of construction workers and plasterers in construction enterprise

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Background. Construction industry is one of the oldest industries in Latvia. Injuries and muscle pain affecting the wrists, shoulders, neck and back are common problems for these workers, caused by compulsory work postures, repetitive movements and prolonged standing positions. 60 construction workers and 30 plasterers with chronic pain (for four months or more) in the neck, shoulders, arms, hands and legs were chosen for the research. All of the participants agreed to take part in the objective myotonometry measurements.

Objective. of this study was to determine the muscle fatigue caused by physical load for construction workers and plasterers in medium-sized construction enterprise.

Methods. The extended version of Standardised Nordic Musculoskeletal Questionnaire (NMQ-E) was used to assess musculoskeletal problems of construction workers and plasterers. Determination of the functional state of skeletal muscles and muscle fatigue was carried out using myotonometric measurements with the MYOTON-3 device that is a non-invasive method. Myotonometry testing of the muscles was performed at the beginning and at the end of the working week in relaxed state in various muscle groups.

Results. NMQ-E inquiry data showed that construction workers and plasterers most frequently complain about feeling discomfort after work, particularly, fatigue or muscle pain in the neck, shoulders, arms, hands and legs. Myotonometric measurement results show that construction workers' muscle tone at the end of the working week has increased in the most of muscles of the shoulder region (m. trapezius – upper part) and wrists/hands (m. extensor digitorum; m. flexor carpi radialis). Plasterers' muscle tone at the end of the working week increased in the most muscle groups in wrists/hands, in shoulder region, as well as in legs: m. flexor carpi radialis; m. tibialis anterior; m. gastrocnemius. Accordingly, 18 ($\kappa = 0.65$) construction workers can be referred to category III, and 42 ($\kappa = 0.78$) construction workers – to category II, whereas 22 ($\kappa = 0.88$) plasterers have been referred to category II, and 8 ($\kappa = 0.65$) plasterers – to category III. Hence, for both reference groups muscles relax partly and are not able to relax fully, thereby resulting in high muscle fatigue levels.

Conclusions, Myotonometric measurements are suitable for objective determination of the fatigue of various muscle groups. During our research, low muscle frequencies were not examined since the MYOTON-3 device does not allow to measure the deep muscle groups. Therefore, the investigation will be continued. In this case, the electromyography measurements are necessary.

Work-related neck musculoskeletal pain among computer workers

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Background. Work-related musculoskeletal pain is a biopsychosocial phenomenon usually associated with individual and work-related causes. Epidemiological studies have shown that employees who work with computers, are more likely to complain of musculoskeletal disorders (MSDs) and the neck localisation is the most vulnerable in this regard.

Objective. The aim of this study was to evaluate associations between the neck pain and individual and work-related factors among computer workers.

Methods. The investigation was conducted in three randomly selected public sector companies of Kaunas. The study consisted of two parts – a questionnaire-based survey (Nordic Musculoskeletal Questionnaire and Copenhagen Psychosocial Questionnaire) and a direct observation (to evaluate work ergonomics by using RULA (Rapid Upper Limb Assessment) method). The study population consisted of 513 public service office workers whose duties were directly associated with computer work.

Results. The survey showed that MSDs in the neck area were expressly prevalent among the investigated population. The prevalence rate amounted to 65.7 % of respondents. According to our survey, the neck localisation MSDs were significantly associated with older age, greater work experience, high quantitative and cognitive job demands, working for longer than 2 h without taking a break, as well as with higher ergonomic risk score (RULA). According to the full adjusted model (multivariate logistic regression analysis), the strongest predictor for neck pain was found to be the length of experience working with a computer – employees with the greatest experience of working with computers (16–36 years) had a 2.19 times (95 % CI: 1.17–3.98) greater probability of complaints, just like the employees with 6–15 years of experience – 2.16 times (95 % CI: 1.17–3.98), in comparison with the employees, who had been working with computers for the shortest period of time. The group of the respondents who had the high quantitative and average cognitive work demands in comparison with the group of employees who encountered low quantitative and cognitive demands, appeared to have greater probability of experiencing neck complaints – respectively, by 1.67 times (95 % CI: 1.01–2.79) and 1.69 times (95 % CI: 1.05–2.84). In the final model, working for longer than 2 h without taking a break also was associated with a higher probability of neck pain complaints (OR 1.59, 95 % CI: 1.05–2.89).

Conclusions. The applied model of multivariable logistic regression used in our study showed that both individual as well as work environment-related factors were significant to the neck area MSDs.

Acknowledgements. The authors declare the absence of conflict of interests.

From the region to the globe: retrospective analysis of incidence rate of colorectal cancer in the course of decennial period

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Background. Today, colorectal cancer (CRC) is the second most common cause of cancer-related death and, unfortunately, the situation is expected to deteriorate. According to the most optimistic prognosis, CRC incidence rate will rise by 60% until 2030. This growth will probably be caused by the development of countries with transitional economy, which also include Ukraine.

Objective. The aim of the current study is to explore the CRC incidence rates for the last 10 years in Ukraine and Sumy region, arriving at a conclusion about the situation in the region and Ukraine, and assess its correspondence to world trends.

Methods. The analysis was carried out, using the data from the Sumy Regional cancer registry, Ukrainian national cancer registry, National Cancer Institute, Center for Disease Control and Prevention, American Cancer Society. Standard statistical methods were used. The 10th and 11th editions of International Statistical Classification of Diseases were used for data sorting, therefore the data for colon cancer (C18) and the data for rectum and anus cancers (C19–C21) were analysed separately.

Results. The average morbidity for colon cancer (CC) was 22.76 in 100 thousand people, in cases of rectum and anus cancers (RAC) 23.28 in 100 thousand people, while the average values for Ukraine in the corresponding period were by 10.6 % and 34.3 % lower, respectively. There is no clear trend in the dynamics of the indicators (decrease or increase), the coefficient of variation over the last 10 years for CC was 8.1 % and for RAC 6.1 % (low grades), while the global trend was growing.

In the last 10 years, 2581 new cases of CC (57.3 % in women and 46.7 % in men) and 2643 new cases of RAC (47.1 % in women and 52.9 % in men) were observed. The average age for both sexes and both localizations was 66 years, which corresponded to country level, while the global level was closer to 70 years of age. An interesting fact: since 2012, the number of RAC cases in the age group of 70–74 dropped significantly (51.6 % less), while the number of cases in age groups of 55–59, 60–65, 65–69 years grew. At the same time, the number of CC cases increased in the age group of 75–79 years (58.5 %).

Conclusions. For the last 10 years (2009–2018), the predicted growth of the incidence rate in Sumy region and Ukraine was not observed, but changes in age groups were shown. Among patients with RAC, there was a tendency of recovery, while the tendency in cases of CC was the opposite. In general, the global trends are just partly reflected in Sumy Region and Ukraine.

Acknowledgements. The authors express appreciation of the support by the Medical Institute of Sumy State University.

Trends of ischemic heart disease incidence in Kazakhstan

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Background. Cardiovascular diseases (CVD) are the pandemic and a great challenge of the modern world, bearing a heavy burden of costs for health care and it is expected to run high. Based on the estimates of the World Health Organization (WHO), 17.5 million people died from CVD in 2012, reaching 31 % of all deaths worldwide. 7.4 million people of this number died from ischemic heart disease. IHD epidemiologic monitoring is an integral part of CVD prevention in the Kazakhstani population.

Objective. To study IHD incidence trends in Kazakhstan in 2009–2018.

Methods. The retrospective study covered the data of the Ministry of Health of the Republic of Kazakhstan for 2009–2018 – the annual form No. 12 related to the new cases of IHD (I20–I25). Descriptive and analytical methods of medical and biologic statistics were used to define annual averages (M), mean error (m), 95 % confidential interval (95 % CI), annual average aligned increase/decrease (T, %). The alignment was made according to the formula: $y=a+bx$.

Results. In the study period, 572 612 new cases of IHD were registered. The annual average incidence of IHD in Kazakhstan amounted to 335.4 (CI 95 % = 323.5–347.3) per 100 000 total population. Over time, the index increased from $325.5 \pm 1.4 \text{ ‰}$ (95 % CI = 322.7–328.3) in 2009 to 361.6 ‰ (95 % CI = 358.9–364.4) in 2018, with a statistically significant difference ($R^2 = 0.2129$). The aligned index was also growing, with an annual average rate of $T = +1.0\%$.

Then, we reviewed the regional IHD incidence trends. The upward trends were registered in the Aktobe ($T = +0.2$; $R^2 = 0.0101$), Akmola ($T = +0.6$; $R^2 = 0.0247$), Pavlodar ($T = +1.5$; $R^2 = 0.0684$), West Kazakhstan ($T = +1.5$; $R^2 = 0.3276$), North Kazakhstan ($T = +2.1$; $R^2 = 0.5741$), Karaganda ($T = +3.1$; $R^2 = 0.1359$), East Kazakhstan ($T = +5.7$; $R^2 = 0.875$), Kostanay ($T = +5.8$; $R^2 = 0.858$), and Kyzylorda ($T = +8.4$; $R^2 = 0.7614$) regions, as well as in the cities of Almaty ($T = +0.9$; $R^2 = 0.0243$) and Astana ($T = +1.0$; $R^2 = 0.2869$). The downward trends were registered in the Mangistau ($T = -4.3$; $R^2 = 0.1633$), Zhambyl ($T = -3.4$; $R^2 = 0.2437$), Atyrau ($T = -2.0$; $R^2 = 0.086$), Almaty ($T = -1.0$; $R^2 = 0.0468$), and South Kazakhstan ($T = -0.7$; $R^2 = 0.1027$) regions.

Conclusions. IHD incidence in Kazakhstan was mainly growing by regions, with different growth rates. In some regions, the incidence has decreased. It is important to pay attention to the accounting and registration of new IHD cases, as well as to preventive and diagnostic measures taken in the Republic of Kazakhstan.

Acknowledgments. The authors declare the absence of conflict of interest. The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data and supporting the public association “Central Asian Cancer Institute”.

Ethnoepidemiologic aspects incidence of ovarian cancer in Kazakhstan

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Background. According to the IARC, about 300 000 new cases of OC are annually reported in the world. An epidemiological study of the incidence of cancer in different ethnic groups broadens the understanding of the causative factors that must be considered in order to develop a prevention strategy.

Objective. To study the ethnic characteristics of the incidence of OC in Kazakhstan.

Methods. The material of the study was the data acquired from accounting and reporting documents of oncological institutions of the republic on new cases of OC. The study is retrospective – the study period was 11 years (1999–2009). Descriptive and analytical methods of epidemiology were used to study the incidence of OC.

Results. At the outset, 3 433 cases of OC in patients of Kazakh nationality in the whole country in 1999–2009, which accounted for 40.3 % of all cases (8 523 all the new cases), while among the patients of Russian nationality this pathology was present in 3 866 (45.4 %) cases. The average age of patients with OC among the Kazakh patients (50.7 ± 0.3 years) was lower than among the Russian patients (57.3 ± 0.2 years).

The average annual OC crude incidence rate in Kazakh patients was $7.1 \text{ }^0/\text{ }_{0000}$ (95 % CI = $6.7 - 7.5 \text{ }^0/\text{ }_{0000}$). The incidence in the increase of dynamics from $5.8 \pm 0.4 \text{ }^0/\text{ }_{0000}$ (1999) to $7.2 \pm 0.4 \text{ }^0/\text{ }_{0000}$ (2009), during equalization, the growth rate was $T = +3.1 \text{ } \%$.

The crude incidence of OC in dynamics grew from $14.5 \pm 0.8 \text{ }^0/\text{ }_{0000}$ (1999) to $17.9 \pm 0.9 \text{ }^0/\text{ }_{0000}$ in 2009 for Russian patients, during equalization, the growth rate was $T = +1.8 \text{ } \%$, and the average annual rough indicator was $15.7 \pm 0.3 \text{ }^0/\text{ }_{0000}$ (95 % CI = $15.1 - 16.3 \text{ }^0/\text{ }_{0000}$).

Age-specific incidence rate (ASIR) had a unimodal growth with a peak incidence of 60–69 years in both Kazakh (29.7 ± 1.2) and Russian (37.4 ± 1.1) patients.

Trends in ASIR of OC in Kazakh patients tended to increase. Moreover, the most pronounced growth rate of incidence was established at 70 years and older $T = +3.6 \text{ } \%$.

The trends in ASIR of OC in Russian patients decreased at 40–49 years old ($T = -0.4 \%$) and in people 70 years of age and older ($T = -0.7 \%$). In other age groups, the trends tended to increase, and the growth rate was $T = +1.4 \%$, $T = +4.1 \text{ } \%$, $T = +2.6 \text{ } \%$ and $T = +1.7 \text{ } \%$, respectively, in individuals under 30 years, 30–39 years of age, 50–59 years of age and 60–69 years of age.

Conclusions. Ethnic features of OC have been established, indicating a difference in incidence between of Kazakh and Russian nationality. The data obtained must be used in the planning of anti-cancer measures.

Acknowledgements. The authors declare the absence of conflict of interest. The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data and supporting the public association “Central Asian Cancer Institute”.

REGENERATIVE MEDICINE & NUTRACEUTICAL RESEARCH

Delivery of autologous bone marrow-derived mononuclear cells in wide spectrum of pathologies (experience of 10 years)

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Background. The promising field of regenerative medicine is working to restore structure and function of damaged tissues and organs. The adult heart represents an attractive candidate for cell-based technologies. While there is a wealth of preclinical and clinical data showing the safety, feasibility, and efficacy of stem cells in adults with acute myocardial infarction and heart failure, less is known about possible implementation of stem cell therapy in infants and children with heart failure due to dilated cardiomyopathy and pulmonary arterial hypertension. The challenges facing cardiac stem cell therapy are multiple. There are uncertainties around the destiny of stem cells after their injection into the blood stream. In particular, it regards migration and homing of implanted cells in the target tissues. As yet unclear is the possible role of sympathetic nervous system in the context of osteoreflexotherapy. There is still no definitive answer to the question, which is the preferred type of stem cells to be used for transplantation in different settings. In 2008, we first used autologous bone marrow-derived mononuclear cells (BM-MNCs) in a patient with acute myocardial infarction. Since 2009, we have started stem cell implantation for paediatric patients.

Objective. To determine the role of BM-MNCs in management of critically ill paediatric patients suffering from idiopathic dilated cardiomyopathy and severe pulmonary arterial hypertension.

Methods. Two patients (9 and 15 years old) with trisomy 21 and severe pulmonary arterial hypertension due to uncorrected large ventricular septal defects received intrapulmonary BM-MNCs implantation. Radionuclide scintigraphy showed an improvement of lung vascularization during 36-month follow-up. Seven patients (aged 4 months to 17 years) with dilated idiopathic cardiomyopathy received intramyocardial BM-MNCs injections. During follow-up (up to 10 years), we observed an improvement of left ventricular ejection fraction (LVEF), a decrease of left ventricular end-diastolic dimension by echocardiography and cardio-thoracic index at chest X-ray exams, reduction of serum brain natriuretic peptide serum levels and decrease of the stage of heart failure from stage IV to stage I, by NYHA classification. No periprocedural harmful side effects were observed. Two children had heart transplantation (on the 2nd and 4th year after stem cell implantation).

Conclusions. The results are promising and we suggest that BM-MNCs might be used for the stabilization of the adult and paediatric patients to improve symptoms and outcomes or serve as a bridge for heart or lung transplantation, or to delay joint replacement surgery. It also could be recommended in cases when other more traditional treatment options fail or are contraindicated.

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Single centre safety data for mononuclear autologous bone marrow stem cell intracoronary transplantation in patients with chronic heart disease

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Background. Heart failure is one of the major causes of morbidity and mortality from cardiovascular diseases. Worldwide research of regenerative medicine is among the novel and controversial therapies for improving the function heart's left ventricle.

Objective. To use the current registry data for evaluating safety of regenerative therapy in Latvian Centre of Cardiology patients of chronic heart failure.

Methods. Between February 2009 and September 2018, in the Latvian Centre of Cardiology patients aged 18 to 75 years with echocardiography-documented decreased left ventricle ejection fraction < 50 % and longer than three months with optimal medicament therapy for chronic heart failure were assigned for mononuclear autologous bone marrow stem cell intracoronary implantation ($n = 27$). During the follow-up, we analysed clinical results such as all-cause death, cardiovascular death, device implantation rate, heart transplantation and oncology. We report patient median follow up in five years. Statistical data analysis was performed with SPSS software (IBM SPSS Statistics Version 17, SPSS inc., USA).

Results. The mean patient age was 48.6 ± 12.9 years. The mean population from $n = 27$ patients was 23 (82.1 %). Previous PCI was performed in $n = 15$ (53.6 %), diabetes mellitus was found in $n = 3$ (10.7 %), arterial hypertension – in $n = 11$ (39. 3%), dyslipidaemia – in $n = 20$ (71.4 %), active smoking – in $n = 6$ (21.4 %). The mean left ventricle ejection fraction at the baseline in patients was 28.5 ± 9.6 % ($n = 26$). At one-year follow-up, the mean left ventricle ejection fraction was 34.4 ± 12.8 % ($n = 17$). Mononuclear stem cell implantation was mostly done in left anterior descending artery $n = 16$ (57.1 %), in $n = 5$ (17.9 %) of the cases a dual injection of stem cells was done in the left anterior descending and left circumflex coronary arteries. The mean implanted cell amount was 59.4 ± 31.5 million. Follow-up in 2019 was carried out in $n = 27$ patients (96.4 %). One patient missed the follow-up. $n = 12$ (42.9%) patients underwent a device implantation. One heart pacemaker (3.6 %), two CRT (7.1 %), 6 CRT-D (21.4 %) and 3 LVAD (10.7 %) were implanted to decrease rhythm disorders and increase the left heart function. In total, $n = 5$ (17.9 %) patients died from cardiovascular complaints at the median follow-up time. $n = 19$ patients reached five years follow-up, and the death rate in five years was $n = 2$ (10.5 %). In two patients (7.1 %), a heart transplantation was carried out. No oncology cases were noted during the follow-up.

Conclusions. Autologous stem cell therapy for chronic heart failure patients is safe and probably has a positive clinical effect in optimal chronic heart failure therapy.

Acknowledgements. This registry was supported in part by Latvian National Research Programme "Biomedicine for Public Health" (BIOMEDICINE) and the grant from AS "Sistēmu inovācijas"

Dynamic of clinical signs in hip joint osteoarthritis after mononuclear cell injections during 36-month period

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Background. Osteoarthritis is the one of the most common disease and its prevalence only increases with the average age of the population. The current therapy is based on the reduction of symptoms – analgesia, restoration of joint function and slowing of the progression of the disease. Mesenchymal stem cell therapy (MSC) is considered to be an innovative method that can provide safe and easy treatment due to its immunomodulatory and regenerative properties.

Objective. The aim of the study was to evaluate the changes IN clinical status after a single injection of intraarticular mesenchymal stem cells (MSC) over a long-term follow-up period of 36 months.

Methods. The group of 27 patients and 32 cases of hip joints were analysed. The mean age 58.1 ± 10 , 15 males, 12 females, Kellgren–Lawrence grade: II; III. The intraarticular injection of mononuclear cell suspension in average $53,35 \pm 41,57 \times 10^6$ of pure mononuclear cells was performed. The applied cells were extracted from the red bone marrow.

The control group of 14 patients were treated with pain reducing medications and physiotherapy.

Results. No adverse effects after the BM-MNC injection were observed. At the time period between 12 and 36 months, the patients have been distributed in 3 subgroups:

- 1) No increase of OA signs – 16 joints still have a clinical improvement without other treatment,
- 2) Mild increase of OA signs was successfully treated with intra-articular injections of hyaluronic acid and PRP – 4 joints.
- 3) Severe increase of osteoarthritis signs was reported regarding 12 hip joints of the patients, and the total knee arthroplasty was performed.

The patients were evaluated. using Harris Hip Score. The results of the whole group were, as follows: before the treatment 73.65 SD 10.79, on 12-month HHS 86.97 SD 11.33 and 36-month results for the first group of patients are 90.53 SD 5.28

The patients of control group had 83.00 SD 12.31 at the baseline, and 73.00 SD 16.01 HSS at month 12, indicating a worsening of symptoms.

Conclusions. The single-dose mononuclear cell injection reduces the pain and symptoms of stage II–III osteoarthritis over 12 months in all the patients.

In 36 month-period, no further progression of OA signs was observed in 50 % of the patients.

Acknowledgements. The authors would like to acknowledge the support of AS “Sistēmu inovācijas”, research fund and Latvian National Research Programme “BIOMEDICINE”.

The author declares that the research for and communication of this independent body of work does not constitute any financial or other conflict of interest.

Factors influencing bone marrow mononuclear cell quantity and quality in patients with osteoarthritis

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Background. Osteoarthritis disrupts everyday life of numerous individuals, and its incidence is increasing due to ageing and obesity. The economic burden is immense. New treatment methods are needed, and the use of mononuclear cells (MNC) could be a solution. There is a lack of knowledge of the optimal quantity of cells to be used and the factors affecting the quality and quantity of these cells. According to literature, contamination with erythrocytes, apoptotic cells, diabetes, increased age and different steps in cell processing may affect the final cell product quantity and quality.

Objective. To see whether there are correlations between the patient factors: age, sex, erythrocytes, hemoglobin, thrombocytes, and the quantity of mononuclear cells, CD34⁺ cells and the percentage of CD34⁺ cells.

Methods. The total of 33 patients were included in the study. *DataMed* and *Ārsta Birojs* were used under the supervision and permission of Dr. Gončars. Patients' hemoglobin, erythrocytes, thrombocytes, age and sex parameters were collected from the laboratory data from patient database. Dr. Gončars kindly provided the data about bone marrow mononuclear cell quantity, CD34⁺ quantity and the percentage of CD34⁺ cells from his original study. SPSS 22 was used for analysis.

Results. $n = 33$, 19 were female (57.6 %). The mean age was 59.45 years ($SD \pm 9.42$ years), mean erythrocyte level was $4.13 \times 10^{12}/L$ ($SD \pm 0.80 \times 10^{12}/L$), the mean hemoglobin level was 124.91 g/L ($SD \pm 19.06$ g/L), mean thrombocyte level was $224.36 \times 10^9/L$ ($SD \pm 61.66 \times 10^9/L$), mean mononuclear cell count was 41.40×10^6 ($SD \pm 6.47 \times 10^6$), the mean CD34⁺ cell count was 0.763×10^6 ($SD \pm 0.923 \times 10^6$), mean percentage of CD34⁺ cells 1.611 ($SD \pm 0.932$).

Table. Univariate analysis results of continuous non-normally distributed data analysed with Spearman

	Mononuclear cells		CD34 ⁺ cells		Percentage of CD34 ⁺ cells	
Age	$r_s = 0.187$	$p = 0.297$	$r_s = 0.102$	$p = 0.572$	$r_s = -0.75$	$p = 0.677$
Erythrocytes	$r_s = -0.158$	$p = 0.379$	$r_s = -0.147$	$p = 0.416$	$r_s = 0.213$	$p = 0.235$
Hemoglobin	$r_s = -0.181$	$p = 0.314$	$r_s = -0.209$	$p = 0.242$	$r_s = 0.093$	$p = 0.607$
Thrombocytes	$r_s = 0.132$	$p = 0.464$	$r_s = 0.048$	$p = 0.790$	$r_s = 0.005$	$p = 0.979$

Associations between sex and MNC and percentage of CD34⁺ cells were analysed with independent sample T-test which gave p -value for MNC 0.639 and p -value for percentage of CD34⁺ cells 0.473.

Conclusions. Results show that none of the investigated factors, including age, sex, erythrocyte level, hemoglobin level and thrombocyte level have a correlation with the quantity of mononuclear cells, CD34⁺ cells or the percentage of CD34⁺ cells.

Acknowledgements. The authors declare the absence of conflict of interests.

Optical glucose sensor: comparison of sensor prototypes with automatic and manual parameter setting

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Background. Glucose consumption monitoring is crucial for large scale cell expansion in bioreactor systems. The real-time glucose monitoring by optical sensor could benefit automatization and traceability of bioprocess. Application of sensor that does not come in direct contact with cell cultivation medium significantly lowers the risk of system’s contamination, lowers the bioprocess maintenance time and improves cost effectiveness.

Objective. The aim of the study is to evaluate optical glucose sensor prototype’s performance during adherent cell cultivation and to compare optical sensor readings with verified biochemical analyser.

Methods. To evaluate the optical glucose sensor prototype performance, adherent cells were cultivated in bioreactor system for 3 weeks. The cell cultivation media samples were collected and flash frozen for biochemical analysis. The glucose sensor was integrated into circulation system of cultivation medium. Glucose concentration readings from both optical sensors were compared and validated against biochemical analysis. Optical sensor readings in cultivation media were calculated on the basis of mathematical analysis and physically related to signal variety.

Results. The two photometric sensor systems were developed. The first prototype (A) had an option of manual tuning of several measurement cascades to find the optimal settings. Based on the result, the most informative channel was chosen for studies. The second prototype (B) utilised a single-channel unit and a feature of automatic tuning of the system to examine cultivation medium. Both prototypes showed high precision and immunity to optical interference from environment. The prototype (A) showed average precision of ± 0.1 mmol/l in a glucose range 10–18 mmol/l. The prototype (B) showed average precision of ± 0.4 mmol/l in a glucose range 10–20 mmol/l.

Conclusions. Both sensor prototypes showed similar reading trends, however, the sensor with manual parameter control provided more stable glucose concentration readings than the reader setup with automatic parameter control. Further studies will be aimed at determining the critical points for automatic setting adjustment in order to achieve highest precision.

Acknowledgements. This research was funded under the contract No. 1.2.1.1/18/A/007 between “VMKC” Ltd. and the Central Finance and Contracting Agency, the study was conducted by AS “Sistēmu inovācijas” with support from the European Regional Development Fund (ERDF) within the framework of the project “Smart Material and Technology Competence Centre”. The authors declare the absence of conflict of interests.

Assessment of polycaprolactone application for three-dimensionally printed tissue scaffolds

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Background. Degenerative processes and trauma can lead to joint failure. Three-dimensional (3D) bio printed tissue constructs could contribute to novel treatment strategies. Application of 3D printing technology could make it possible to fabricate biologically compatible tissue segment transplants and provide a solution for lack of treatment. Considering the properties of 3D printing technology, it would be possible to bioprint personalized transplants and restore joint function. Properties of polycaprolactone (PCL) is poorly studied from perspective of 3D bioprinting and it is essential to evaluate potential material application compatibility.

Objective. The aim of this study is to develop enhanced architecture PCL scaffold suitable for live cell imaging.

Methods. The scaffolds were designed by computer-aided design (CAD) in Simplified 3D software. The combined thermoplastic/bioink extrusion system was utilized to fabricate tissue scaffold models. The system was developed in first stage of this study. The scaffold molten were printed on glass slide, after cooling were removed and fixed to 24 well plate surface.

Results. Two printing protocols were developed. The first scaffold – two-layer grid, 12 mm diameter, tread width 100 µm, space between grids 50 µm, density of grid filling 33 %, dimension of strut 100 µm, outside perimeter layer width 400 µm. The second scaffold – two-layer grid, 6 mm diameter, tread width 100 µm, space between grids 50 µm, density of grid filling 33 %, dimension of strut 100 µm, outside perimeter layer width 400 µm. Scaffold was modified with 8 beams and outside perimeter support ring. Total construct diameter 12 mm.

Printing quality were assessed by series of scaffold fabrication. Initial extrusion temperature was + 130 °C, molten bed temperature + 5 °C, tread laminating speed 4 mm/s. Selected printing parameters showed uniform tread positioning, lamination, condensate forming that led to deformation of scaffold. By extrusion temperature +130 °C, molten bed temperature + 10 °C, tread laminating speed 6 mm/s no deformations were observed and all scaffolds were released for further studies.

Conclusions. Developed PCL scaffolds are suitable for live cell imaging and are morphologically suitable for cell size, cells can proliferate and attach to them. Further research of scaffold fixation in 24 well plates is needed, as they tend to disengage during cultivation.

Acknowledgements. This study was funded in part by grant from corporation JSC “SISTEMU INOVACIJAS” and European Regional Development Fund (ERDF) in accordance with the contract No. 1.2.1.1./16/A/002 between “LEO PĒTĪJUMU CENTRS” Ltd. and the Central Finance and Contracting Agency, the study was conducted by “Pauls Stradins Clinical University hospital”. Authors declare no conflict of interest.

Predictive biomarkers for therapy-resistant cells

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Background. Despite of the improving cancer screening methods and applied therapy, mortality from this disease still remains high. Polymorphism of cancer cells and different functional activity in the same tumour tissue cause cell mass heterogeneity. It is associated with cancer cell resistance. Therefore, it is necessary to identify and describe cancer cell population after treatment is applied. Performing an experiment with cell cultures and treating them with conventional chemotherapy revealed the development of small-sized cells – microcells. Microcells are small (3–5 μm), roundish, intensively DAPI or haematoxylin – stained cells with small amount of cytoplasm. The PCNA overexpression in microcells represents replication activity, as well as DNA repairing after stress. The embryonic stem cell markers as NANOG and SOX2 are strongly expressed in microcells.

Objective. The aim of the current study was to describe predictive cancer microcell biomarkers.

Methods. SK-MEL-28, melanoma cells (from ATCC Company) were seeded into multi-well plate on coverslips with an initial density of $\sim 1 \times 10^5$ cells per well and grown as recommended by manufacturer.

The paclitaxel (PTX, Paclitaxel-TEVA) was used as stress factor at the end concentration 0.6 mg/ml.

Immunocytochemistry primary antibodies SOX2, NANOG and anti-PCNA, conjugated with relevant secondary antibody Alexa fluor 488 or Alexa fluor 594 as manufacturer recommended (Abcam, Origene), DAPI (MP Biomedicals) as nuclei stain. RNA label (Abcam) and EdU Click-iT (Thermo) kits were used for DNA and RNA synthesis identification in microcells.

Results. Microcells show a stronger antibody expression than other cells in culture. PCNA expression mainly is related to cell replication and involved in DNA repair. Increased expression of PCNA represents high replication activity in microcells and it indicates their high capacity for renewal. After PTX treatment, SOX2 shows higher expression in nuclei of microcells than in control cells. Intriguingly, NANOG – cell nucleus marker, is expressed in cell cytoplasm equally strongly in both control and treated cells, and it is associated with cell malignancy and therapy resistance.

Conclusions. Using NANOG⁺/SOX2⁺/PCNA⁺ markers and DNA/RNA synthesis markers it is possible to evaluate microcells as a possible predictive factor for effectiveness of tumour therapy.

Acknowledgements. This project is supported by University of Latvia patron SIA “Mikrotikls”. The donation is administered by the University of Latvia Foundation.

The confocal microscopy was implemented in collaboration with Carl Zeiss Microscopy Democenter Oberkochen, Germany.

Aziridin-2-carbonic acid derivatives as novel class of promising protein disulphide isomerase (PDI) inhibitors with anticancer activity

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Background. Protein disulphide isomerases (PDIs) are recently recognised as a very promising novel target for cancer treatment. However, none of the known PDI inhibitors is currently approved for clinical use.

Objective. The aim of the current study was to search for novel PDI inhibitors among aziridin-2-carbonic acid derivatives (N-Aza), who reacts with cysteine of PDI on cancer cell surface.

Methods. Around 200 N-Aza were synthesized and tested as inhibitors for PDI A1 in the insulin turbidity assay. Unlabelled and ¹⁵N,¹³C-double-labelled versions of PDI A1a domain (residues 18–137) and PDI A1a' domain (residues 367–475) were expressed and purified from *E. Coli* and used in NMR experiments for the ligand binding site identification. The 2D ¹H-¹⁵N-HSQC spectra for the *apo* form and protein-ligand complexes of the PDI A1 thioredoxin domains were acquired in the 10 mM AcOH pH 5.1, 50 mM NaCl, 2 mM DTT buffer on 600 MHz Bruker Avance Neo spectrometer equipped with the cryo-probe. Anti-proliferative activity of N-Aza was tested *in vitro* on HT-1080, CaCo-2, MCF-7, MDA-MB-231, anti-adhesive property was tested in MDA-MB-231 co-cultured with endothelial cells whereas *in vivo* activity was assessed in the murine model of Lewis Lung Carcinoma on C57BL/6 mice. Modelling of ligand-protein binding was done using Maestro modelling interface.

Results. N-Aza with electron-withdrawing (preferably aromatic) substituents at nitrogen atom are potent PDI A1 inhibitors (30–500 nM). NMR experiments demonstrate irreversible potent binding of the N-Aza to the cysteines of the catalytic CXXC motif of the PDI A1 at 1-to-2 protein-ligand ratio, indicating that both cysteines of the active site are involved in the covalent bond formation. N-Aza with electron-donating substituents at N-atom of aziridine ring possesses much lower activity. N-Aza are cytostatic *in vitro* at low µM concentrations, inhibit cancer cell adhesion to endothelium in concentration dependent manner, and have *in vivo* anticancer activity in dosages 50–100 mg/kg in the murine model of Lewis Lung Carcinoma without significant toxicity.

Conclusions. For the first time, isoform-selective low nano-molar, PDI A1 inhibitors among N-Aza were discovered. *In vitro* and *in vivo* antitumor activity of N-Aza is based on the covalent and irreversible binding to the catalytic centres of PDI A1.

Acknowledgements. Authors declare absence of conflict of interest and acknowledge Latvian National Fundamental and Applied Research Grant No. lzp-2018/1-0143 “Isoform-selective PDI inhibitors: design, synthesis and SAR”, and The National Centre for Research and Development (STRATEGMED1/233226/11/NCBR/2015) for financial support.

How to reduce the residual cardiovascular risk: Focus on Resveratrol

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Background. Polyphenols have received increased attention due to a plethora of health promoting properties attributed to them. Particularly, **resveratrol, quercetin and pycnogenol** are in the focus of cardiovascular health.

Taking into consideration the promising data of multifactorial effect of polyphenol compounds on human health, the thesis about significance of their combinations in secondary prevention of cardiovascular diseases (CVD), particularly coronary artery disease (CAD), can be raised. While statins are the treatment of choice for lowering low-density lipoprotein cholesterol (LDL-C) in the majority of patients, many patients retain a high CVD risk despite achieving the recommended LDL-C targets with statins (residual risk). This 'residual risk' is mainly due to elevated triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels.

Objective. To evaluate the impact of original composition of food supplement containing resveratrol on lipid profile and level of C reactive protein (CRP) in patients with angiographically verified CAD.

Methods. 167 patients were selected during their scheduled post-event elective bicycle stress-test examination. All the patients received standard CAD and permanent statin therapy and had elevated total cholesterol (TC > 5.0 mmol/L) and/or CRP (> 3.5mg/L) levels. The study consisted of 2 days of polyphenol depletion followed by a 12-week supplementation period in a randomized, blinded, placebo-uncontrolled parallel design. Composition of quercetin, linseed oil and resveratrol was tested.

Results. All investigated parameters have been changed from baseline to 1 and 3 months after the treatment. However, only CRP decrease from 2.48 ± 1.62 mg/L at baseline to 1.97 ± 1.15 mg/L, HDL increase from 1.18 ± 0.31 to 1.38 ± 0.34 mmol/L and decrease of TG from 1.5 ± 0.9 to 1.29 ± 0.8 mmol/L after 3 month treatment can be counted as statistically significant ($p < 0.001$). Nevertheless, the average decrease of TC from 5.12 to 5.03 mmol/L, the decrease of LDL-C from 2.91 to 2.81 mmol/L is necessary to note. Following the optimisation of statin therapy, additional pharmacotherapy should be considered as a part of multifaceted approach to risk reduction.

Conclusions. Our results demonstrate that resveratrol exerts cardioprotective benefits through improvement of inflammatory markers and atherogenic profile. Since the origin of residual risk is multifactorial, the adoption of individual patient management should be considered as a serious option to reach therapeutic goals.

Acknowledgements. The authors declare the absence of the conflict of interest regarding this study. This study was partially financed by ERAF project No. 2DP/2.1.1.1.0/14/APIA/VIAA/008, and state programme "BIOMEDICINE".

Potential application of sea buckthorn extracted bioactive compound for residual risk reduction of cardiovascular disease

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Background. One of the major cardiovascular disease risk factors is elevated levels of low-density lipoprotein (LDL) in blood plasma. Use of statins and polyunsaturated fatty acids (PUFA) substantially reduce biosynthesis of LDL. To find a rich source of PUFA's with optimal composition of omega - 3, 6 and 9 fatty acids and to create efficient manufacturing technology is of great importance. Sea buckthorn seeds (SBS) are recognized as one of the best candidates to extract PUFA's due to its unique fatty acid composition. In addition, SBS oil extraction using supercritical CO₂ technology from sea buckthorns harvested in Latvia have not been studied so far.

Objective. Aim of the study was to develop extraction protocol using supercritical CO₂, evaluate extraction yield and analyse extracted oil composition from SBS grown in Latvia.

Methods. After juice pressing sea buckthorn press cake was freeze-dried (residual moisture content – 8.99%). SBS were separated (using blender and vibrating sieves) and grinded (particle size: 0.35 – 0.50 mm). SBS was extracted using supercritical CO₂ (extraction parameters 3 h /310 bar/40°C). Extracted SBS oil composition was analysed by GC and HPLC methods.

Results. Extraction yield of SBS was 10.4± 0.11%. Main compounds of extracted oil were - linolenic acid 36.1± 0.1%, linoleic acid 34.9± 0.1%, oleic acid 12.5± 0.2%, palmitic acid 7.5± 0.2%, stearic acid 2.7 ± 0.1%. Tocopherol and sterol content were 173.5± 15.2 mg/100 g and 693.8 ± 12.5 mg/100g respectively.

Conclusion. Study results lead to conclusion that SBS grown in Latvia are good source of PUFA's as the extracted oil have desirable ratio of omega-3/omega-6 fatty acids and notable amount of other fat-soluble bioactive compounds. Furthermore, SBS extracted oil might play a role in CVD residual risk reduction and could be used in nutraceuticals products. Developed SBS extraction protocol using supercritical CO₂ is environment friendly, provide reasonable extraction outcomes and valuable composition of lipophilic compounds. Residual defatted sea buckthorn cake could be used for further extraction of polar bioactive compounds.

Acknowledgements. This research was funded in accordance with the contract No. 1.2.1.1/18/A/002 between "Latvian Food Sector Competence center" Ltd. and the Central Finance and Contracting Agency, the study is conducted by JSC "SISTEMU INOVACIJAS" with support from the European Regional Development Fund (ERDF) within the framework of the project "Latvian Food Sector Competence center". Authors declares no conflict of interests.

Extraction yield of flavonoid apigenin from *Matricaria recutita* flowers

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Background. Apigenin is a polyphenolic compound that belongs to the class of flavonoids and is considered to be a potent antioxidant. Flavonoids along with other natural substances present in fruits and vegetables exert a variety of pharmacological effects on various disease risk factors including anti-inflammation, antioxidant, anti-allergic, anti-thrombotic, anti-tumour, and have sedative properties. Chamomile (*Matricaria recutita*) is one of the plants which contains a significant amount of flavonoid apigenin.

Objective. The aim of study was to develop flavonoid extraction protocol utilising chamomile flowers.

Methods. Chamomile flowers were extracted using 90 % ethanol with solid/liquid ration 1:20, extraction time 45 min., at 40 °C temperature. After extraction, the solvent was removed by application of vacuum rotatory evaporator. The obtained aqueous extract was assessed on total polyphenol, total flavonoid and apigenin content in extract.

Results. Chamomile flowers (*v. Zloty Lan*) were hand-harvested in late September 2019, in northern part of Latvia. Prior to processing, chamomile flowers were dried at a temperature of 45 °C for 24 hours and had the final moisture content of 5.21 %. Before the extraction, dried flowers were crushed in powder to enlarge surface area for better solvent penetration. HPLC analysis of the aqueous extract showed the presence of various compounds including apigenin and apigenin-7-O-glucoside. The assessment of extraction yield resulted in average total polyphenol count – 0.88 ± 0.12 mg/ml, average flavonoids 0.16 ± 0.02 mg/ml and average apigenin 0.12 ± 0.01 mg/ml.

Conclusions. The conducted study of apigenin extraction led to conclusion that chamomile flowers can be perceived as a good source of apigenin. Application of ethanol as solvent can provide sufficient apigenin yields to consider extraction scale-up. Ethanol is considered as GRAS (“generally recognised as safe” by FDA and EFSA), providing dietary intake application of apigenin extract. Further experimental activities will be focused on ultrasound-assisted pre-treatment of substrate in order to improve extraction yield and apigenin outcomes.

Acknowledgements. This research was funded under the contract No. 1.2.1.1/18/A/002 between “Latvian Food Sector Competence Centre” Ltd. and the Central Finance and Contracting Agency, the study is conducted by “CELLARTE” Ltd. with support from the European Regional Development Fund (ERDF) within the framework of the project “Latvian Food Sector Competence Centre”. The authors declare the absence of conflict of interests.

ANESTHESIOLOGY & INTENSIVE CARE

Monitoring of continuous femoral nerve block using remote photoplethysmography. A randomized double-blind placebo study

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Background. Any regional anaesthesia has a risk of failure with late and subjective success prediction. Remote photoplethysmography (rPPG) is a non-invasive imaging method of monitoring the microcirculation of the skin, with potential regional anaesthesia-induced vasodilatation monitoring.

Objective. The aim of the study was to measure the changes in the microcirculation of knee skin after femoral nerve block by using rPPG to evaluate whether rPPG can differentiate between placebo and local anaesthetic (LA) injection in peripheral nerve block.

Methods. After local Ethics Committee approval and written informed consents were obtained, we enrolled four patients in our prospective randomized double-blind pilot study. The patients preoperatively received a continuous femoral nerve block with two pre-filled 20 ml syringes (40 ml in total). All participants involved in procedure were blinded to syringe content: one was containing Ropivacaine 0.375 % 20 ml, and the other NaCl 0.9 % 20 ml placebo. Two patients (50 %) randomly received LA in the first syringe, while the other two patients (50 %) randomly received placebo in the first syringe. The rPPG camera was adjusted to the selected skin area, the medial side of the knee. The imaging started few minutes before insertion of the femoral block catheter and continued for 12 minutes after the injection of the first syringe, and for 12 minutes after injection of the second syringe. In addition to rPPG statistical analysis, we assessed the block using cold sensation and visual online rPPG mapping. The design of this study (inserted perineural catheter) secured regional postoperative analgesia in every patient enrolled in this study.

Results. After blind analysis, the first syringe injection in all four cases showed statistically significant increases in rPPG signal AC/DC ratio in Kruskal-Wallis ($p_{1-4} < 0.001$) and showed a positive time correlation ($r_1 = 0.125$, $r_2 = 0.161$, $r_3 = 0.186$, $r_4 = 0.378$, $p_{1-4} < 0.001$), with no statistically significant increase after injection of the second syringe ($r_1 = -0.131$, $r_2 = 0.037$, $r_3 = 0.059$, $r_4 = 0.064$, $p_{2-4} > 0.05$).

Conclusions. In this small double-blind study rPPG could not distinguish local anaesthetics from placebo, compared to 100 % sensitivity of cold sensation assessment. However, in *post hoc* analysis time series the 1st syringe LA group showed more positive correlation coefficients ($r_3 = 0.186$, $r_4 = 0.378$). Knee skin type is considered to be less prone to temperature and microcirculation changes, furthermore, the vascular coverage of anterior knee (angiosomes) may not represent dermatome concept. Subjective methods like cold sensation remains the gold standard in clinical practice and further research in this field is needed.

Acknowledgements. The authors are grateful to the hospital staff who helped with the measurements.

Effect of dexamethasone on acute pain relief, blood glucose and lactate level after hip arthroplasty

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Background. Dexamethasone relieves inflammation and swelling, enhances endogenous opiate synthesis and therefore could provide a great analgesic effect, allowing to reduce high opioid doses for multimodal pain management. However, glucocorticoids cause hyperglycaemia and may also increase lactate level. Blood glucose and lactate changes during perioperative period and may reach recovery-affecting level.

Objective. The aim of this study is to determine the effect of dexamethasone on pain, blood glucose and lactate level in patients after total hip replacement.

Methods. This prospective randomized study includes 50 patients undergoing hip arthroplasty under spinal anaesthesia. After surgery they received multimodal analgesia, using Sol. Morphini 10 mg s/c as a rescue medication (if pain >5 by VAS). The experimental group additionally received dexamethasone 8 mg i/v at the start of surgery and 4 mg i/v in 6 and 12 hours after the first dose. The control group did not receive glucocorticoids. Blood glucose and lactate levels were measured before surgery, at 6:00 p.m. and 6:00 a.m. on the 1st post-operative day (POD-1). The patients filled in a pain questionnaire (VAS scale) for the perioperative period. The amount of injected rescue analgesic was counted for a 24 h period after surgery. Data were processed using SPSS program.

Results. Pain level in rest in the experimental and control group accordingly was 1.2 and 3.1 ($p < 0.001$) at 18:00; 0.8 and 2.3 ($p < 0.001$) at 6:00 on POD-1; 1 and 2.2 ($p < 0.015$) at 18:00 on POD-1. Pain level on movement in the experimental and control group accordingly was 2.0 and 3.9 ($p < 0.001$) at 18:00; 1.8 and 4.2 ($p < 0.001$) at 6:00; 2.2 and 3.8 ($p < 0.001$) at 18:00 on POD-1. Lactate level in the experimental and control group accordingly was 1.02 and 1.57 mmol/l ($p > 0.05$) before surgery; 1.32 and 1.08 mmol/l ($p = 0.38$) at 18:00; 1.9 and 1.54 mmol/l ($p = 0.2$) at 6:00 on POD-1. Glucose level in the experimental and control group accordingly was 5.5 and 5.4 mmol/l ($p > 0.05$) before surgery, 8.3 and 6.4 mmol/l ($p < 0.001$) at 18:00; 7.5 and 5.8 mmol/l ($p < 0.001$) at 6:00 on POD-1. There are no significant differences in the amount of used rescue analgesic between these groups.

Conclusions. Dexamethasone provides excellent analgesic effect. Serum glucose and lactate do not reach a level affecting recovery during perioperative period after hip replacement. Dexamethasone does not allow the use of lower rescue medication dose.

Acknowledgements. The authors declare the absence of conflict of interest.

Efficiency of infiltration between popliteal artery and capsule of the knee (IPACK) together with adductor canal blockade (ACB) in post-operative analgesia after knee replacement surgery – a preliminary analysis

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Background. Postoperative pain reduces patient mobility, increases the hospitalization time and the risk of complications. Many models of post-operative analgesia have been studied, but the problem persists. Recently, the adductor canal block (ACB) was introduced as the selective sensory fascial block for post-operative analgesia. ACB does not cause muscle weakness and may contribute to faster recovery. However, there is evidence indicating that ACB does not relieve pain in the posterior part of the knee capsule and therefore it is combined with the infiltration between popliteal artery and capsule of the knee (IPACK), which is performed under ultrasound guidance. This combination provides a significant analgesia of the knee without causing muscle weakness.

Objective. The aim of the current study is to determine the efficiency of IPACK in addition to the ACB for post-operative analgesia after knee replacement surgery.

Methods. Prospective randomized study, which was conducted in the Hospital of Traumatology and Orthopaedics from October 2019 to March 2020. The study evaluated patients who underwent unilateral knee joint replacement. Patients were randomized into 2 groups – ACB and ACB in combination with IPACK (ACB+IPACK).

Pain was evaluated using Numeric Rating Scale (NRS). Pain intensity was evaluated on movement and at rest 6 hours after surgery, as well as on the 1st and 2nd post-operative day (POD). Muscle strength was evaluated using Oxford scale on the 1st and 2nd post-operative day.

Statistical data processing was performed using IBM SPSS Statistics 25.0 and Microsoft Office Excel 365 software.

Results. In total, 18 patients (12 women, 6 men) were included in the study – 8 into ACB and 10 into ACB+IPACK group. No statistically significant differences in pain NRS and muscle strength were found between groups ($p > 0,05$). A tendency of a lower pain NRS in ACB+IPACK vs ACB group was observed on movement on the 2nd POD – 4,8 vs 6,3 ($p = 0,081$).

Conclusions. The results suggest that ACB+IPACK possibly provide a better analgesia on movement on the 2nd post-operative day after knee replacement surgery without compromising muscle strength.

Acknowledgements. The authors declare the absence of conflict of interest.

Pain assessment with Critical-Care Pain Observation tool and Behavioural Pain Scale for critically ill patients undergoing mechanical lung ventilation

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Background. Critically ill patients may suffer from pain, and it is a challenge to assess the pain of patients who are not able to communicate due to their illness. It is important to recognize pain in these patients, because untreated pain may interfere with recovery, and over-sedation also can have a negative effect.

Objective. The main aim of the current study is to compare critical care, pain observation tool (COPT) and behavioural pain scale (BPS) in pain assessment for unconscious patients with mechanical lung ventilation (MLV). The other aim is to establish, in which period of recovery patients could experience the greatest pain and discomfort.

Methods. This was an observational study encompassing 30 patients. They were assessed with COPT, BPS in the 1st, 3rd and 7th day from admission in the intensive care department, the patients were assessed with COPT and BPS in rest, during oral cavity sanitation, which is a non-painful manipulation and trachea sanitation, which is a painful manipulation. The patients were also assessed with Glasgow Coma Scale (GCS) and Richmond Agitation Scale (RASS)

Results. Both COPT and BPS in all 7-day period showed that rest patients did not have pain or discomfort, but during painful manipulation – trachea sanitation on the 1st day COPT showed an increase by 3 points, while BPS showed increase by 2 points, GCS was median 4 (3, 5) and RASS was median -4 (-5, -3). On the 3rd day during trachea sanitation, COPT showed a rise by 3.5 points, and BPS by 3 points, GCS was median 5 (4, 6) and RASS was median -3 (-4, -2). On the 7th day, the measurements showed an increase during tracheal sanitation COPT by 5 points and BPS by 4 points, GCS was median 7 points (5, 8) and RASS was median -1 (-2.5, 0). During oral cavity sanitation in all 3 measurements COPT did not show any difference, whereas BPS showed an increase by 1 point median.

Conclusions. In rest, patients did not much show signs of discomfort or pain, but during painful manipulations they did have a painful reaction. The patients were most reactive to pain stimuli on the 7th day. COPT showed a higher increase during painful manipulation – tracheal sanitation, and COPT showed no significant rise during non-painful manipulation, while BPS had a rise of 1 point during mouth cavity sanitation. COPT appears to be a more sensitive tool to evaluate pain for this patient group.

Acknowledgements. The authors declare the absence of the conflict of interest.

Health-related quality of life assessment before and after open heart surgery

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Background. Well-being is a positive outcome that is meaningful for people and for different sectors of society, because it tells that people perceive fact that their lives are going well. The SF-36 is a 36-item self-report measure of health-related quality of life. Two component scores are derived from the eight subscales: a physical health component score and a mental health component score. Higher scores on all subscales represent better health and functioning. Operative mortality is a good quality measure of cardiac surgical care, as long as patient risk factors are taken into consideration. EuroSCORE is a method of calculating predicted operative mortality for patients undergoing cardiac surgery.

Objective. To compare health-related quality of life before and after open cardiac surgery.

Methods. A prospective, observational study was held in the Cardiac Surgery Centre of Pauls Stradiņš Clinical University Hospital in 2019 including patients undergoing open heart surgery. The predicted operative mortality was calculated according to EuroSCORE. Patients were asked to fill in SF-36 questionnaire before surgery and 1 month afterwards. Data about postoperative period and length of hospital admission were analysed in SPSS statistical analysis platform.

Results. In total, 22 patients with the mean age of 63.3 (\pm 2.9) were selected, from which 81.8 % (n = 18) were men. The median hospitalization days of patients were 16 (minimum = 7, maximum = 76). Before cardiac surgery, the mean score of SF-36 questionnaire was 65 %, and 1 month after surgery – 58.6 %. There were statistically significant correlation between hospitalization days and physical health after surgery (physical function [Spearman's r = -0.58; p = 0.004], role limitations due to physical health [r = -0.59; p = 0.004], general health [r = -0.62; p = 0.002]), and mental health after the surgery (vitality [r = -0.44; p = 0.043], emotional well-being [r = 0.56; p = 0.007], social function [r = 0.66; p = 0.001]. Patients' quality of life 1 month after surgery statistically correlates with the days spent in ICU. EuroSCORE does not correlate with mortality (p = 0.094).

Conclusions. Overall, health-related quality of life was lower 1 month after open cardiac surgery than beforehand. According to patients' guidelines, moderate physical activities are allowed not sooner than six weeks after surgery, and intensive activities after three months. Only 1 month after surgery some patients still were not discharged and a significant part of research group had not fully recovered in their daily activities. This statement confirms the results that health-related quality of life is affected by days spent in ICU and overall hospitalization time.

Perineural nerve stimulation for acute pain management after shoulder joint replacement

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Background. The major goal of postoperative pain management is a successful pain relief without side effects. Adequate control of acute pain prevents the development of chronic pain. Perineural catheter provides injection of analgesic directly to a nerve and performs effective pain relief. Nerve stimulation by this catheter could become an extra option of it, improving pain control without additional medications.

Objective. The aim of this study is to explore the effect of perineural nerve stimulation on acute pain level for patients after total shoulder joint replacement.

Methods. This prospective randomized pilot study includes 2 patients undergoing shoulder joint replacement under general anaesthesia and interscalene brachial plexus block was provided for both patients before surgery. Perineural catheter was placed to the *nervus suprascapularis* after surgery and Sol. Ropivacaini 0.375 % 5 ml was administered there, if pain level by NRS > 4. Both patients also received multimodal analgesia, using morphine 10 mg s/c as a rescue medication if pain level > 6 by NRS. Nerve stimulation was additionally applied for experimental group at 19:00 (operation day); 7:00 and 19:00 (POD-1). The parameters of stimulation were: 0,4 mA, 100 Hz, 30 min. The pain level was measured by NRS scale at 19:30 on the day of surgery, 7:30 and 19:30 (POD-1) and 7:30 (POD-2).

Results. Pain level in control group in rest and on movement accordingly was 0 and 0 at 19:30 (operation day), 3 and 8 at 7:30 (POD-1), 2 and 6 at 19:30 (POD-1), 2 and 5 at 7:30 (POD-2). The amount of injected Sol. Ropivacaini 0.375 % was 15 ml and the amount of morphine was 20 mg.

Pain level in experimental group in rest and on movement accordingly was 0 and 0 at 19:30, 0 and 3 at 7:30 (POD-1), 1 and 4 at 19:30 (POD-1), 0 and 4 at 7:30 (POD-2). The amount of injected Sol. Ropivacaini 0.375% was 20 ml, the amount of morphine was 0 mg.

Conclusions. Our data suggests that perineural stimulation might improve postoperative pain relief after total shoulder replacement surgery and could allow to reduce high doses of narcotic drugs. The study should be continued and more patients enrolled to see the effectiveness of perineural stimulation.

Acknowledgements. The authors indicate the absence of conflict of interest.

Automated cardiopulmonary resuscitation device for pre-hospital cardiac arrest: a single-centre experience of AutoPulse-CPR

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Background. A low quality of cardiopulmonary resuscitation (CPR) predicts adverse outcome. The usage of A-CPR following out-hospital cardiac arrest remains poorly described.

Two automatic mechanical chest compression devices – LUCAS and AutoPulse – have been used in Latvia in order to optimize the circulation in patients with cardiac arrest.

Objective. To determine the implementation and effectiveness of LUCAS and AutoPulse for out-of-hospital cardiac patients in Latvia.

Methods. A retrospective cross-section study was carried out, involving adult patients with out-of-hospital cardiac arrest with sustained circulatory arrest.

The data from State Emergency Service of Latvia regarding the patients resuscitated with mechanical chest compression device – AutoPulse was used in the study.

Results. From May 2016 to December 2018, 232 patients, 182 (78.4 %) of those men and 50 (21.6 %) women ($p < 0.001$) were resuscitated with AutoPulse. The median age for women was 62.5 (12.0–92.0) years and 59.0 (17.0–88.0) for men ($p = 0.101$).

Of those patients, in 70/232 (30.2 %) cases the return to spontaneous circulation and a successful admission to the hospital, 59/70 (84.3 %) were male and only 11/70 (15.7 %) were women.

The median age (min-max) of patients who had survived was 58.50 (17–92) years, but in patients' group who died, the median age 60.0 (12–88) years ($p = 0.375$).

The aetiologies of cardiac arrest were followed: unknown cause 126/232 (54.31), the second most common cardiac arrest reason was an acute myocardial infarction in 44/232 (19 %) cases, and Chronic Ischemic heart disease in 23/232 (9.9 %) cases, while non-cardiogenic cause was present in 39/232 (17 %) cases.

68.2 % (30/44) of the patients with myocardial infarction and 14/23 (60.9 %) of the patients with the diagnosis CIHD ($p = 0.549$) experienced the return of spontaneous circulation and were admitted to hospital.

The most common location of cardiac arrest was found to be a patient's residence – 137 (59.1 %) cases, and 95 (40.9 %) – in public places.

Conclusions. AutoPulse is effectively used in Latvia and the study shows a positive outcome.

Acknowledgements. The authors declare the absence of the conflict of interest.

NURSING

Heated tobacco product impact on health and wellbeing – user experience, behaviours and attitude

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Background. Heated tobacco products (HTP) have become popular over the past decade, in Latvia HTPs are sold since 2018. It becomes more common for people to choose this mode of smoking. Although World Health Organization reports there is no evidence, which would confirm that HTPs are less harmful to health than conventional cigarettes, that does not mean society shares this view towards HTPs.

Objective. The aim of the study was to assess HTPs user experience, behaviours and attitude towards heated tobacco product impact on health and wellbeing.

Methods. 438 current HTPs users were enrolled in this study. They were interviewed using an anonymous questionnaire on the web. At least 18 years old current HTPs users were included (age range 18–62). The collected data were analysed using IBM SPSS program v. 22.

Results. 70.3 % of all study participants use less than 1 pack of disposable tobacco sticks daily. Before turning to HTPs, 95.2 % were conventional cigarette smokers, whereas 13 respondents did not smoke at all before using HTPs. The indicated reasons for starting to use HTPs included less unpleasant smell of smoke (90.6 %), belief that it is less harmful to their health (53.0 %), recommendation of friends (39.7 %), as a method to reduce/quit smoking (33.1 %). 66.9 % said they believed HTPs was less harmful to their health than conventional cigarettes. When asked who had informed them about the impact of HTPs on health, respondents stated that mostly the information came from their kinspeople (50.0 %), the seller (37.9 %), nobody (29.5 %). Changes in their health and wellbeing were noted by 46.1 % ($n = 202$), of those 42.2% ($n = 185$) noted improvement. 41.1 % ($n = 76$) stated that their cough had decreased, but 15.7 % said that their breathing had improved and shortness of breath decreased, physical endurance has improved for 11.9 % of respondents, 13 % claimed improvement in sense of taste and smell. A statistically significant association ($\chi^2 = 8.658$, $p < 0.005$) was found between choosing to use HTPs because of the belief that this habit is less harmful and claiming their health has improved.

Conclusions. The most common reason for starting to use HTPs was the less unpleasant smoke smell. More than a half of users believe that HTPs is less harmful to their health than conventional cigarettes. Four out of ten HTPs users claim their health has improved, the main improvements are decreased cough, sense of taste and smell, breathing, physical endurance has also been reported to have improved.

Relationship between self-esteem and sleep in RSU medical students

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Background. The level of self-esteem represents individual's subjective beliefs and evaluation of their own worth. It has a significant impact on many important aspects of life, such as interpersonal relationships, work and academic achievements, physical and mental health. It is a well-known fact that medical students have high stress level due to demanding study programme and lack of time to complete all of the necessary assignments. Moreover, they need to keep up with other time-consuming activities like work and personal life. In order to do so, some students regularly or from time to time cut down on sleep. Even though sleep is often neglected, it is a vital component of well-being.

Objective. This study aimed to investigate whether there was a relationship between self-esteem and sleep in RSU medical students.

Methods. To assess students' level of self-esteem, Rosenberg Self-Esteem Scale (1965) was used. Scale ranges from 0 to 30 points with 30 representing the highest level of self-esteem. For sleep evaluation, Physical Health Questionnaire's section regarding sleep was used. The section includes 4 questions about sleep with the total range of points from 4 to 28. More points mean better sleep. Also, some demographic data was collected, including age, gender, and study year. The questionnaire was made using Google Forms and distributed among students via Facebook students' groups.

Results. Out of the total of 266 students, 15.79 % ($n = 42$) were male and 84.21 % ($n = 224$) were female. The mean age of responders was 21.39 (SD 2.40) years. The mean score on the Physical Health Questionnaire regarding sleep was 19.88 (SD 5.01) points. The lowest score on the scale was 7, while the highest – 28 points. The mean score on the Rosenberg Self-Esteem Scale was 18.18 (SD 4.30) points. The lowest score on the scale was 7, and the highest – 29 points. The results showed a weak correlation between RSU medical students' level of self-esteem and sleep: Spearman's rho correlation coefficient was 0.299 ($p < 0.01$).

Conclusions. There is a weak correlation between the level of self-esteem and sleep in RSU medical students, indicating that a higher self-esteem level might result in better sleep. Further studies are needed to investigate the effect of self-esteem on general physical health and well-being.

Acknowledgements. The utmost gratitude is expressed to medical students for dedicating their time to complete the questionnaires.

Impact of high physical load exercises on anthropometric parameters of military personnel

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Background. The problem has a particular importance in planning Combat Training Course (CTC) that is a compulsory part of study process in the National Defence Academy of Latvia. Its duration is ten days and it includes various high physical load components, tactical, psychological activities in military conditions with sleep deprivation and dietary limitation. High standards of physical fitness and health standards are essential for military personnel training under field conditions.

Objective. The aim of the current study was to evaluate the changes of anthropometric characteristics, implementing analysis of data of bio impedance register before and after CTC.

Methods. Altogether, 56 participants of both genders (50 males and 6 females) aged 23 to 30 years enrolled in the study group. Military Medical Centre specialists examined participants of CTC. Sports medicine doctor carried out the examination of physical health status. The height established by anthropometry with an accuracy to 0.001 m. The body mass was established by scale with an accuracy to 0.01 kg. The body mass indexes (BMI) calculated as the quotient of body mass (kg) and the square of height (m²). The body composition (fat mass, muscle mass etc.) were controlled by using the body impedance equipment. Anthropometric data established in three measurement sessions: before (at the beginning (February) of preparing period for CTC, at the end (May) of preparing period for CTC, and after CTC (June).

Results. We provided analysis and evaluation of anthropometric parameters. The participants lost body weight during the CTC: 31.4 % of the participants lost 6–9 % of the body weight; in 54.9 % of the participants, the loss of body weight was about 10–12 %, and in 13.7 % of the participants lost 13–15 % of the initially established body weight. The analysis of anthropometric characteristics showed that body mass index (the mean value with standard deviation) in the 1st measurement session changed, as follows: 24.80 ± 2.53 ; in the 2nd measurement session the change was 25.28 ± 2.33 , and at the 3rd measurements session it was 24.41 ± 2.0 . The changes of body composition parameters like those that body mass, body fat and visceral fat level decreased, while the muscle mass increased.

Conclusions. The summary of results contributes to management of the pre-courses training programme and optimization of adaptation of participants to high physical load under field conditions during Combat Training Course. Analysis of anthropometric parameters yielded general and individual changes during high physical load exercises.

Acknowledgements. The current study is a part of the project funded by National Defence Academy of Latvia, and the authors declare absence of any conflict of interest.

Necessity to improve the Civil Procedure Code to accelerate proceedings in patients' rights cases

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Background. Civil Procedure Code of Latvia does not provide the option to ensure proceedings in patients' rights cases in accelerated order, however, Latvian court practice indicates that disputes between hospitals and patients or their relatives occur on a regular basis. Patients' rights cases have an explicitly personal character and should be treated as such. Taking into account the consideration that civil disputes in healthcare have a significant role, and earnest impact not only on individuals and hospitals but also on the public, it is essential to find an appropriate legal solution to guarantee patients' rights cases along with the children rights cases and other specific groups of cases to be examined by a court in accelerated order.

Objective. The aim of this research is to expand the understanding of the necessity of specific procedural regulation that provides accelerated order in which patients' rights cases could be examined by court. The author has chosen to identify the most relevant group of cases along with the patients' rights cases that could be combined and implemented into the regulation as a new concept of accelerated order in proceedings under Latvian Civil Procedure law.

Methods. For the interpretation of the Civil Procedure Code of Latvia, the author has used grammatical, historical, systemic and teleological methods. In addition, the author has analysed modern and historical cases of Latvian court practice and legal literature on this topic from various periods.

Results. Research results are: 1) an expanded understanding of the necessity of specific procedural regulation to provide accelerated order in which patients' rights cases could be examined by a court; 2) a more precisely reviewed group of civil cases that could be exposed under the new concept of proceedings in accelerated order; 3) an identified proposal to the legislator for improvement of the regulation.

Conclusions. Civil Procedure Code of Latvia should be supplemented with at least one new article in the General Provisions to stipulate that in the planning of the division of cases and in examination by a court, the preference applies to patients' rights cases, the cases with claims arising from personal injuries that have resulted in mutilation or other damage to health, or the death of a person, the cases with claims regarding the recovery of child maintenance, as well as other cases of a highly personal character.

Acknowledgements. The author would like to pay his respects and express gratitude to the Dean of Faculty of Medicine, Professor Valdis Folkmanis.

Validity and reliability test of Latvian translation of Neuropsychiatric Inventory – Nursing Home Version

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Background. Nursing homes are increasingly faced with clients affected by dementia with superimposed manifestations of neuropsychiatric symptoms (such as delusions, hallucinations, agitation, depression, etc.). Neuropsychiatric Inventory (NPI) is a widely used evaluation tool in clinical practice and research for quantifying the above symptoms and thus evaluating the effectiveness of pharmacological and non-pharmacological interventions in treating these symptoms. This tool is validated and freely available online in English.

Objective. The aim of the current study was to prepare a Latvian translation of NPI – Nursing Home Version, and to test its validity and reliability.

Methods. In December 2019, a quantitative study was conducted at a nursing home in Riga. Inclusion criteria were an age above 65; a Minimum Mental State Examination (MMSE) score < 26; duration of stay at the nursing home for more than one month; a stable clinical condition, and voluntary participation in the study. A Latvian translation of NPI – nursing home version was prepared according to the translation guidelines of psychometric tests. The respondents were formal caregivers, who were involved in 24/7 care of the study participants. The interrater reliability was tested by interviewing another respondent, also a formal caregiver involved in 24/7 care of the study participants. The participants were re-evaluated at intervals of 7–14 days. The data were processed using SPSS 20.0 software. Rīga Stradiņš University Ethics Committee approved the study (decision No. 6-2/10/39 of 28/11/2019).

Results. Altogether, 55 seniors were enrolled in the study, 85.5 % of whom were women. The median age was 87 years (IQR 82–90). The median duration of stay was 23 months (IQR 15–45). The mean MMSE score was 10.4 ± 6.4 . Cronbach's alpha for the Latvian version of NPI – Nursing Home Version was 0.751, indicating acceptable internal consistency. Cronbach alpha for individual neuropsychiatric symptoms varied between 0.738 (apathy) and 0.919 (agitation/aggression), which is a good indicator for internal consistency. The interrater reliability was excellent, as intraclass correlation coefficient (ICC) was 0.906 (95 % CI: 0.84–0.95). Test-retest reliability was excellent, as ICC was 0.965 (95 % CI: 0.88–0.99).

Conclusions. The Latvian translation of NPI – Nursing Home Version is a valid and reliable evaluation tool to be used in the field of long-term care of clients with dementia. A further study in a larger group would be needed to determine the correlation of neuropsychiatric symptoms with MMSE values.

Acknowledgements. Both authors declare the absence of conflict of interests and funding.

Evaluation of an efficiency of the second nurse in general practice

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Background. One of the goals of the primary health care system (PHC) is to reduce the consumption of secondary level health care, including emergency medical care (EMC). A part of executed mobile ambulance calls (EMAC) would possibly be avoided if a wider access to PHC were to be available. A programme of second nurse was launched in Latvia to improve the access to PHC – the general practitioners (GP) with more than 1200 registered patients have an option to receive supplementary financial support, if additional healthcare professional is employed. The efficiency of this support system has not yet been evaluated.

Objective. The aim of the study is to evaluate the number of EMAC per one patient registered to each of GP and to find out, whether there is a correlation between this index and the fact of employment of additional nurse in GP praxis.

Methods. The number of patients registered to each individual GP, the number of EMAC to those patients, as well as the information regarding the employment of the second nurse by particular GP was requested from the Centre for Disease Prevention and Control. The study included analysis of data for the 5-year period starting from 2014.

This retrospective study included GP with more than 500 registered patients older than 20 years of age. The number of EMAC in each GP was attributed to the number of registered patients. The GPs with and without a second nurse/physician assistant were compared.

All the acquired data were analysed using Microsoft Excel and IBM SPSSv22.-

Results. Within inclusion criteria, there were 484 GP with 2 nurses and 344 GP with 1 nurse. The medium number of EMAC per 1 patient within a period of 5 years in a GP with 1 nurse was 2.17 ($SD = 0.47$), while in a GP with 2 nurses it was 2.13 ($SD = 0.46$) with no statistically significant difference ($p = 0.19$).

In Latvia, the number of EMAC per 1 patient increased from 0.27 to 0.31 calls from 2014 to 2017, whereas in 2018 there was a reduction by 0.03 calls in comparison with 2017 ($p < 0.001$).

The average of EMAC per 100 patients for the period of 5 years was 2 calls less for the GPs with 2 nurses compared to the GPs with one nurse.

Conclusions. The study revealed a positive impact of a second nurse in GP. The number of EMAC could be considered as an efficiency index of GP, but further studies are necessary to exclude localization of GP and proportion of chronic diseases as influencing factors.

Assessment of the staff hand antiseptics performance

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Background. The investigations show that in 10 % to 78 % of cases, hands of the medical personnel are contaminated with *Staphylococcus aureus*, gram-positive VRE, *Clostridium difficile* bacteria. According to European standard EN 1500, in performing hand hygiene, soap or antiseptics must be applied to all areas of hands (palm and fingers) and wrists. In this way, after a contact with an infected patient, elimination of contaminants is ensured; colonisation of skin on hands by transit micro-organisms is reduced. Correctly performed hand hygiene can reduce contamination of hands by 50 to 70 per cent.

Objective. To assess the preparation of the hands of the nursing staff for the procedure.

Methods. A three-year investigation was carried out at one of university hospitals in Lithuania, involving a total of 272 research subjects (nursing staff). The hand hygiene procedure of the research subjects was observed prior to carrying out the penetrating procedures. The observation was made in three stages (one stage once a year). After each stage of observation, the mistakes made by the nursing staff were discussed with them (preparation for the procedure, the methods of applying antiseptics).

Results. Skin of all the investigation participants was healthy and unblemished. During the first observation stage, it was established that working clothes (gowns) of 22.8 % ($n = 62$) of the research subjects failed to completely cover the clothes of a person; 34.6 % ($n = 94$) of the nursing staff wore jewellery on their hands; 23.8 % ($n = 65$) of the research subjects performed movements of rubbing antiseptics into their hands incorrectly; more mistakes (30.9 %; $n = 84$) were discovered in rubbing antiseptics into the left rather than right hand (17.6 %; $n = 48$). The results of the second stage of observation were better than those of the first one: no wrong working clothes was registered in 14.3 % ($n = 39$) of the cases; 16.5 % ($n = 45$) wore jewellery; 14.0 % ($n = 38$) of the research subjects performed movements of rubbing in antiseptics incorrectly. The results of the third stage of observation showed that inadequacies in working clothes had decreased to 4.0 % ($n = 11$); 6.3 % ($n = 17$) of the research subjects wore jewellery on their hands; 10.7 % ($n = 29$) of the research subjects performed movements of rubbing in antiseptics incorrectly.

Conclusions. Application of standard methods of hand antiseptic and the discussion of the mistakes with the staff improve the skills of performing hand antiseptic.

NEUROLOGY & ONCOLOGY

Anxiety among Charcot-Marie-Tooth disease patients

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Background. Charcot-Marie-Tooth (CMT) disease is the most common inherited disease of the peripheral nervous system affecting approximately 1 in 2500 individuals. In patients with CMT disease, generalized anxiety, phobias, posttraumatic stress and panic are found. According to recent studies, the most common psychiatric disorders in patients with neuromuscular disorders are depression and phobias, these conditions are not related to disease severity.

Objective. The aim of the study was to estimate the prevalence of anxiety in CMT patients, and possible associations with disease severity.

Methods. Participants were recruited in outpatient setting. We used the GAD-7 (General Anxiety Disorder-7) to screen for anxiety. Patients also responded to sociodemographic questionnaire and were assessed clinically using Charcot-Marie-Tooth Neuropathy Score version 2 (CMTNSv2).

Results. The total of 87 adult patients with CMT disease were included in study. There were 47 (54.0 %) female and 40 male (46.0 %) patients with the mean age of 43.4 ± 15.7 (the range was 18–81 years of age). The GAD-7 was indicating at least mild anxiety ($\text{GAD-7} \geq 5$) in 20.0 % ($n = 17$) of patients. The mean GAD-7 value for those patients was 10.9 ± 3.2 , ranging from 5 to 17. The CMTNS ranged from 0 to 33, with the mean score 11.6 ± 7.7 . It was found that patients with a higher CMTNS had a higher GAD-7 score indicating more severe symptoms of anxiety ($r = 0.259$; $p = 0.05$), however, GAD-7 score was not associated with patient's age.

Conclusions. Every fifth patient with CMT disease has symptoms of anxiety. Patients with a more severe disease phenotype tend to have more severe anxiety symptoms. These results could be related to the level of disability and chronic course of CMT disease that influences patient's well-being and quality of life.

Acknowledgements. The authors declare absence of conflict of interest.

Epilepsy stigma in Lithuania

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Background. As much as 50 million people worldwide have epilepsy, which makes it one of the most common neurological diseases, that has been stigmatized since before 4000 years ago and is still surrounded by stigma today. For this and also to our knowledge for lack of stigma evaluation in Lithuania, we deemed this study topic to be very relevant.

Objective. The study aimed to evaluate the severity of epilepsy stigmatization in Lithuania's general population.

Methods. The study sample consisted of 180 healthy participants (72.2 % – women, the mean age 42.7 ± 14.8), all of whom completed a newly developed questionnaire in several public institutions. Our questionnaire was composed of 8 socio-demographic and 20 closed questions designed to assess epilepsy stigma. Stigma level was calculated by scoring the aforementioned 20 questions, higher score number indicating stronger stigmatization level. Statistical analysis was conducted using MS Excel and SPSS 21.0. Statistical significance was assumed at $p < 0.05$.

Results. 95.6 % of respondents indicated having heard or read about epilepsy. 54.4 % indicated not personally knowing anyone with epilepsy. 59.4 % reported having seen a seizure at least once in their lifetime. 29.4 % indicated believing that people with epilepsy (PWE) are treated differently in society, although 73.9 % thought PWE encounter difficulties in the occupational field and 57.3 % would be worried if their relative lived with a PWE. 21.2 % reported that epilepsy is a psychiatric disorder, 22.8 % thought that epilepsy cannot be controlled and 66.1 % – that epilepsy cannot be cured. The mean epilepsy stigma score was 23.2 ± 8 , which equals 43 ± 14.8 on a scale from 0 (no stigma) to 100 (strongest stigma). We found that if respondents knew something about epilepsy they more often thought of epilepsy as an incurable sickness ($p = 0.027$). The belief that epilepsy is a psychiatric illness was found to have a link with the overall higher stigma scores ($p < .05$). Having the mentioned link with higher epilepsy stigma scores were also respondents' beliefs that society views and treats PWE differently ($p < 0.05$); that PWE are more often dependent on other people ($p < 0.05$) and encounter prejudice ($p < 0.05$).

Conclusions. Healthy Lithuanians still tend to stigmatize people with epilepsy, despite all the efforts of education.

Acknowledgements. The authors declare the absence of conflict of interest.

Exploring influence of weather on migraine

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Background. Many migraine patients claim that some weather changes trigger their headaches. However, research data is contradictory.

Objective. Investigate the possible correlation between parameters of weather conditions and frequency as well as intensity of headaches.

Methods. A prospective study was carried out, involving 100 patients with migraine (study group, SG) and 100 people without migraine (control group, CG), but statistical analysis was performed for 82 and 80 respectively. The study was conducted in Health Centre 4, in the headache consultation office. Outpatient record data, headache diary and questionnaire were used for analysis. The intensity and frequency (FR) of pain were correlated with temperature, humidity, atmospheric pressure, the number of sun-hours within an interval of 12 hours over a month (November).

Results. In SG ($M = 42.6$; $SD = 13.28$) 56 % noted themselves as weather-sensitive. In CG ($M = 44.8$; $SD = 13.4$) – 36 %.

In SG a weak correlation of FR and atmospheric pressure ($r = -0.2$), as well as air humidity ($r = 0.25$) was revealed (more headache days with lower pressure and higher humidity).

In CG – an average correlation of FR and humidity ($r = 0.49$) and temperature ($r = 0.31$) (pain occurred more often on humid and warmer days). In SG, a tendency of headache intensification with a decrease in air humidity, and an increase of sun-hours was revealed. In CG – a tendency of pain intensification with a decrease in atmospheric pressure. In SG 7 (8.5 %) patients were identified with an average correlation of headache intensity and humidity, most of them ($n = 5$) had a negative correlation ($r = (-0.35 - -0.57)$). In CG 4 (5 %) patients with an average correlation, mainly to temperature, were identified.

Conclusions. The incidence and intensity of headaches show a weak correlation with various weather conditions. In the migraine group, among patients with an average correlation to the weather, an increase in headache intensity with a decrease in humidity was detected. The percentage of patients with an average correlation was small.

Acknowledgements. The authors would like to acknowledge the contribution of State Ltd “Latvian Environment, Geology and Meteorology Centre”.

Perceived trigger and inhibiting factors of seizures in people with epilepsy

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Background. Perceived provocative and inhibiting seizure factors can be helpful for seizure control. To our knowledge, no study to date has established an electroencephalogram (EEG) based link between precipitant factors and seizures, neither has the predictive value of subjective reports been objectively demonstrated.

Objective. The study aimed to determine seizure precipitating and inhibiting factors and evaluate the link between self-awareness and epileptiform activity on EEG, while performing standard and cognitive tests.

Methods. Ninety patients with epilepsy (50 % – women, 72.2 % had focal epilepsy, the mean age 38.4 ± 16.6 years; the mean duration of epilepsy – 9.5 ± 10.6 years) completed a comprehensive questionnaire on different factors that can have a triggering or suppressing effect on their seizures. Later, EEGs were registered using standard and cognitive tests. Subjective (questionnaires) and objective (EEG) data were coded as having provocative, suppressive or no effect on epileptiform brain activity (EA). MS Excel and IBM SPSS 21.0 were used for data analysis. Statistical significance was assumed at $p < 0.05$.

Results. 83.3 % of patients reported at least one factor facilitating or triggering seizures: triggering factors include mental stress (18.7 %), sleep deprivation (17.3 %), negative feelings (14.7 %), loud noise (10.7 %), alcohol intake (10.7 %); facilitating factors include sleep deprivation (48.9 %), emotional stress (46.7 %), negative feelings (36.7 %), alcohol intake (24.4 %). Women more often reported mental calculation, striped patterns, flickering light and unexpected noise ($p < 0.05$), and those with generalized epilepsy (GE) indicated flickering light ($p = 0.036$) as seizure-provoking. 43.3 % indicated that they had at least one seizure-inhibiting factor: positive feeling (15.6 %), thinking or concentrating (15.6 %), mental calculation (10 %). Patients with GE more often reported specific memories and specific thought tasks ($p < 0.05$) as seizure inhibiting. Weak or no correlation between subjective and objective data was found ($R < 0.2$). A subjective opinion on hyperventilation, lightning and cognitive tasks did not correlate with EEG changes during these tasks ($p > 0.05$).

Conclusions. Based on our study, we conclude that many people with epilepsy believe that their seizures may be triggered or inhibited by some factors. However, EEG with standard and cognitive tests showed no statistically significant correlation.

Acknowledgements. The authors declare the absence of conflict of interest.

Cognitive impairment estimation of patients with Parkinson's disease

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Background. Parkinson's disease (PD) is one of the most common neurodegenerative disorders [1, 2]. Approximately 20–50 % of patients from the beginning of diagnosis have a mild cognitive impairment [3]. It often remains undetected due to low sensitivity of neuropsychological tests [4].

Objective. We aimed to evaluate executive functions as a possible early sign of cognitive disturbance in PD patients.

Methods. The study involved 32 PD patients and 32 healthy controls (HC). Everyone completed a general questionnaire and subjective evaluation of memory and sleep quality. The cognitive functions were tested by 9-hole peg (9HP) test with dominant hand (9HP-DH) and with non-dominant hand (9HP-NdH), Stroop test, Mini-Mental State Examination (MMSE), Trail Making Test part A and part B (TMTA and TMTB). All the collected data were analysed by IBM SPSS version 23.0.

Results. The PD and HC groups were similar according to age (PD mean 66.06 years (± 10.41), HC mean 66.38 years (± 10.21)) and gender (females: PD 46.88 %, HC 62.5 %). 43.8 % of PD patients had subjective memory impairment and 56.3 % complained of poor sleep quality. The mean duration (years) of disease after confirmed diagnosis was 5.78 (± 4.5).

Significant differences between PD and HC were detected in MMSE (PD mean 26.91 pts (± 2.36) vs HC mean 27.76 pts (± 2.88); $p = 0.035$), Stroop test (PD mean 5.16 mis. (± 5.79) vs HC mean 2.66 mis. (± 3.04); $p = 0.027$), 9HP test (PD: 9HP-DH mean 37.28s (± 15.58), $p = 0.017$; 9HP-NdH 41.41s (± 16.67), $p = 0.001$; vs HC: 9HP-DH 29.19s (± 6.97), $p = 0.017$; 9HP-NdH 30.81s (± 8.77), $p = 0.001$).

PD patients were divided into subgroups – subjects with subjective cognitive impairment (SCI) (39.1 %) and those with no complains regarding memory or other cognitive dysfunction (nonSCI), 60.9 %). Significant differences between SCI and nonSCI were detected in 9HP-NdH (SCI mean 48.86s (± 20.98), nonSCI mean 35.61s (± 9.42 , $p = 0.008$)).

In PD subgroups, according to TMTA (cut off value > 78 s), the subjects with pathological TMTA (37.5 %) were significantly slower in 9HP-DH (mean 47.75s (± 19.72), than PD patients with normal performance of TMTA (62.5 %; the mean 31s (± 7.76); $p = 0.026$) and in 9HP-NdH, respectively (median (IQR): 43.0 (36; 94) vs 32.5 (23; 87), $p = 0.001$).

Moderate correlation between tests of TMTA and 9HP-DH were detected (Pearson corr. 0.536, $p = 0.002$) in PD patients, as well as in HC (Pearson corr. 0.430, $p = 0.014$). Weak correlation between tests of 9HP-DH and MMSE was found (Pearson corr. -0.364, $p = 0.040$) in PD, and strong correlation in HC (Pearson corr. -0.636, $p = 0.000$).

Conclusions. 9HP could be useful for early detection of executive functions' impairment in PD patients.

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The role of activating transcription factor 3 gene functional polymorphisms in early-stage breast cancer prognosis

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Background. A higher expression of activating transcription factor 3 (ATF3) facilitates breast cancer radioresistance and metastasis. Functional single nucleotide polymorphisms (SNPs) in *ATF3* gene have influence on ATF3 production and therefore are potential breast cancer prognostic biomarkers.

Objective. The aim of this study was to evaluate the associations of functional SNPs in the *ATF3* gene with the early-stage breast cancer phenotype, locoregional and distant disease progression.

Methods. Genomic DNA and clinical data were collected for 202 adult Lithuanian women with primary I–II stage breast cancer. Genotyping of the SNPs was performed using TaqMan genotyping assays. Three functional polymorphisms in *ATF3* gene (rs3125298, rs1119982 and rs1877474) were analysed. The associations of polymorphisms with clinicopathologic variables (age at diagnosis ≤ 50 y/ > 50 y), tumour size (≤ 2 cm/ > 2 –5cm), lymph node status (positive/negative), estrogen receptor (ER) status (positive/negative), progesterone receptor status (positive/negative), HER2 status (positive/negative), differentiation grade (G1+G2/G3) were evaluated by Pearson's chi-square or Fisher's exact test. Survival endpoints were locoregional recurrence-free survival (LRFS) and metastasis-free survival (MFS). Kaplan-Meier's procedure and Cox regression models were used for survival analysis. Patients were prospectively followed until April 30, 2019.

Results. All the studied genotypes were in Hardy-Weinberg equilibrium. Evaluating the associations between polymorphisms and clinicopathologic variables it was found that carrying of at least one G allele (GG+GT vs TT) in *ATF3* rs3125289 SNP was associated with younger age at diagnosis (OR 2.59; 95 % CI 1.12–5.98; $p = 0.038$), negative ER status (OR 4.07; 95 % CI 1.17–14.09; $p = 0.022$) and negative PR status (OR 3.19; 95 % CI 1.15–8.85; $p = 0.030$). *ATF3* rs1119982 CC genotype (CC vs TT+TC) was associated with positive lymph node status. In the mean follow-up time of 67 months (range 28–202), locoregional recurrence was observed for 11 patients, 28 patients developed distant metastases. Univariate Cox survival analysis revealed that *ATF3* rs1119982 CC genotype carriers had worse MFS (hazard ratio (HR) 2.36; 95 % CI 1.12–4.96; $p = 0.024$). The mean MFS for CC genotype carriers was 122 months vs 173 months for TT+TC genotype carriers (log-rank $p = 0.019$). Multivariate Cox survival analysis, adjusted for clinicopathologic variables, revealed that *ATF3* rs1119982 CC genotype is an independent negative prognostic marker for MFS (HR 2.43, 95 % CI 1.11–5.34; $p = 0.027$). No other significant associations were observed.

Conclusions. Functional polymorphisms in *ATF3* gene may help to identify patients with more aggressive breast cancer phenotype. Furthermore, *ATF3* rs1119982 SNP might contribute to the identification of early-stage breast cancer patients who are at a higher risk to develop metastases.

Acknowledgements. The authors declare the absence of conflict of interest.

Investigation of circulating tumor DNA dynamics in patients with breast cancer

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Background. Breast cancer is one of the most urgent problems in clinical oncology. This issue remains extremely relevant despite significant advances in medicine to date. Improvement of genomic and molecular methods of diagnostics expands the range of their application in oncology. One of the most promising methods in this field is liquid biopsy, focused on the analysis of circulating tumor DNA (ctDNA) in the blood.

Objective. The aim of our research is to investigate the dynamics of circulating tumor DNA in patients with locally advanced breast cancer in order to monitor the efficacy of neoadjuvant therapy.

Materials and methods. The study includes patients with histologically and immunohistochemically verified breast cancer. The determination of ctDNA, namely, the quantitative detection of the TP53 gene mutation, is performed using the digital PCR method on a QuantStudio 3D Digital PCR System device (Thermo Fisher Scientific). On screening step, formalin-fixed and paraffin-embedded tumor tissue samples are used for analysis. Next, for patients with detected mutation in the tissue samples, the TP53 gene mutation is investigated in circulating tumor DNA from the plasma samples. Collection of blood samples for digital PCR is performed throughout the treatment period. The results of the quantitative determination of gene mutations are compared with clinical and CT data.

Results. Quantitative determination of TP53 gene mutation was performed for 13 patients with locally advanced breast cancer. The TP53 gene mutation rate was 31 % (4/13). In all cases where a TP53 gene mutation was confirmed in tumor tissue, the same mutation was detected in the corresponding ctDNA from plasma. Investigation of serial plasma samples showed changes in circulating tumor DNA amount of various degrees throughout all cycles of neoadjuvant chemotherapy, reflecting the dynamics of the tumor process on CT scans.

Conclusions. At this stage, it can be concluded that quantitative determination of TP53 gene mutations (ctDNA) reflects the tumor burden and the dynamics of the disease during neoadjuvant treatment in patients with locally advanced breast cancer. The obtained data are comparable with the results of computed tomography. Further sample collection and inclusion of more patients in the study is planned.

Acknowledgements. This research has been performed with the financial support of of the Ministry of Education and Science of Ukraine grant No. 0118U003570 “The efficiency of “liquid biopsy” and tissue biopsy in the diagnosis and treatment of malignant tumors”.

Prevalence trends and years of life lost due to bladder cancer among the inhabitants of Latvia over past 28 years

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Background. Bladder cancer (BCa) is the 10th most common cancer worldwide. According to GCO number of estimated 5-year prevalent cases of BCa, in 2018 it has risen to 1 648 482 worldwide. It ranks 13th in mortality rate from cancer globally. Moreover, men in Latvia have one of the highest mortality rates in the world and in Europe. It would be important to analyse and compare the bladder cancer prevalence trends and the years of potential life lost due to it in Latvia, since such an epidemiological trend study has not been implemented to date.

Objective. The aim of the study was to determine the years of potential life lost (YPLL) as an indicator of premature mortality and to evaluate BCa prevalence trends in Latvia over the past 28 years.

Methods. Altogether, 10 533 BCa survivors between January 1990 and December 2017 were included in the retrospective study. Data were taken from the Register of Latvian Centre for Disease Prevention and Control. The research data were analysed for the prevalence of BCa, according to patients' gender and age. Data pertaining to 4790 deaths were analysed for calculating YPLL. The cut-off age for YPLL calculation was 65 years. Data was analysed using Microsoft Excel 2017, SPSS version 22 and Joinpoint version 4.6.0.0.

Results. The standardized prevalence rates (per 100.000) had increased from 25.2 in 1990 to 69.7 in 2017 with AAPC 3.8 (95 % CI 3.1 to 4.6) during the whole period, and 3 join points were observed in 1999, 2002 and 2015. Both genders experienced an increase (per 100.000) in the standardized prevalence (men, 53.4 in 1990 to 132.5 in 2017 versus women, 8.9 in 1990 versus 29.2 in 2017) throughout the study period. The total number of YPLL due to BCa in Latvia over 28 years was 7450. Comparing the YPLL by periods, 959 (12.1 per 100 000 general population) years were lost between 1990 and 1992, and then decreased to 474 (7.9 per 100 000) years between 2015 and 2017. Every person who died due to BCa in the beginning of period, lost an average of 8 years of life, while in the end of the period, this factor fell to 6.5 years.

Conclusions. The prevalence of bladder cancer fluctuates throughout the reviewed period, but overall AAPC increased. A considerable number of years of potential life has been lost in Latvia due to bladder cancer.

Acknowledgements. The authors express their gratitude to Latvian Centre for Disease Prevention and Control for the provided data.

Incidentally found vs non-incidental thyroid carcinomas

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Background. The term “incidental” denotes malignant tumours of the thyroid gland detected in morphology of surgical specimens resected for benign disease. Whether there are differences between incidental and non-incidental carcinomas is still widely discussed.

Objective. To analyse and compare clinicopathological features in incidental and non-incidental thyroid cancers.

Methods. Retrospective thyroid patient data since 2015 were analysed. Altogether, 1219 patients had had a thyroid operation. Thyroid cancer was diagnosed in 373 (30.6 %) patients, and out of these, 94 (25.2 %) were incidental. Data were analysed regarding indications for surgery, operation type, morphology, tumour size, thyroid weight.

Results. The incidentally found thyroid cancers were diagnosed in 94 patients operated due to benign reasons – Group A, while 279 were non-incidental carcinomas – Group B. The main indications for surgery in Group A were compression symptoms – 62 and thyrotoxicosis – in 32 cases. Group B – a suspected malignancy in 119 cases, a proven malignancy – in 160 cases. Fine needle aspiration (FNA) was performed in 47 (50.0 %) patients from Group A, and 268 (96.1 %) from Group B. Thyroidectomy was the method of choice in both groups: A – 59 (62.8 %), B – 241 (86.4 %). Unilateral procedures were more common in Group A – 35 (37.2 %) than B – 38 (13.6 %). Dominant morphological cancer type in both groups was papillary thyroid cancer: Group A – 69 (73.4 %), B – 251 (90.0 %). Follicular cancer prevalence was higher in group A than B: 20 (21.5 %) vs 17 (5.7 %). Medullary cancer and anaplastic cancer were found in Group A and B respectively: 2 (2.2 %) and 1 (1.1 %) vs 8 (2.7 %) and 0 (0 %) respectively. Multiple different cancers noticed in 2 (2.1 %) cases in Group A and in 3 (1.1 %) in B. The majority of tumours in Group A were microcarcinomas – 62 (66.6 %), B – 121 (43.4 %). The mean tumour size in Group A was 14.3 mm (1–95 mm), B – 14.6 mm (1–75 mm). Multifocality in Group A was noticed in 18 (19.1 %), while in B – 72 (24.2 %) cases. The mean excised thyroid weight in Group A – 73.2 g, B – 28.1g. Metastatic lymph nodes were diagnosed in 4 (4.3 %) in Group A, in B – 61 (21.9 %) cases.

Conclusions. Unexpected thyroid cancers could be found in patients operated due to benign pathologies. Although FNA is commonly performed and effective in cancer diagnostics, a large part of follicular cancers is still found incidentally.

Acknowledgements. The authors declare the absence of conflict of interest.

Analysis of lncRNA ANRIL SNP rs4977574 association with bladder cancer development in persons with overweight

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Background. Long non-coding RNA (lncRNA) ANRIL (Antisense Non-coding RNA in the INK4 Locus) is RNA transcribed from antisense strand of INK4b-ARF-INK4a gene cluster. Experimental studies have revealed that ANRIL overexpression is linked to emergence and progression of various oncological pathologies. Also, the role of ANRIL gene polymorphism in development of tumours, including tumours of genitourinary system, is shown. In addition, it is also known that overweight is a significant risk factor for development of malignant tumours.

Objective. The aim of the current study was to check the possible relation between ANRIL gene rs4977574-polymorphism and bladder cancer development in Ukrainian persons with normal and elevated body mass index (BMI).

Methods. Venous blood of 241 Ukrainian population representatives (141 patients with transitional cell carcinoma of urinary bladder (TCCUB) and 100 persons of control group) was used for study. Genotyping of ANRIL gene rs4977574-polymorphism was performed by real-time polymerase chain reaction (Real-time PCR) method using TaqMan assay C_31720978_30. Statistical analysis was done using SPSS software package (version 17.0). *P* values of < 0.05 were considered as statistically significant.

Results. ANRIL rs4977574-genotypes frequency was not significantly different in general group between control and TCCUB subjects ($p = 0.809$). Stratified analysis by BMI revealed no significant difference in rs4977574-genotypes distribution both in individuals with BMI $< 25 \text{ kg m}^2$ ($p = 0.501$) and BMI $\geq 25 \text{ kg/m}^2$ (0.935). The results of binary logistic regression showed no association between rs4977574 site and TCCUB risk in general group ($p_{\text{obs}} > 0.05$) and in groups with normal ($p_{\text{obs}} > 0.05$) and elevated BMI ($p_{\text{obs}} > 0.05$). Significant link was not found even after adjusting for gender, age, body mass index (for general group), and smoking habit ($p_{\text{adj}} > 0.05$).

Conclusions. Thus, for the first time, ANRIL rs4977574-genotypes distribution in individuals of Ukrainian population was established. There is no association between ANRIL gene rs4977574 SNP and bladder cancer risk development in persons with normal and elevated BMI.

Acknowledgements. The authors declare the absence of conflict of interests.

Poster presentations

GYNECOLOGY

Partner support in labour – impact on perinatal and obstetric outcomes

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Background. The World Health Organization encourages women to have a companion present during labour and childbirth due to beneficial effects on both the mother and the newborn.

Objective. The aim of the study was to compare perinatal and obstetric outcomes in births with and without partner support.

Methods. Retrospective case – control study, carried out in Riga Maternity Hospital, included 993 women. The patients were divided into two groups based on whether they had a companion present during labour. Both groups were compared on the basis of perinatal outcomes, including foetal distress during labour, neonatal transfer to intensive care unit (ICU), the mean Apgar scores in the 5th minute; and obstetric outcomes, including oxytocin use, episiotomy rates, vacuum extraction and acute caesarean section rates. The use of epidural anaesthesia was also compared. The variables were compared using the Chi-square test and Mann-Whitney U test in IBM SPSS.

Results. Both groups were comparable based on maternal age, gestation and body mass index. In cases of partner support, a significant reduction in ICU transfers ($p = 0.023$) and a higher mean Apgar scores in 5th minute ($p = 0.02$) were observed. In cases with no partner participation, there were lower rates in oxytocin use ($p < 0.01$) and episiotomy ($p < 0.01$). Epidural anaesthesia was used more frequently by women with partner support ($p < 0.01$). There were no significant differences in vacuum extraction and caesarean section, nor in foetal distress frequencies.

Conclusions. We found partner support to improve neonatal outcome and to be associated with higher rates of episiotomy, oxytocin use and epidural anaesthesia. In future studies, women's satisfaction with partner participation in labour and delivery should be taken into consideration.

Acknowledgements. This study was not funded.

Apoptosis and proliferation in kidneys of full-term newborns from mothers whose pregnancy was complicated by preeclampsia

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Background. Maternal diseases, pregnancy and childbirth complications are the main factors leading to damage of the fetuses' and newborns' kidneys. Preeclampsia (PE) is a common pregnancy complication.

Objective. To determine the features of apoptotic and proliferative processes in the kidneys of full-term newborns from mothers whose pregnancy was complicated by PE.

Methods. The tissue of the kidneys of full-term newborns was the study material. Four groups were formed: I – 15 newborns from mothers with physiological pregnancy; II – 13 newborns from mothers whose pregnancy was complicated by mild PE; III – 14 newborns from mothers whose pregnancy was complicated by moderate PE; IV – 13 newborns from mothers whose pregnancy was complicated by severe PE. The immunohistochemical study was conducted using monoclonal antibodies to p53 and Ki-67. Microspecimens were studied using microscope «Olympus BX-41».

Results. In group I p53-, Ki-67-positive cells were found in glomerular and tubular apparatus of nephrons, in collecting ducts, among stromal vessels endotheliocytes and polymorphic cell infiltration, represented mainly by immune cells, fibroblast line cells. The average value of the absolute number (AVAN) of p53-positive and Ki-67-expressed cells was (6.80 ± 0.31) and (6.93 ± 0.42). The apoptotic and proliferative processes were equally pronounced in stroma and parenchyma. In group I, a balance was found between apoptotic and proliferative processes.

In groups II–IV, a maximal p53 expression was noted in nuclei of the cells of renal corpuscles, tubules, collecting ducts, vascular endothelial cells and minimal expression in nuclei of the fibroblast line cells, immune cells. The AVAN of p53-positive cells in groups II (19.23 ± 0.43), III (22.43 ± 0.37) and IV (25.08 ± 0.38) significantly ($p < 0.05$) increased compared to group I. The expression of p53 was predominant in parenchyma compared to stroma. Ki-67 expression was maximal in nuclei of the fibroblast line cells, while minimal in nuclei of the cells of renal corpuscles, tubules, collecting ducts, vascular endothelial cells, immune cells. The AVAN of Ki-67-positive cells in groups II (22.18 ± 0.58), III (20.36 ± 0.68) and IV (19.23 ± 0.45) increased significantly ($p < 0.05$) in comparison with group I. Ki-67 expression was predominant in stroma compared to parenchyma. In groups II–IV an imbalance was noted between apoptosis and proliferation, associated with the predominance of proliferative processes in group II, and apoptotic processes in groups III and IV.

Conclusions. In the kidneys of full-term newborns, PE activates apoptotic and proliferative processes with the development imbalance between them.

Acknowledgements. The authors declare the absence of conflict of interest.

Corpus uteri cancer incidence in Kazakhstan

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Background. According to International Agency for Research on Cancer about 382 062 new cases of ovarian cancer are registered annually in the world, age-standardized incidence rates amounted to 8.4 per 100 000 of the population. High incidence rates were found in North America (20.5 $\frac{0}{0000}$), Central and Eastern Europe (19.0 $\frac{0}{0000}$), while the lowest figures were found in South Central Asia (2.5 $\frac{0}{0000}$) and Central Asia (2.6 $\frac{0}{0000}$). The highest indicators were in the age groups 75 years and older – 29.1, the cumulative risk (0–74) was 0.7.

Objective. The purpose of this research was to study the characteristics of corpus uteri cancer incidence in Kazakhstan.

Methods. Data on new cases of ovarian cancer during 2009–2018 were collected from cancer institutions of the republic. Crude (CR), age-specific incidence rates and age-standardized (world standard) incidence rates per 100 000 female population were calculated. The incidence trends were determined by the method of least squares. The mean error, 95 % confidence interval (CI) were calculated.

Results. During the study period, 10 522 new cases of corpus uteri cancer were registered in Kazakhstan. The age distribution was, as follows: < 30 years – 60 (0.6 %), 30–39 years – 295 (2.8 %), 40–49 – 1 339 (12.7 %), 50–59 – 3 440 (32.7 %), 60–69 – 3 319 (31.5 %) and \geq 70 years – 2 069 (19.7 %). The average age of patients with ovarian cancer was 60.4 ± 0.2 years ($T = +0.2$ %), ($t = 1.4$; $p = 0.2$). Crude rate of corpus uteri cancer was $6.2 \pm 0.2 \frac{0}{0000}$ (95 % CI = 5.9–6.5) and was statistically higher ($t = 0.7$; $p < 0.5$) than age-standardized rate $6.4 \pm 0.1 \frac{0}{0000}$ (95 % CI = 6.2–6.7). The incidence trends tended to grow $T = +1.7$ % (crude rate), $T = +0.6$ % (age-standardized rate). The highest age-specific incidence rate of ovarian cancer $33.4 \pm 0.9 \frac{0}{0000}$ (95 % CI = 31.6–35.2), and the highest growth rate $T = +0.7$ % were found in the age group 60–69. The cumulative risk (0–74 years) amounted to 0.76 ± 0.02 %.

Conclusions. The corpus uteri cancer incidence in Kazakhstan had a tendency to grow and it was typical for all age-specific indicators. Moreover, for the age-specific incidence rates a unimodal growth with a peak in 60–69 years was revealed, where the incidence trends were most pronounced. Further epidemiological study of corpus uteri cancer in Kazakhstan will be a priority for future researches.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude for the contribution of the Ministry of Healthcare of the Republic of Kazakhstan for provided data and supporting the public association “Central Asian Cancer Institute”

Assessing enhancing factors for successful external cephalic version

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Background. External cephalic version (ECV) is a procedure whereby the foetus is rotated from a noncephalic to a cephalic presentation by manipulation through the mother's abdomen near the 37th of the gestational week. The effectiveness of ECV supported by studies is 49%.

Objective. To predict statistically significant factors for successful external cephalic version performed at near term.

Methods. A retrospective study was conducted in Riga Maternity Hospital. The ECV data at Riga Maternity Hospital was reviewed over a period of 4 years, between 2016 and 2019. The study encompassed 160 women who accepted performance of ECV (age range 16–45 years old). Data was analysed with the method of descriptive statistics. Women were divided into 2 groups: successful and non-successful external version. A p -value of < 0.05 was considered significant. Association was calculated by Pearson chi-square and Independent Samples t Test.

Results. The mean age of women was $M = 30.16$; $SD = 5.15$ years, gestational age at ECV $M = 261$ (37+2 weeks); $SD = 6.61$ days. Successful reversion rate was 45.6 %. Days from successful ECV to delivery $M = 19.64$; $SD = 8.31$. Independent Samples t Test showed no significant difference in the mean gestational age at delivery between successful ECV and non-successful ECV group ($p = 0.74$; 95 % CI: -2.21 – 3.13). 40.63 % had vaginal deliveries and 5 % caesarean deliveries after successful external version. There was a statistically significant association between posterior ($p = 0.04$) and anterior ($p = 0.02$) placental location, parity ($p = 0.01$), non-longitudinal lie ($p = 0.03$), maternal age ($p = 0.01$; OR = 2.27, 95 % CI: 0.63–3.80) (significant only at age 16–20 ($p = 0.04$)) and successful external version. There was no statistically significant association between fundal location of placenta ($p = 0.67$), complete breech ($p = 0.63$), Frank breech ($p = 0.69$), footling breech ($p = 0.72$), low birth weight ($p = 0.19$), an amniotic fluid index < 10 and > 10 ($p = 0.64$) and successful external version. Independent Samples t Test showed no significant difference in the mean gestational age at delivery between 2 groups ($p = 0.74$; 95 % CI: -2.21 – 3.13).

Conclusions. Enhancing factors for successful version are nonlongitudinal lie, parity, posterior and anterior placental location, maternal age. Factors that are not connected with successful version are frank, footling and complete breech, fundal placenta, low birth weight and amniotic fluid index.

Acknowledgements. The authors declare the absence of conflict of interest. No funds and financial support were received for this study.

Cervical length, measured in the third trimester, as a prognostic factor for preterm labour for nullipara women

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Background. Measurement of cervical length (CL) between 18 and 24 gestational week (GW) is a part of routine examination to prevent preterm labour (PL). The same diagnostic tool is not unarguably recommended in the 3rd trimester – indicative CL rates at that time vary by source. For this reason, for now there is no clear idea about CL as a prognostic factor of PL.

Objective. To analyse cervical length as a prognostic factor for preterm delivery depending on presence of PL symptoms.

Methods. A prospective cohort study, conducted in Riga Maternity Hospital (RMh), included 68 women, who came for routine 3rd trimester USG screening (Group 1) or were admitted to RMh with complaints of abdominal pain and contraction (Group 2). Transvaginal ultrasound was performed, measuring CL. Afterwards women were followed-up until the day of delivery. Data was processed with SPSS-Statistics 22.0.

Results. The mean (SD) GW when CL was measured was 32 + 5(3.1) and 32 + 5 (2.3) GW for Group 1 ($n = 44$) and Group 2 ($n = 24$) respectively, $p = 0.06$. The mean CL was 37.97 (7.4) mm and 33.50 (9.8) mm for Group 1 and Group 2 respectively, $p = 0.053$, the mean difference – 7.44 (2.3) mm. The mean GW at delivery were 39 + 4 (2.14) and 38 + 6 (4.4) GW for Group 1 and Group 2, respectively, $p = 0.017$. PL (< 37 GW) occurred in 4.5 % ($n = 2$) and 26.1 % ($n = 6$) in Groups 1 and 2 respectively, $p = 0.02$. PL (< 34 GW) occurred in 2 cases in total, 2.9 % ($n = 2$) both in Group 2. CL below 25 mm was found in 11.8 % ($n = 8$) of the cases: 4.5 % ($n = 2$) in Group 1 and 25 % ($n = 6$) in Group 2, $p = 0.02$. CL below 30 mm was found in 23.5 % ($n = 16$) cases: 15.9 ($n = 7$) in Group 1 and 37.5 % ($n = 9$) in Group 2, $p = 0.046$. CL < 30 mm and CL < 25 mm both had correlation with PL < 37 GW ($p = 0.11$, $p = 0.00$).

Conclusions. CL, measured in the third trimester both in symptomatic and asymptomatic patients, could be valuable for the diagnosis of PL and effective management. Further evaluation, including bigger group of symptomatic women is required

Acknowledgements. The authors declare the absence of conflict of interest.

Weekend effect: does it exist in caesarean deliveries?

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Background. A caesarean section (CS) can be a life-saving procedure and the urgency for performing it appears at any minute and day of the week. Despite the well-known clinical indications, the decision to perform a CS in some cases may be influenced by human factor.

Objective. The aim of this study was to evaluate the incidence of CSs based on hours and day of the week.

Methods. A retrospective study of a 3-year period was carried out in randomly selected hospitals providing secondary and tertiary level obstetrical care. Days of the week were divided into 3 groups: Monday through Thursday were considered as weekdays, Saturdays, Sundays and holidays – as weekends and days preceding leisure periods, including Fridays, were the pre-holiday group. Weekdays and pre-holidays were divided into morning, evening and night, weekends into day and night hours. Data analysis performed with SPSS Statistics 26 program. Chi square test for independence (homogeneity) was used for statistical analysis of research data.

Results. Our study included 20 646 women, whose mean age was 27 (SD 4.756) years. Overall, CS rate was 18.3 %. Elective CS rates were significantly higher on weekdays 417 (3.6 %) and pre-holidays 131 (3.9 %) relative to weekends – 60 (1.1 %); ($p < 0.05$). The majority of elective CS took place in the morning compared to evening and night, respectively: 140 (10.2 %) vs 19 (0.8 %), and 30 (2.4 %) in 2014, ($p < 0.05$); 139 (9.9 %) vs 18 (0.7 %) and 19 (1.5 %) in 2015, ($p < 0.05$); 143 (11.1 %) vs 20 (0.8 %) and 20 (1.7 %) in 2016, ($p < 0.05$). Higher emergency CS rates were observed in the evenings rather than nights or mornings, respectively: 462 (18.8 %) vs 179 (14.1 %) and 181 (13.2 %) in 2014, ($p < 0.05$); 449 (18.0 %) vs 177 (14.3 %) and 164 (11.7 %) in 2015, ($p < 0.05$); 371 (15.4 %) vs 160 (13.3 %) and 149 (11.6 %) in 2016, ($p < 0.05$). More elective CS were performed in tertiary care compared to secondary A and secondary B, respectively: 293 (3.6 %) vs 59 (1.5 %) and 256 (3 %); ($p < 0.05$). There was no significant difference in emergency CS rates between hospital care: 1 261 (15.7 %) in tertiary, 619 (15.7 %) in secondary A and 1 293 (14.9 %) births in secondary B.

Conclusions. A “weekend effect” exists, as elective CS rates are significantly higher on weekdays in comparison to weekends. The majority of elective CS are performed in the mornings, whereas most of the emergency CS – in the evenings. No changes are observed in the tendency of CS rates each year.

Acknowledgements. The authors declare the absence of conflict of interest. No funding was provided for this study.

Changes in indicators of cervix uteri cancer in Kazakhstan

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Background. According to estimates, about 569 847 new cases of cervix uteri cancer (CUC) are registered in the world every year and annually about 311 365 lives are lost to this disease (IARC, 2018). 55.3 % of all the cases are in Asian countries, and high standardized incidence rates are established in Southern Africa ($43.1 \text{ }^0/_{0000}$) and Eastern Africa ($40.1 \text{ }^0/_{0000}$).

Objective. The aim was to evaluate the tendencies in CUC incidence in Kazakhstan.

Methods. The material of the study was the data of the MOH Kazakhstan, concerning CUC (form 35). We analysed indicators in the period of the beginning and end of the screening program for CUC (2009–2018) within the National Program of Cancer Care Development. The retrospective study employed descriptive and analytical methods of epidemiology.

Results. In 2009, 1 347 people were registered with the first-ever diagnosis of CUC and the incidence (crude rate, CR) was $15.8 \pm 0.4 \text{ }^0/_{0000}$. In 2018, 1 814 new cases of CUC were registered (table), and the incidence increased to $18.3 \pm 0.4 \text{ }^0/_{0000}$ ($t = 4.42$; $p = 0.000$).

Table. CUC indicators in Kazakhstan, 2009–2018

Indicators	2009	2012	2015	2018
New cases	1 347	1 616	1 806	1 814
Morphological verification	1 336 (99.2 %)	1 602 (99.1 %)	1 795 (99.4 %)	1 802 (99.3 %)
I–II stage	1 075 (79.8 %)	1 299 (80.4 %)	1 507 (83.4 %)	1 599 (88.1 %)
III–IV stage	253 (18.8 %)	305 (18.9 %)	233 (12.9 %)	210 (11.6 %)

The rate of morphological verification of CUC in the researched years increased from 99.2 % in 2009 to 99.3 % in 2018. In dynamics, the indicators of early diagnosis (I–II stage) increased from 79.8 % (2009) to 88.1 % in 2018, and the incidence of the female population of stage I–II in these years was $13.0 \pm 0.4 \text{ }^0/_{0000}$ and $17.1 \pm 0.4 \text{ }^0/_{0000}$ accordingly ($t = 7.25$; $p = 0.000$). The incidence of stage III tended to decrease from $2.50 \pm 0.17 \text{ }^0/_{0000}$ (2009) to $1.72 \pm 0.14 \text{ }^0/_{0000}$ in 2018 ($t = 3.54$; $p = 0.000$), and the incidence of stage IV in these years was 0.56 ± 0.08 and 0.52 ± 0.07 , respectively ($t = 0.38$; $p = 0.71$).

Conclusions. Kazakhstan reflects the global tendency of rising incidence of CUC. Indicators of cancer service are characterized by positive trends (increase in morphological verification and early diagnosis, decrease in the proportion of patients with stage III–IV), which may be associated with the screening conducted in the country.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the Ministry of Healthcare of the Republic of Kazakhstan for provided data and supporting the public association “Central Asian Cancer Institute”.

Review of laparoscopic supracervical hysterectomies performed in Vilnius City Clinical Hospital in 2016–2018

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Background. It is well-established that laparoscopic hysterectomy has several advantages compared to traditional abdominal hysterectomy, such as faster recovery, less postoperative pain, lower intraoperative blood loss and improved cosmetic appearance. However, at present it is difficult to establish the upper uterine size limit for successful performance of a laparoscopic hysterectomy, and it is still a common opinion that laparoscopic surgery is limited by the weight of uterus.

Objective. The aim was to review laparoscopic supracervical hysterectomies (LSH) performed during the period of 2016–2018 and to compare surgical outcomes for LSH in the large uterus (equal or greater than 800 g) compared with smaller (< 800 g).

Methods. The clinical data of 189 patients, who have undergone LSH in 2016–2018 was analysed retrospectively. The following information was evaluated and analysed: medical history, complaints, surgery and its characteristics, operative complications, weight of the removed uterus, histological results. Data was collected and processed by MS Excel and IBM SPSS Statistics v23 applications. The difference was considered statistically reliable when $p < 0.05$.

Results. In the study group of 189 patients, 28 had a large uterus (maximum uterine size 4400 g). The mean operation time did not differ between groups ($p > 0.05$), intra-operative blood loss was greater in the larger uterus cohort ($p < 0.05$). The hospital stay and intra-operative complication rate were similar for the two study cohorts. There were no conversions to laparotomy in both groups.

Conclusions. We believe that LSH could be performed in the presence of large uterus, if not contraindicated by the patient's comorbidities or anatomical conditions, moreover, it is feasible and safe due to the low level of operative complications and short hospital stay, as demonstrated in our study.

Acknowledgements. The authors declare the absence of conflict of interest.

Medical indications for transfer of women in prenatal, perinatal and postnatal period to a higher-level hospital

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Background. In order to improve maternal and child health and to promote quality of health care services provided to women in prenatal, perinatal and postnatal period and newborns, on June 6, 2018, the Cabinet of Ministers Order No. 259 “On Maternal and Child Health Improvement Plan 2018–2020” approved the developed Maternal and Child Health Improvement Plan 2018–2020 by the Ministry of Health. The care of women in prenatal, perinatal and postnatal period and newborns was identified as one of the areas of action to achieve the maternal and child plan goal, leading to the study analysing medical indications for cases of transfer of women in prenatal, perinatal and postnatal period from maternity wards to higher-level hospitals in Latvia.

Objective. The aim of this study was to establish and analyse the most common medical indications for transfer of women in prenatal, perinatal and postnatal period to a higher-level hospital in the period from 1 January 2018 to 30 June 2019.

Methods. The analysis included self-assessments of maternity wards and higher-level hospitals in Latvia, data from the Centre for Disease Prevention and Control and medical records for assessment of specific cases.

Results. The study examined and analysed medical records for cases meeting the set medical indications: 1) women in prenatal, perinatal and postnatal period with diagnosis requiring urgent transfer to higher-level hospital according to medical indications – preeclampsia, eclampsia, hypertensive complications, bleeding, preterm birth, premature discharge of amniotic fluid, sepsis; 2) algorithm of action – performed necessary activities for diagnosis, condition stabilization therapy, transfer organization; 3) timeliness of transfer in time interval.

Conclusions. The problems identified in the analysis of medical records enabled to identify the necessity to develop an action plan for care of high-risk women in prenatal, perinatal and postnatal period:

1. It is necessary to establish a protocol for the choice of antimicrobial therapy, taking into account the resistance of the growing microflora.
2. The reasons for late diagnosis of sepsis development and the choice of antimicrobial medication for all Level II hospitals must be reviewed.
3. The indicators (processes and outcomes) for analysis and feedback on the treatment performance of Level II inpatient maternity wards and perinatal care centres must be defined.
4. A classification/distribution of complications for high-risk women in prenatal, perinatal and postnatal period must be established.

PUBLIC HEALTH & EPIDEMIOLOGY

Characterization of complementary and alternative medicine in Latvia: evidence-based formal aspects

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Background. In the countries of the world, the concept of complementary and alternative medicine (CAM) has been studied and interpreted, and generally is well understood. Unfortunately, it has been observed that in Latvia experts who belong to the fields of official medicine sometimes continue to express their views on CAM as pseudoscience, unacceptable medical practices, etc. The Foundation "Institute of Conflictology" (FIC) does not agree with the above statements. Using scientific methods, the institute clarifies the truth and dispels the myths that circulate about CAM in Latvia.

Objective. The aim of study is to test the thesis "In Republic of Latvia, CAM (science, education, and clinical practice) are the legally valid specific sub-field of medicine and health".

Methods. The content of 23 policy and legislative documents has been analysed by systemic approach and comparative meta-analysis.

Results

1. CAM and science. It follows from the Classification of Scientific Fields and Sub-fields of Latvia in compliance with the documents of the Organization for Economic Co-operation and Development (OECD), European Commission (EC), the *Saeima* of Republic of Latvia (SRL), the Cabinet of Ministers of Republic of Latvia (CMRL), that study of CAM formally belongs to 3.2. subfields "Clinical Medicine", sub-branch "Other Subfields of Clinical Medicine".

2. CAM and clinical practice. According to the Classification of Occupations of the Republic of Latvia, based in documents of EC, the SRL, the CMRL, International Labour Organization (ILO), CAM practitioners, if they have obtained higher education, formally belong to the basic sub-group "2.2. Senior healthcare professionals", subdivision "Senior CAM professionals". If CAM practitioners have a secondary vocational education, they formally belong to the basic sub-group "3.2. Healthcare professionals", subdivision "CAM professionals". Physicians (medical doctors) belong to subdivision "Doctors", they do not belong to professional group of CAM senior professionals.

3. CAM and education. According to the legislation of the European Union and the Republic of Latvia, clinical practice of CAM specialists is not included in the practice system of regulated professions. The clinical practice of CAM specialists is based on a relatively different body of medical knowledge. According to the World Health Organization (WHO) benchmarks, CAM education could be organized as well-established programs of non-formal education. The WHO states that the scope and content of CAM education programs should be tailored to the formal and non-formal educational background of the learner.

Conclusions. The thesis stated in the objective of this study is fully proved.

Acknowledgments. The R&E&D Program "Possibilities for the development of complementary and alternative medicine system in Latvia", FIC.

Promoting healthy eating with methods of behavioural economics

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Background. Overconsumption, poor quality of diet and inactivity can lead to weak health. Even with the plethora of weight-loss programs and diet books currently available, diet-related health conditions like obesity and diabetes continue to expand. Traditional economic analyses seem inadequate for explaining why so many people choose risky health behaviours. Consequently, we decided to turn to behavioural economics, which tries to explain why people act as they do and what incentives can modify behaviour.

Objective. The aim of the current study was to promote healthy eating among students using methods of behavioural economics.

Methods. We founded the Students Nutrition Programs, which led to the creation of the “Smarter Lunch”, based on development of behavioural interventions for students’ lunchrooms.

Results. Our research was conducted in the student cafeteria and highlighted the impact that simple behaviour-based interventions can have on the nutrition-related decisions made by individuals. Research findings:

- use of more interesting and descriptive names for healthy foods can increase their sales by 23 %;
- providing choice of vegetables (e.g., carrots and beetroots), instead of just one option (e.g., just carrots), increased the likelihood that students will consume vegetables by 26 %
- having cafeteria workers explicitly ask students whether they would like a salad can increase salad sales by over 33 %;
- moving the salad bar to a more prominent location near the checkout can lead to a threefold increase in salad sales;
- displaying fruit in a bowl and thereby making it more attractive and accessible resulted in doubling of fruit sales;
- implementing an express line exclusively for students who buy healthy items was found to significantly increase the sales of healthy food (36 %).

Conclusions. Our research has shown that many factors pertaining to eating environment can affect people’s nutrition choices and portion sizes. Some of the findings can also be used to help individuals make healthier food choices. Finding successful ways to promote healthier students’ nutrition choices could be an important tool in preventing a considerable portion of chronic diseases. By understanding how these behavioural interventions influence food choice and diet quality, possible strategies can be devised, using methods of behavioural economics in other fields of medicine.

Acknowledgements. The authors declare the absence of conflict of interests. This study was performed with support from Sumy State University.

Herpes zoster vaccination: opinion of medical specialists in Lithuania

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Background. Herpes zoster (HZ) is a painful skin eruption due to reactivation of latent varicella zoster virus (VZV) and occurs most frequently in the elderly [1]. The lifetime risk of HZ in general population ranges from 20 to 30% but the risk increases dramatically after 50 years of age with a lifetime risk of HZ reaching 50 % at age 85 years [2]. 5 %–20 % of those with HZ go on to develop a complication – postherpetic neuralgia (PHN) [3]. The risk of HZ and PHN will grow as a result of an aging population in Europe. Therefore, vaccination is one of the most significant strategies to prevent shingles and reduce the cases of PHN. Currently two HZ vaccines are available – the recombinant zoster vaccine (RZV) and zoster vaccine live (ZVL) [4]. However, there is no vaccination available in Lithuania until now.

Objective. The aim of this study was to analyse and evaluate the view of medical specialists regarding vaccination against HZ.

Methods. An internet survey was conducted in December of 2019 in Lithuania. In total, 331 medical specialists filled in the anonymous questionnaire. Statistical analysis was performed using IBM SPSS Statistics 24.0 software.

Results. 88.5 % of women and 11.5 % of men completed the questionnaire. Almost a half (48 %) of the respondents belong to the group of 25–34 age. Family physicians and residents made up 33.2 %, physicians and residents of other specialties – 53.8 % of the surveyed. We also included medical students, who made up 12.7 % of respondents. We found out that more than a half (57.7 %) of respondents confirmed that vaccination against shingles was necessary in Lithuania. However, a significant part (30.2 %) of respondents answered “don’t know”. In addition, we aimed to elucidate how often patients ask their physicians about the possibility of vaccination against HZ. The results show that patients very rarely (21.8 %) inquire about this opportunity, and 73.7 % of patients never ask about it.

Conclusions. Our study reveals that patients in Lithuania during visiting the doctor very rarely or never inquire about vaccination against shingles. The situation causes concern among medical professionals, as more than a half of them maintain that vaccination is definitely necessary in order to prevent complications of HZ. However, a number of medical specialists do not have an opinion regarding this issue. Presumably, there is a lack of knowledge about the benefits and effectiveness of HZ vaccination both among physicians and patients.

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Indicators for benchmarking of research and clinical trials

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[for more information, please visit <https://www.interreg-central.eu/Content.Node/INTENT.html>]

Background. Research and clinical trials in the field of oncology are of great value and supply infrastructure and public service providers with highly important information, which could be, eventually, saving lives. In the last quarter of 2018, the INTENT group carried out a survey targeting relevant non-medical stakeholders – the patients – to understand their views on research. Based on this survey, the INTENT group has developed specific indicators, which are to be used as a base for a hospital benchmarking online tool.

Objective. The aim of the survey was to collect stakeholder replies and to identify the key issues – as viewed by the patients – contributing to the creation of specific indicators targeting the field of research and clinical trials.

Methods. Questionnaires were disseminated among cancer centres in four Central European countries (Czech Republic, Hungary, Slovenia, Italy). Survey stakeholders were oncologic patients, who were presented with anonymous form of survey in their mother tongues. Questions targeting research and clinical trials were placed into a separate category of the questionnaire. Over 1000 questionnaires were collected and registered. For reply options with highest quantitative value, key words were identified and translated into specific indicators for Research and Innovation.

Results. Over 80 % of the surveyed persons agreed on the importance of cancer centres to perform research in order to improve future care of cancer patients. More than 70 % stated that they would agree to donate samples to Biobank for possible future research. About a half of the patients were not interested in general introduction on how clinical research (e.g., clinical trials) is conducted. Over a half of the patients thought that it was important to easily obtain information about the clinical trials eligible for their illness.

Conclusions. Patients seem to value the fact that a cancer centre is performing research, and they could contribute a great deal of participation in researches. They are interested in specific relevant clinical trials, but less interested in how the research is conducted. Based on those replies, the set of indicators shall include evaluation of information on research provided to patients, information on Biobank, comprehensibility of research data given to patients.

Acknowledgements. The work was carried out as a part of INTENT project, supported by EU cohesion policy programme Interreg Central Europe.

Should only outstanding school graduates become medical students?

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Background. The first two years of university studies for medical students are particularly severe because of increased physical and mental load and changed living conditions. The students who try to execute all requirements of university are under a great stress. Responses of respondents indicate the negative health effects of stress: sleep disorders, panic attacks, weight changes, etc. A longitudinal study on evaluation of the health status of medical students in six study years has been launched.

This is the first phase of the study commenced by following the statement of the Ministry of Education and Science hereafter to restrict university enrolment of students with the average grade below 7 (good).

Objective. The aim of the study is to find a correlation between the success of the first-year medical students in University and their performance at the secondary school.

Methods. A survey method was applied, involving 70 students of the University of Latvia Faculty of Medicine, who answered targeted questions about the average grade at school, marks in centralized examinations and the results of the first four semesters. A particular attention was paid to the assessment of subjects required for medical studies (chemistry, physics, biology). The study results of students from schools in Riga and schools in the other regions of Latvia have been evaluated separately. The obtained data were processed by SPSS method.

Results. The study found that during the first years of studies the students from Riga demonstrate worse results than the students from other schools in Latvia.

This is evidenced by the fact that those students who had completed their secondary education outside Riga had earned higher grades.

No statistically significant association was found between the average grade at school and the results of examinations of the first four examination sessions.

Conclusions. Based on the obtained results, it can be concluded that the students who scored lower in secondary school and in centralized examinations show good academic achievement, thus, there is no direct correlation between the average grade at school and success in studies at university.

It is not expedient to differentiate graduates according to grades received at school, but instead it is suggested to take in consideration other criteria.

Bacterial food zoonosis in Ukraine

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Background. Food zoonoses are a serious threat to public health. In recent years, there has been a tendency of increasing their share in the structure of intestinal infections. Most of them are caused by *Salmonella spp.* and *Campylobacter spp.* These are the most dangerous infections for children and the elderly.

Objective. To investigate the epidemic situation of salmonellosis, campylobacteriosis, intestinal yersiniosis in Ukraine.

Methods. Data from the official statistical reporting of the Ministry of Health of Ukraine are presented in the work, and processed by using epidemiological and statistical methods. Materials were analysed using the C-STAT (Oxford Statistic) package.

Results. In Ukraine, the incidence of salmonellosis in 2011–2018 ranged from 18.2 to 22.1 per 100 000 people. The highest incidence is reported in the powerful scientific and industrial region – Kharkov region, where the median incidence exceeds the average Ukrainian by 2.5 times. The epidemic situation is periodically complicated by outbreaks. The most frequent outbreaks occur in catering establishments (38.4 %) and preschool institutions (23.5 %). We believe that the high incidence of salmonellosis in the region is supported by the continued flow of salmonella-contaminated food into the trading network.

Campylobacteriosis is a widespread diarrheal infection in the world. In Ukraine, the incidence of campylobacteriosis ranges from 0.19 to 0.32 per 100 000 people, which is indicative of the hypodiagnosis of the disease in connection with cost-effective research methods.

Intestinal yersiniosis occupies a leading position in the structure of etiologically undeciphered intestinal forms. In modern conditions, the median incidence of intestinal yersiniosis in Ukraine is 0.23 per 100 000, thus remaining 10 times below the European average. One of the reasons for this is the low informativeness of laboratory tests.

Conclusions. The unstable epidemic situation regarding the food zoonoses in Ukraine requires the optimization of epidemiological and epizootic surveillance by sanitary and epidemiological and veterinary services, with further development of unified approaches to the control system. Laboratory research methods should include advanced technology (PCR).

Acknowledgements. We would like to thank the employees of the state institution “Sumy Oblast Laboratory Center” for their assistance in carrying out scientific work.

Colorectal cancer in Kazakhstan: the impact of age and gender on the incidence

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Background. Colorectal cancer (CRC) belongs to the most common causes of cancer death in the world. According to the statistics of the IARC 880 792 of people died because of CRC (484 224 among men, 396 568 among women).

Objective. To study the incidence of CRC in the country as a whole, taking into account age and sex.

Methods. The source used was data on new cases of CRC (form 7), as well as population data for 2009–2018, taking into account the age- and sex-related structure. A retrospective study using descriptive and analytical methods of epidemiology. The crude rate (CR), age-specific incidence rates (ASIR) and age-standardized rate (ASR) is calculated at 100 000.

Results. In the Republic of Kazakhstan, 28 950 new cases of CRC were recorded during this period: of these, 13 779 were men (47.6 %) and 15 171 (52.4 %) were women. The average annual incidence rate of CRC was 16.7 ± 0.5 ‰ for men and 17.2 ± 0.3 ‰ for women, while the overall incidence ratio was $0.97 \div 1.0$, and the largest difference in incidence by sex was set at the age of 70–79 (see table).

Table. ASIR of CRC in Kazakhstan

Age	Both sexes (T, %)	Male (T, %)	Female (T, %)	M÷F
< 30	0.3 ± 0.0 (–2.4)	0.3 ± 0.0 (–5.8)	0.2 ± 0.0 (+0.9)	$1.27 \div 1.0$
30–39	2.9 ± 0.1 (+2.7)	3.0 ± 0.2 (+0.9)	2.9 ± 0.2 (+1.8)	$1.02 \div 1.0$
40–49	10.1 ± 0.2 (+0.6)	10.5 ± 0.3 (+0.1)	9.8 ± 0.4 (+0.2)	$1.07 \div 1.0$
50–59	35.3 ± 0.7 (+0.8)	37.8 ± 1.1 (+2.3)	33.3 ± 0.9 (+2.5)	$1.14 \div 1.0$
60–69	91.0 ± 3.0 (+1.7)	107.8 ± 4.2 (+1.2)	79.1 ± 2.5 (+4.9)	$1.36 \div 1.0$
70+	131.3 ± 1.4 (+0.4)	175.5 ± 2.2 (+0.3)	109.2 ± 1.6 (+0.9)	$1.61 \div 1.0$
CR	16.9 ± 0.4 (+2.0)	16.7 ± 0.5 (+2.1)	17.2 ± 0.3 (+1.4)	$0.97 \div 1.0$
ASR	18.1 ± 0.31 (+1.0)	21.9 ± 0.48 (+0.7)	15.9 ± 0.27 (+1.0)	$1.38 \div 1.0$

ASIR of CRC are characterized by growth with a peak in the older age group (70+) – 175.5 ‰ and 109.2 ‰, respectively for men and women. The evidence of the one-way ANOVA indicates the influence of the gender on the CRC incidence, which is 87.8 % versus other random factors 12.2 % ($F = 130.0$, $p < 0.001$).

Conclusions. The study confirms the influence of age and gender as a risk factor on the increase in the incidence of CRC. Thus, the identified age- and sex-related epidemiological aspects of CRC have to be used to conduct comprehensive and targeted interventions to strengthen prevention and reduce incidence.

Acknowledgements. The authors report the absence of conflict of interest. The study was supported by public association “Central Asian Cancer Institute”.

Component analysis of changes in incidence of malignant neoplasms of central nervous system in Kazakhstan

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Background. International Agency for Research on Cancer reports that about 300 000 new cases of malignant neoplasms of the central nervous system (MN CNS) are registered in the world every year, and 240 000 people die of this cause. In this view, a detailed study of the incidence of MN CNS, with an assessment of the role of exogenous and endogenous factors, is of a great importance. The study will serve as a platform for further scientific research and monitoring of preventive and therapeutic measures.

Objective. The purpose of the current work is to study the dynamics of MN CNS incidence indicators in Kazakhstan using component analysis.

Methods. MN CNS incidence (ICD 10 – C70-71) in 2009 and 2018 was retrospectively studied, mainly using Dvoirin and Aksel guidelines.

Results. In 2018, the number of MN CNS (812 cases) was by 26.1 % higher than in 2009 (600 cases).

Crude MN CNS incidence in 2009 was 3.8 ⁰/₀₀₀₀ vs. 4.5 ⁰/₀₀₀₀ in 2018, with a total growth of $T = +0.72$ ⁰/₀₀₀₀. At that, the increase of $T = +0.22$ ⁰/₀₀₀₀ was age-related; $T = +0.58$ ⁰/₀₀₀₀ was due to the risk of acquiring illness, and $T = -0.08$ was due to joint influence.

According to the study results, the increase in the number of new NM CNS cases in Kazakhstan could be mainly associated with the following components:

1. Population growth ($\Delta_p = +38.5$ %).
2. Changes in the age structure of the population ($\Delta_A = +16.4$ %).
3. The combined effect of changes in the population and its age structure ($\Delta_{pA} = +3.6$).
4. Changes in the risk of acquiring illness ($\Delta_R = +24.6$ %).
5. The combined effect of changes in the risk of acquiring illness and changes in the population ($\Delta_{RP} = +2.2$ %).
6. The combined effect of changes in the risk of acquiring illness and changes in the population age structure ($\Delta_{RA} = -6.2$ %).
7. The combined effect of changes in the risk of the population to acquire illness and the population age structure ($\Delta_{RPA} = -0.8$ %).

Conclusions. Based on the results of the component analysis of MN CNS incidence dynamics, the demographic components and the risk of acquiring illness had a separate direct influence on the revealed growth in incidence. However, the joint influence of the study components (factors) resulted in a decrease in the growth of incidence. The provided data complement our knowledge and are recommended for the monitoring of anti-cancer activities in the country.

Acknowledgments. The authors declare the absence of conflict of interest. The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data and supporting the public association “Central Asian Cancer Institute”.

Evaluation trends of hospital intracranial trauma incidents in Kazakhstan

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Background. Traumatic brain injury (TBI) is an important global public health problem due to the rise of urbanization, scientific and technological progress. The incidence of TBI is in the range of 150–300 cases per 100 000 of the population in the major part of the world.

Objective. To investigate the dynamic of hospital incidence rate of intracranial trauma in Kazakhstan.

Methods. A retrospective data from 2009–2018, form 14 (ICD – S06) of the Ministry of Health of Kazakhstan was analysed by using modern methods of biomedical statistics.

Results. In total, during the study period in the state hospitals 475 478 patients were registered with intracranial injury. The group with the biggest number of patients over 18 years of age was equal to 333 885 (70.9 %) (see table below).

Table. Hospital incidence of intracranial injury in Kazakhstan, 2009–2018

Indicators	Total	< 15 years	15–17 years	≥ 18 years
Number (%)	475 478 (100.0)	113 526 (23.9)	25 069 (5.3)	336 883 (70.9)
P ± m, ⁰ / ₀₀₀₀	280.3 ± 11.2	284.8 ± 14.2	337.6 ± 8.4	257.7 ± 3.8
95 % CI, ⁰ / ₀₀₀₀	258.3–302.2	256.9–312.6	321.1–354.1	250.3–265.1
T, %	–4.3	–5.5	–0.6	–1.2

The average annual value of intracranial injury in the Kazakhstan amounted to 280.3 cases per 100 000 of the total population and tended to decrease from 326.5 ± 1.4 (2009) to 237.5 ± 1.1 in 2018 ($t = 49.99$, $p = 0.0000$), the average annual rate of decrease of the equalized indicator amounted to $T = -4.3$ ($R^2 = 0.9129$). The average annual rate of decline in children under 15 years old was $T = -1.2$ ($R^2 = 0.405$), showing a tendency to slightly decrease from 262.9 ± 2.6 (2009) to 231.5 ± 2.1 in 2018. 15–17 years), the incidence increases from 333.5 ± 5.9 in 2009 to 378.9 ± 8.0 in 2018, with $T = -0.6$ ($R^2 = 0.0428$). Whereas in adults there is a pronounced decrease in $T = -5.5$ ($R^2 = 0.9299$).

Conclusions. The analysis showed a decrease in hospital morbidity of intracranial injury in the Republic of Kazakhstan. In our opinion, clinical incidence declined due to the improvement of preventive and diagnostic measures, modern neurosurgery equipment, also to the implementation of the WHO recommendations on the road safety programme 2011–2020.

Acknowledgments. The authors declare the absence of conflict of interest. The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data and supporting the public association “Central Asian Cancer Institute”.

Aspects of melanoma incidence in Kazakhstan

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Background. According to the WHO, there were 287 723 new cases of melanoma in 2018. 50.1 % of them were young adults living in Europe. IARC anticipates that in 2040 there will be 470 000 new cases of melanoma.

Objective. To study specific aspects of melanoma incidence in Kazakhstan.

Methods. The material for this retrospective research from 2009 to 2018 consisted of the data from all cancer institutions in our republic. According to the research, the following parameters were defined: extensive, age-specific incidence rates, crude rate, and age-standardized rate (World), annual average (P), mean error (m), 95 % confidence interval (95 % CI), and annual average rate of growth/decrease (T, %).

Results. Over the period of study, 3 143 new cases of melanoma were registered in Kazakhstan. At the same time, a high share of patients was aged 70 and older (30.7 %) (See table below).

Table. Melanoma in Kazakhstan (2009–2018)

Age	Number (%)	M ± m	95 % CI	T, %
< 50	798 (25.4)	0.59 ± 0.02	0.56–0.63	–0.7
50–59	610 (19.4)	3.4 ± 0.1	3.1–3.6	+9.9
60–69	769 (24.5)	7.7 ± 0.3	7.1–8.3	+2.1
≥ 70	966 (30.7)	12.4 ± 0.7	11.1–13.8	+4.3
Total	3 143 (100.0)	1.8 ± 0.1	1.7–2.0	+2.1

The average age of patients with melanoma was 60.1 ± 0.5 (95 % CI=59.1–61.0). Over time, this indicator decreased from 58.5 ± 1.0 (2009) to 62.0 ± 0.8 in 2018, this difference was statistically significant ($t = 2.73$; $p = 0.006$), while the annual average rate of growth of equated indicators was $T = +0.6$ %.

The annual average ASIR showed unimodal growth with a peak at the age of 70 and older – 12.4 ± 0.7 $^0/_{0000}$ (table). At the same time, these differences in age-specific incidence rate were statistically significant ($p < 0.05$). Melanoma incidence trends were different: tended toward reduction before the age of 50, and growth with the age of 50 and older (table). The annual average crude incidence rate of melanoma was 1.8 ± 0.1 $^0/_{0000}$ (95 % CI = 1.7–2.0 $^0/_{0000}$); the incidence rate grew ($T = +2.1$ %, $R^2 = 0.4507$). ASR (World) was 2.0 ± 0.1 $^0/_{0000}$ (95 % CI = 1.8–2.1 $^0/_{0000}$), and this indicator also was on the rise ($T = +1.6$ %, $R^2 = 0.3115$).

Conclusions. The obtained data show that the republic follows the worldwide trend of increased incidence of melanoma. Therefore, the identified age-related melanoma incidence aspects have to be used to conduct comprehensive and targeted interventions to strengthen prevention and reduce incidence.

Acknowledgments. The authors declare the absence of conflict of interest. The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data and supporting the public association “Central Asian Cancer Institute”.

Assessing the incidence of vasomotor and allergic rhinitis in Kazakhstan

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Background. Over the past decades, the number of allergic diseases has increased significantly with allergic and vasomotor rhinitis taking the leading place. According to WHO forecasts by 2050, most of the world's population will be affected by seasonal or year-round vasomotor and allergic rhinitis.

Objective. To study the incidence of allergic and vasomotor rhinitis in Kazakhstan.

Methods. Analysis of the accounting data of the Ministry of Health of the Republic of Kazakhstan (Form 12) on new cases (ICD 10 – J30) in the republic as a whole for 2009–2018. The incidence rates per 100 000 ($^0/_{0000}$) of the relevant population are calculated. The incidence trends are determined by the least squares method and the rates of increase/decrease are calculated (T, %). Calculated annual average values, 95 % confidence interval (CI).

Results. 115 817 new cases of allergic and vasomotor rhinitis were registered in Kazakhstan, of which in children (under 15 years of age) – 193 689 (43.0 %) cases, in adolescent population (15–17 years of age) – 39 127 (8.7 %) cases, and among the adults (18+) – 217 292 (48.2 %) cases (see table).

Table. Allergic and vasomotor rhinitis in Kazakhstan (2009–2018)

Age group	Number (%)	$P \pm m, ^0/_{0000}$	95 % CI, $^0/_{0000}$	T, %
Children under 15 years	193.689 (43.0)	444.1 ± 19.3	406.3–482.0	–5.0
Adolescent (15–17)	39 127 (8.7)	529.8 ± 17.1	496.3–563.4	+0.04
Adults (18+)	217 292 (48.3)	183.4 ± 5.2	173.2–193.6	–3.7
Total	450 108 (100.0)	265.1 ± 8.6	248.2–282.1	–3.8

The average incidence among the population of the republic was $265.1 \pm 8.6 ^0/_{0000}$ and in dynamics it had a tendency to decrease, dropping from $324.0 \pm 1.4 ^0/_{0000}$ (2009) to 215.1 ± 1.1 in 2018, and the average decrease rate of the equal indicator was $T = -3.8$ %. Among the studied population groups, the high rates were detected in adolescent population – $529.8 ^0/_{0000}$ (95 % CI = 496.3–563.4 $^0/_{0000}$), while the incidence in children under 15 years and adults was significantly lower and amounted to $444.1 ^0/_{0000}$ and $183.4 ^0/_{0000}$, respectively. In dynamics, the indicators tended to decrease ($T = -3.7\%$) in adults, and the incidence trends in children decreased (table).

Conclusions. In Kazakhstan, we can observe a decrease in the incidence of vasomotor and allergic rhinitis. It was found that in adolescents (15–17 years of age), the data shows the highest results. The obtained data require a further in-depth study and are recommended for evaluating prophylaxis, early diagnosis and treatment.

Acknowledgments. The authors confirm the absence of conflict of interest. The authors express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

Crohn's disease in Kazakhstan: Some aspects of incidence

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Background. Crohn's disease (CD) at the present stage is considered as an interdisciplinary problem and a polyetiological incidence. There are multiple factors that can influence its development: genetic aberrations, eating habits, disturbance in hormone metabolism, and other causes. Despite the high level of diagnosis and treatment of Crohn's disease, for many years, the study of its clinical and epidemiological features retain its relevance.

Objective. To study the incidence of CD in Kazakhstan.

Methods. Analysis of the accounting and reporting data of the MoH of Kazakhstan (Form 12) on new cases of CD (ICD 10 – K50) for 2013–2018. The incidence rates per 100 000 ($^0/_{0000}$) of the relevant population are calculated. The trends are determined by the least squares method and the rates of increase/decrease are calculated (T, %).

Results. 4 617 new cases of CD were registered in Kazakhstan, of which in children (under 15) – 341 (7.3 %), in adolescents (15–17) – 84 (1.8 %) and in adults (18+) – 4 246 (90.9 %). The average annual incidence of CD among the all population of the republic was 4.49 ± 0.96 $^0/_{0000}$ (table) and in dynamics it had a tendency to increase, showing a rise from 8.90 ± 0.23 $^0/_{0000}$ (2013) to 2.70 ± 0.12 in 2018 ($t = 23.90$, $p = 0.000$), and the average annual growth rate of the equal indicator was $T = -30.3$ % ($R^2 = 0.8191$).

Table. Crohn's disease in Kazakhstan

Age	P \pm m	95 % CI	T, %
< 15 years	1.21 ± 0.06	1.09–1.32	+1.1
15–17	2.12 ± 0.33	1.47–2.77	–11.8
≥ 18	5.86 ± 1.36	3.20–8.53	–33.8
Total	4.49 ± 0.96	2.62–6.37	–30.3

Among the studied population groups, the high incidence of CD was detected in adults – 5.86 ± 1.36 $^0/_{0000}$ (95 % CI = 3.20–8.53 $^0/_{0000}$), while the incidence in children under 15 years of age and adolescent population was statistically significantly lower and amounted to 1.21 $^0/_{0000}$ and 2.12 $^0/_{0000}$ respectively. In dynamics, the indicators tended to increase: ($T = +1.1$ %, $R^2 = 0.0181$) in children, and the incidence trends in adolescents ($T = -11.8$ %, $R^2 = 0.1869$) and adults ($T = -33.8$ %, $R^2 = 0.8168$) decreased.

Conclusions. Thus, the analysis of the incidence of CD in Kazakhstan shows a steady decrease trend. It is important to pay attention to a sharp drop of the disease rates which might possibly be linked to the accounting, registration and diagnosis of the disease. The obtained data require a further, more detailed study and are recommended for monitoring and evaluating prophylaxis, early diagnosis and treatment.

Acknowledgements. The authors confirm the absence of conflict of interest. The authors express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

Epidemiological features of breast cancer in Ukraine, Latvia and Europe

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Background. Breast cancer is the most common malignancy among the female population of economically developed countries. Breast cancer is a polyetiological disease, the risk of development of which is facilitated by various factors, such as genetic, hormonal and environmental factors, factors of reproductive anamnesis, etc.

Objective. The aim was to analyse the features of breast cancer among the population of Ukraine, Latvia and Europe as a whole.

Materials and methods. Retrospective analysis of breast cancer incidence data for 2018.

Results. According to the epidemiological data of The Global Cancer Observatory, the incidence of breast cancer among all malignant diseases in Ukraine and Europe as a whole, takes the 1st place, while in Latvia it takes the 2nd place.

In 2018, the percentage of patients with breast cancer from the total number of cancer patients, regardless of gender and age, in Latvia and Ukraine was 10.4 % and 12.4 %, respectively, which was lower than the percentage calculated for Europe as a whole (12.4 %). In the female population, the same tendency was observed. The percentage of women with breast cancer from the total number of cancer patients was the lowest in Latvia (20.8 %), in Ukraine it was marginally higher (21.6 %), but these levels were lower than the pan-European ones (24.6 %).

To assess the incidence and mortality of breast cancer, the ASR (Age Standardized Ratio) per 100 thousand women and the ASR mortality rate are used. The lowest incidence rate of breast cancer was observed in Ukraine and was 44.6 per 100 thousand women, which is by 18.2 lower than in Latvia (62.8) and by 29.8 lower than in Europe as a whole (74.4). Regarding mortality, there is an opposite tendency. Latvia is characterized by the highest mortality rate from breast cancer (17.7 per 100 thousand), the mortality rate is slightly lower in Ukraine (16.7), while the European level is the lowest (14.9). Mortality from breast cancer takes the 3rd place in Ukraine and Europe, while in Latvia it takes the 2nd place.

Conclusions. The incidence of breast cancer in Ukraine and Latvia is characterized by a lower level than in Europe overall, but the mortality rates in these countries are higher than the pan-European ones. This situation can be caused by problems in the early diagnosis of the disease and the detection of the disease in the advanced stage, as well as in the low level of coverage of specialized treatment.

Acknowledgements. The authors declare the absence of conflict of interest.

Geographic variability of lung cancer incidence in Kazakhstan

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Background. Spatial estimation of lung cancer incidence in the world evidences its variability (gco.iarc.fr). At that, the global map shows a high incidence in such countries as China (35.1 $^{0}/_{0000}$), the US (35.1 $^{0}/_{0000}$), Canada (30.0 $^{0}/_{0000}$), and Turkey (36.9 $^{0}/_{0000}$). The study of regional specifics in lung cancer incidence allows revealing new exogenic and endogenic causes that influence the occurrence and development of tumours in this localization.

Objective. To study the geographic variability of lung cancer incidence in Kazakhstan.

Methods. The cartograms were prepared on the basis of the age-standardized (world standard, WHO 2001) incidence for 10 years (2009–2018) using the mapping method based on the determination of the standard deviation (σ) from the mean (\bar{x}).

Results. In the study period, the standardized lung cancer incidence in Kazakhstan was 23.0 ± 0.5 $^{0}/_{0000}$ (95 % CI = 22.1–23.9 $^{0}/_{0000}$). To do the mapping, we determined the lung cancer incidence levels for the whole population based on the following criteria: low – up to 21.3 $^{0}/_{0000}$, average – 21.3 to 26.5 $^{0}/_{0000}$, high – 26.5 $^{0}/_{0000}$ and above. As a result, the regions were grouped, as follows:

1. Regions with low incidence (up to 21.3 $^{0}/_{0000}$) – South Kazakhstan (14.0 $^{0}/_{0000}$), Almaty (17.0 $^{0}/_{0000}$), Mangistau (18.0 $^{0}/_{0000}$), and Zhambyl (19.1 $^{0}/_{0000}$) regions, as well as the city of Almaty (18.7 $^{0}/_{0000}$);
2. Regions with average incidence (21.3 to 26.5 $^{0}/_{0000}$) – Qyzylorda (22.5 $^{0}/_{0000}$), Aktobe (24.1 $^{0}/_{0000}$), Karaganda (24.3 $^{0}/_{0000}$), West Kazakhstan (26.0 $^{0}/_{0000}$), Atyrau (26.1 $^{0}/_{0000}$), and Qostanai (26.1 $^{0}/_{0000}$) regions.
3. Regions with high incidence (26.5 $^{0}/_{0000}$ and above) – East Kazakhstan (28.2 $^{0}/_{0000}$), Akmola (29.4 $^{0}/_{0000}$), Pavlodar (30.3 $^{0}/_{0000}$), and North Kazakhstan (31.0 $^{0}/_{0000}$) regions, as well as the city of Astana (currently, Nur-Sultan) (28.1 $^{0}/_{0000}$).

Conclusions. Thus, the established epidemiological peculiarities of incidence indicate a geographic variability of lung cancer, with a territorial differentiation of loci with low values in the southern regions and high values in the environmentally unfriendly regions.

The results obtained will provide the public health managers with a clear spatial picture of lung cancer frequency and incidence, which is to be used to monitor and assess the conducted anti-cancer activities and for further research.

Acknowledgments. The authors confirm the absence of conflict of interest. The authors express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

Incidence of nonspecific ulcerative colitis in Kazakhstan

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Background. Nonspecific ulcerative colitis (NUC) is a chronic recurrent disease of the colon, characterized by severe ulcerative-inflammatory lesion of its mucous membrane with the development of local and systemic complications. NUC is most widely distributed in European countries, Australia and North America. In those countries (regions), the frequency of new cases reaches 8–15 per 100 000 people.

Objective. To study the incidence of NUC in Kazakhstan.

Methods. The research is based on accounting-reporting forms of the MoH of the Republic of Kazakhstan relative to the NUC (ICD 10 – K 51). A retrospective research was conducted in the period from 2013 to 2018. According to the generally accepted methods of sanitary statistics computed extensive and intensive incidence of NUC.

Results. Intensive average annual incidence of NUC was 13.5 ± 1.7 ‰ (95 % CI = 10.1 – 16.8) for all population (table), the dynamics of the rate are decrease from 21.7 ± 8 ‰ (2013) to 10.6 ‰ in 2018 ($t = 24.82$; $p = 0.000$), the average annual growth rate of aligned index $T = -17.7$.

Table. NUC in Kazakhstan, 2013–2018

Age	< 15	15–17	≥ 18	Total
Number (%)	2 160 (15.3)	679 (4.8)	11 240 (79.8)	14 079 (100)
Incidence, ‰ P ± m (95 % CI)	7.9 ± 2.1 (3.8–12.0)	16.5 ± 5.0 (6.7–26.2)	15.4 ± 1.9 (11.8–19.1)	13.5 ± 2.1 (9.4–17.5)
T, %	–43.7	–35.5	–12.3	–17.7

The highest incidence rates were found among adolescent population (16.5 ‰), followed by adults (15.4 ‰), while the lowest were found among children under 15 years of age (7.9 ‰). Trends in the incidence of NUC in all age groups have a tendency to significant decrease ($T_{<15} = -43.7$ %, $R^2 = 0.8612$; $T_{15-17} = -35.5$ %, $R^2 = 0.8057$; $T_{\geq 18} = -12.3$ %, $R^2 = 0.5326$).

Conclusions. Kazakhstan refers to regions with high rates of the incidence of NUC, but at the same time, data have a sharp decrease, especially among the child population. This fact is alarming and emphasizes the need to increase the knowledge of general practitioners and narrow specialists in the field of accounting, registration and diagnosis of this disease.

Acknowledgments. The authors confirm absence of conflict of interest. The authors express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

On myopia incidence in major cities of Kazakhstan

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Background. The study of myopia incidence peculiarities, and the attempts to find the reasons for increase in its frequency, the knowledge of this etiology, and to support the development of measures to prevent it. Myopia is one of the most critical and common issues of modern health care. WHO forecasts that by 2050 about 4.5 M persons (half of the world population) will have myopia, and about 115 M persons will be blind.

Objective. To study myopia incidence in the major cities of Kazakhstan.

Methods. The study materials included the retrospective data from the Ministry of Healthcare of the Republic of Kazakhstan for 2009–2018 on the new cases of myopia (ICD 10 – N52.1) registered in major cities of Kazakhstan. The data was obtained from the annual form No. 12.

Results. In the study period, 659 463 new cases of myopia were registered in Kazakhstan; of them, 95 694 (14.5 %) in the city of Almaty, and 48 282 (7.3 %) in the city of Astana. Among the study groups, the high incidence was registered in adolescents – 4 325.0 $\frac{0}{0000}$ and 2 860.8 $\frac{0}{0000}$ in Almaty and Astana, respectively (Table).

Table. Myopia in Kazakhstan (2009–2018)

Indicators	Kazakhstan	Almaty	Astana
< 15 years	593.9 \pm 21.8 (551.1–636.7)	1 232.3 \pm 56.9 (1120.9–1343.8)	1 024.5 \pm 93.3 (841.6–1207.5)
15–17 years	2 003.7 \pm 162.6 (1 685.1–2 322.4)	4 325.0 \pm 478.4 (3 387.4–5 262.6)	2 860.8 \pm 478.1 (1 923.7–3 798.0)
\geq 18 years	212.0 \pm 4.7 (202.8–221.1)	314.1 \pm 15.1 (284.4–343.7)	325.2 \pm 28.9 (268.6–381.9)
Total	385.7 \pm 11.3 (363.5–407.9)	615.8 \pm 29.9 (557.2–674.5)	580.4 \pm 46.4 (489.5–671.2)

The incidence rate in children below 15 and adults was statistically significantly lower and amounted to 1 232.3 $\frac{0}{0000}$ and 1 024.5 $\frac{0}{0000}$ in children in Almaty and Astana, and 314.1 $\frac{0}{0000}$ and 325.2 $\frac{0}{0000}$ in adults in Almaty and Astana, respectively. Over time, the incidence was growing ($T = +2.4 \%$) in children and adolescences ($T = +10.5 \%$) and decreasing in adults ($T = -1.2 \%$).

Conclusions. Thus, according to the analysis, myopia incidence is significantly growing among adolescents and children living in major cities of Kazakhstan. The obtained data requires further advanced study and is recommended for monitoring and assessment of prevention, early diagnostics, and treatment.

Acknowledgments. The authors confirm absence of conflict of interest. The authors express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

The epidemiology of onychomycosis in Latvia during the last 5 years

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Background. Onychomycosis is an important public health issue, caused by dermatophytes, yeasts or moulds. Fungal infection of nails creates an entry gate for other infections, maintains allergic reactions and also causes severe psychological discomfort and complications in treatment. *Trichophyton rubrum* and *Trichophyton mentagrophytes* are isolated most frequently; however, the causative agent may vary depending on the geographic region that influences the choice of therapy.

Objective. The purpose of our study was to find out the most frequent causative agent of onychomycosis in Latvia during the last 5 years and observe epidemiological variables.

Materials and methods. A retrospective study concerned 900 cases of onychomycosis, confirmed by direct examination and/or a positive culture, was conducted in private aesthetic dermatology clinic of prof. J. Kīsis in Riga over a five-year period (01.01.2015–31.12.2019). SPSS version 25.0 was used for analysis.

Results. Our study included 402 men (44.67 %) and 498 women (55.33 %). The mean age of the group was 48.24 ± 16.65 years (range 10–95). Toenail infections were the most common occurrence, observed in 836 cases (92.89 %), hand nail infections – in 64 cases (7.11 %). Direct examination was positive in 891 samples (99 %), culture in 462 (51.33 %). In hand nails, most common (66.67 %) infectious agent was *Candida sp.*, in toenails was *Trichophyton sp.* ($P_{\chi^2} = 2.33 \times 10^{-16}$). The relationship between fungal pathogen and nail localization is moderately strong ($V = 0.47$). In total, 11 pathogens were identified. The causative agents of these onychomycoses were dominated by *Trichophyton rubrum*, which was found in 194 patients (44.09 %), followed by *Trichophyton mentagrophytes*, which was found in 34 (7.73 %), then *Candida albicans* with 22 patients (5.00 %). Two different species were detected in 21 samples (4.55 %). Most frequent combinations were *Trichophyton sp.* and *Candida sp.* in 9 samples (42.86 %), followed by *Aspergillus sp./Candida sp.* (14.29 %) and *Trichophyton sp./Aspergillus sp.* (14.29 %).

Conclusions. This study demonstrated that *Trichophyton rubrum* and *Trichophyton mentagrophytes* were the main species causing onychomycosis in our region. Our results are supported by the literature.

Acknowledgements. The current study has not received any funding. The authors confirm the absence of conflict of interest.

Bronchial asthma in Kazakhstan: Epidemiological aspects incidence

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Background. Asthma is the most common respiratory disorder in Kazakhstan. It is also the most frequently encountered chronic disease in childhood. Over the past decades, the number of bronchial asthma incidences has increased significantly, with allergic and vasomotor rhinitis taking the leading place. According to WHO examination by 2017, currently there are about 235,000 million people affected.

Objective. To study the incidence of bronchial asthma in Kazakhstan.

Methods. Analysis of the accounting data of the Republic of Kazakhstan Ministry of Health (Form 12) on new cases (ICD 10 – J45) in the republic as a whole for 2009–2018. The incidence rates per 100 000 ($\frac{0}{0\ 000}$) of the relevant population were calculated. The incidence trends were determined by the least squares method and the rates of increase/decrease were calculated (T, %). Annual average values were calculated with 95% confidence interval (CI).

Results. In Kazakhstan, 99 079 new cases of bronchial asthma were registered, of which in children (under 15 years of age) these were – 36 619 (37.0 %), in adolescents (15–17 years of age) – 4 775 (4.8 %) and adults (18+ years of age) – 57.685 (58.2 %) (table).

Table. Bronchial Asthma in Kazakhstan (2009–2018)

Age group	Number (%)	P ± m, $\frac{0}{0000}$	95 % CI, $\frac{0}{0000}$	T, %
Children under 15 years	36 619 (37.0)	79.9 ± 8.9	62.5–97.3	+16.0
Adolescents (15–17)	4 775 (4.8)	67.5 ± 6.9	53.9–81.1	+14.5
Adults (18+)	57 685 (58.2)	48.1 ± 4.2	39.8–56.4	+11.6
Total	99 079 (100.0)	57.3 ± 5.7	46.2–68.4	+13.5

The table above shows the total population of republic, that took about $57.3 \pm 5.7 \frac{0}{0000}$ (95 % CI = 46.2–68.4 $\frac{0}{0000}$) and in dynamics it had tendency about T = +13.5 % ($R^2 = 0.9376$). The highest numbers showed in children under the 15 years of age $79.9 - 8.9 \frac{0}{0000}$ (95 % CI = 62.5–97.3 $\frac{0}{0000}$), and also the tendency of T = +16.0 % ($R^2 = 0.93$). However, the lowest numbers were found in adults $48.1 \pm 4.2 \frac{0}{0000}$ (95 % CI = 39.8–56.4 $\frac{0}{0000}$) and the tendency T = +11.6 % ($R^2 = 0.9154$). In the middle stood the adolescents with $67.5 \pm 6.9 \frac{0}{0000}$ (95 % CI = 53.9–81.1 $\frac{0}{0000}$) and took T = +14.5 % ($R^2 = 0.9413$).

In Kazakhstan, we can observe an increase in the incidence of bronchial asthma. It was found that in children under 15 years of age, the data shows the highest results. The obtained data require a further in-depth study and studies are recommended for the purposes of evaluating prophylaxis, early diagnosis and treatment.

Acknowledgments. The authors confirm the absence of conflict of interest and acknowledge the support of the Ministry of Health of the Republic of Kazakhstan in providing the primary material.

ONCOLOGY

Neuroendocrine tumours: relationship between survival and morphology

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Background. Current classification divides NENs into neuroendocrine tumours (NETs) and neuroendocrine carcinoma (NEC). In many organ systems, NETs are based on mitotic count and/or Ki-67 labelling index, and/or the presence of necrosis are graded as G1, G2, G3, corresponding to low-grade, intermediate-grade, and high-grade. All 3 grades are defined as well-differentiated neoplasms. On the contrary, NEC is a high-grade, poorly differentiated neoplasm. NENs at different anatomic sites require site-specific applications for the classification.

Objective. In this study, we sought to define correlation between type and grade of NEN in different locations based on biopsy findings with survival rate.

Methods. In this retrospective study, we used medical files of all patients with NEN followed up in Oncology Clinic, Pauls Stradiņš Clinical University Hospital, Riga, Latvia from January 2010 to October 2019. The patients without an immunohistochemical report were excluded.

Results. The study included 41 patients. Median age was 61.4 (range 26–83). 48.78 % of the patients were diagnosed at stage IV, 21.95 % at stage I, at stage II and III – 14.63 % each. 20 patients were excluded from the survival analysis due to the short period (less than 3 years) from the date of diagnosis. Survival analysis summary showed that overall survival in patients with NEN is 57.1 %: in patients with G1 NET – 70 %, with G2 NET – 44.4 %, with G3 NET – 0 %. 3-year survival analysis showed 80 % 3-year survival for patients with G1 NET, 77.8 % in G2 NET, and 0 % in G3 NET.

Conclusions. According to the WHO classification, type and grade of NEN is a strong prognostic factor. In our study, type and grade of NEN based on newest classification was confirmed by reviewing immunohistochemical reports of all patients with NEN. In terms of incidence, certainly the leading type of NEN is NET, the majority of cases were low-grade and intermediate-grade NETs, respectively – G1 NET and G2 NET. The overall survival analysis showed a higher survival rate in G1 NET in comparison with G2 NET, a significant difference in overall survival analysis indicates that the grade of the tumour is a significant prognostic factor.

Acknowledgements. The authors declare the absence of conflict of interest concerning this abstract.

Laryngeal cancer incidence trends in Kazakhstan, 2009–2018

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Background. The epidemiological studies exploring incidence of malignant tumours, particularly laryngeal cancer (LC), remain relevant because they allow building new hypothesis of cancer origin. This is especially actual with changes occurring under anthropogenic influence and evolution of risk factors.

Objective. This thesis focuses on the descriptive epidemiological evaluation of LC incidence in the whole country.

Methods. Data was sourced from the republic cancer institutions about new cases of LC over the period of 2009–2018. We used descriptive and analytical methods of the modern epidemiology of oncological diseases.

Results. The study included the 4 026 patients newly diagnosed during the study period, of these 3 680 (91.4 %) were males and 346 (8.6 %) – females. Men to women ratio was $10.6 \div 1$. The average age of LC patients in the whole population was 61.9 ± 0.3 years, men – 62.3 ± 0.3 years, women – 58.5 ± 1.0 years ($p < 0.05$).

The average annual incidence rate of LC in males was $(5.5 \pm 0.1 \text{ } ^0\text{ } _{0000})$ (95 % CI = $5.3\text{--}5.7 \text{ } ^0\text{ } _{0000}$), and in females – 13.75 times lower, i.e., $0.4 \pm 0.03 \text{ } ^0\text{ } _{0000}$ (95 % CI = $0.3\text{--}0.4 \text{ } ^0\text{ } _{0000}$), ($p < 0.05$). In general, the population incidence was $2.5 \pm 0.05 \text{ } ^0\text{ } _{0000}$ (95 % CI = $2.4\text{--}2.6 \text{ } ^0\text{ } _{0000}$). The trends of LC levelled incidence rates in the general population declined ($T = -0.2 \%$), thus, in males ($T = -0.5 \%$), unlike in females ($T = +3.8 \%$).

We found that the trends of LC incidence increased in the following age groups: “under 30” – ($T = +0.5 \%$), “30–39” ($T = +2.0 \%$), “60–69” ($T = +6.8 \%$), where the growth was the most pronounced. The decline was observed in the age groups “40–49” ($T = -2.5 \%$), “50–59” ($T = -2.3 \%$), and “70 and older” ($T = -4.4 \%$). Due to the expressive increasing trend in the age groups older than 60, the incidence rate in the whole population had an upward trend.

The trends of age-specific rates of LC incidence among men repeated the above pattern, and the rates of growth were mostly expressive among the patients older than 60. For women, the age-specific rates, when adjusting, had a declining tendency in the age groups “40–49” ($T = -15.8 \%$) and “60–69” ($T = -22.0 \%$), in other age groups the rates were increasing.

The cumulative risk in the whole population of Kazakhstan for the studied period was $(0.31 \pm 0.01 \%)$ (95 % CI = $0.29\text{--}0.32 \%$), according to gender, the results were, as follows: males – $(0.69 \pm 0.01 \%)$ (95 % CI = $0.66\text{--}0.71 \%$), females – $(0.04 \pm 0.003 \%)$ (95 % CI = $0.03\text{--}0.05 \%$), a statistically significant difference ($p < 0.05$).

Conclusions. The established characteristics of LC incidence depend on the influence of various risk factors in the occurrence of this disease. These incidence features should be used to reduce the burden of LC.

Acknowledgements. The authors declare the absence of conflict of interest and express their appreciation of the assistance of the Ministry of Healthcare of the Republic of Kazakhstan in providing data and supporting the public association “Central Asian Cancer Institute”.

Assessment of response to chemotherapy in patients with lymphoma

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Background. Lymphomas are malignant tumours of the lymphoid tissues. Hodgkin's lymphoma (HL) and non-Hodgkin's (nHL) lymphoma have some similar clinical symptoms, however, the incidence and mortality of nHL is higher. Patients with HL and aggressive types of nHL can be cured with the current chemotherapy. For patients with indolent nHL, the goal of chemotherapy is induction of remission. Assessment of response to chemotherapy is done by computed tomography (CT). Response evaluation criteria in lymphoma (RECIL 2017) include complete response, partial response, minor response, stable and progressive disease.

Objective. To analyse and statistically summarize the response of different types of lymphomas to chemotherapy, using RECIL.

Methods. A retrospective study was conducted at the PSCUS Cancer Clinic. 85 patients with histologically confirmed lymphoma, who had undergone chemotherapy, were enrolled. Data was processed using IBM SPSS Statistics 22.

Results. The minimum age of the patients was 24 years, the maximum was 89 years (M = 58; SD = 16.5). CT results after chemotherapy are unknown for 27 % of patients ($n = 23$).

In 21 % ($n = 17$) of the patients HL was confirmed. In this group, men ($n = 12$) prevailed with a 2:1 ratio. 71 % ($n = 12$) of the patients reached complete remission, 29 % ($n = 5$) had a partial remission after chemotherapy.

In 79 % ($n = 64$) of the patients, nHL was confirmed. This group did not have a sex predominance. The aggressive type of nHL was confirmed in 71 % ($n = 46$), the most common histological form in this group was diffuse large B cell lymphoma. After chemotherapy, 53 % ($n = 24$) of the patients achieved a complete remission, while 6 % ($n = 3$) – a partial remission, and 11 % ($n = 6$) showed disease progression.

The indolent form was confirmed in 29 % ($n = 19$) of the patients. The most common histological type in this group was follicular lymphoma. In this group, complete remission was achieved by 43 % of the patients ($n = 6$), partial – by 29 % ($n = 4$) of the patients, stable disease – by 21 % ($n = 3$) of the patients, whereas disease progression – by 7 % ($n = 1$) of the patients.

Conclusions. All lymphomas are sensitive to chemotherapy. The best result in achieving a complete remission had HL. In the second place is the aggressive nHL, however, it has a rather high percentage of disease progression. In the third place to achieve a complete remission is the indolent nHL, however, it has a relatively high percentage of partial remission and stable disease.

BRAF V600 E mutational status correlated with increased numbers of tumour – infiltrating lymphocytes in patients with melanoma

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Background. Despite new opportunities for treating one of the most aggressive skin cancers, the prognosis for a melanoma patient depends on the stage of the disease at diagnosis.

Tumour – infiltrating lymphocytes (TIL) in primary melanoma have been found to correlate with patient outcomes. In most tumours, including melanoma, a high density of intratumoural FOXP3+ Tregs has been associated with poor prognosis. However, it is insufficiently understood whether these cells also influence the response to BRAF inhibition therapy in metastatic melanoma.

Objective. To evaluate tumour – infiltrating lymphocytes (TIL) in patients with BRAF V600E mutant and wild type melanoma.

Methods. 71 patients were enrolled in the study. The patients were surgically treated in Riga East University Hospital from 2011 to 2017 with primary skin melanoma. The study was approved by the Central Ethical Committee. The histopathological characteristics were assessed according to the current WHO and AJCC 8th. edition guidelines. DNA from formalin – fixed paraffin – embedded melanoma tissues was isolated using GeneRead™ DNA FFPE kit (Qiagen). The melanoma BRAF mutation status was assessed by RT-PCR/Sanger sequencing in both directions using primers: forward 5'-TCATAATGCTTGCTCTGATAGGA-3' and reverse 5'-GGCCAAAATT-TAATCAGTGGA-3'.

Results. 71 patients (47 were females and 24 were males) with the mean age 62.08 ± 14.15 years were enrolled in the study. Distant metastases were detected in 18 patients (10 were females and 8 were males). A mild TIL infiltration was identified in 45.1 % of the patients, 31.0 % had non-metastatic and 14.1 % had metastatic melanoma. A moderate TIL infiltration was observed in 52.1 % of the patients, 40.8 % had a non-metastatic disease, whereas 11.2 % had a metastatic melanoma. A prominent TIL infiltration was identified only in patients with non-metastatic melanoma (in 4.2 % of the cases). The significant correlation between BRAF mutational status and TIL infiltration was observed ($\text{Rho} = + 0.32$; $p = 0.003$).

Conclusions. TIL play an important role in the prognosis of the disease. The presence is associated with the best prognosis of melanoma and the highest life expectancy. In addition, the intratumoural density of TIL was higher in melanomas with mutant BRAF compared to those with wild type BRAF status.

Contrast enhanced mammography – the first experience at the Oncology Centre of Latvia

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Background. Contrast enhanced mammography (CEMG) is an emerging X-ray modality with developing clinical applications, which exploits breast tissue and tumour uptake of iodinated contrast agents. This modality has never been used in Latvia before for detecting breast diseases.

Objective. The aim of the current study was to compare BIRADS assessment categories of the same breast lesions using 2D mammography (MG), CEMG and to confirm final diagnosis by pathohistological assessment.

Methods. Altogether, 20 patients were enrolled in the study. They had various clinical backgrounds and various mammographic lesions according to BI RADS lexicon in one breast. Retrospective data about every patient's MG and CEM detected same breast lesion BI RADS assessment category (0–5) was obtained. The final diagnosis, if possible, was confirmed by pathohistological assessment. Data were registered and analysed in MS Excel.

Results. All the enrolled patients were female with the mean age of 56 years. Of all the patients, 40 % (8 patients) had palpable lesions. In asymptomatic women, according to BIRADS mammography lexicon, the following lesions were found: mass, asymmetry, architectural distortion or calcifications. Of all the patients, 20 % (4) had BIRADS 0, 65 % (13) had BIRADS 4 and 15 % (3) had BIRADS 5 final assessment category after MG. Of the entire BIRADS 0 group after CEM findings were assessed as BI RADS 3 in 75 % (3) of the patients and BIRADS 5 in 25 % (1) of the patients. Of the entire BIRADS 4 group after CEM findings were assessed as BIRADS 4 in 8 % (1) of the patients, and BIRADS 5 in 92 % (12) of the patients. Of the entire BIRADS 5 group after CEM findings all of the patients (3) in this group were still assessed as BI RADS 5. Histopathologically invasive malignancy was confirmed in 14 patients (from BIRADS 5 group after CEM), *in situ* malignancy was confirmed in 1 patient (from BIRADS 5 group after CEM), malignancy was denied in 1 patient (from BIRADS 4 group after CEM) and a report was not available in 1 patient (from BIRADS 5 group after CEM).

Conclusions. All the patients with suspicious or highly suspicious lesions in MG (BI RADS 4 or 5) CEM confirmed or upgraded lesions in BI RADS category. For most of the patients with suspicious or highly suspicious lesions in CEM invasive or *in situ* malignancy was confirmed.

Electron microscopic examination of skeletal muscle regeneration in rats with chronic hyperglycaemia

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Background. Chronic hyperglycaemia (CH) is one of the most common metabolic disorders worldwide, especially in developed countries. Recent studies have shown that CH impairs the function of striated muscle progenitor cells, inhibits the formation of new vessels and disrupts the immune system function within skeletal muscles. However, to date, there is virtually no data regarding ultrastructural changes in striated muscles during their post-traumatic recovery under CH conditions.

Objective. The aim of the current study was to investigate the ultramicroscopic features of skeletal muscle post-traumatic regeneration in rats with CH.

Methods. 80 laboratory white male rats were used in the study: 40 animals – control group; 40 animals – experimental group (animals with CH). CH simulation was carried out by two-week 10 % fructose solution loading followed by a single intraperitoneal administration of streptozotocin (40 mg/kg). Traumatic injury of triceps surae muscle was reproduced by linear deep incision perpendicular to muscle fibres course. The ultrastructural features of striated muscle regeneration were studied at 3, 7, 14 and 28 days after traumatization. Ultramicroscopic examination was performed using PEM-100 m electron microscope (Sumy, Ukraine).

Results. On the 3rd day of experiment, formation of the new vessels in animals with CH was less intense compared to control rats. Segmented neutrophils had a large number of electron-dense autophagosomes and electron-transparent vacuoles. On the 7th day of experiment, the nuclei of non-destructive myosimplast were pyknotic. The sarcomeres had fragmented myofibrils and impaired transverse darkness. On the 14th day, no noticeable signs of progenitor cell activation were observed. In addition, fibroblasts were characterized by a highly developed granular endoplasmic reticulum with dilated cisterns, significantly hypertrophied mitochondria with expanded matrix. On the 28th day after the injury, the defective site was filled with fragmented muscle fibres, multiple vacuoles, muscle detritus, and connective tissue elements. Microcirculatory vessels were mostly defective. The weak signs of post-traumatic myogistogenesis were observed in the marginal areas of defect. The myosimplasts contained groups of vesicles that were located under sarcolemma. The basement membrane over activated myosatellites was destroyed.

Conclusions. Thus, it was found that chronic hyperglycaemia leads to the decrease in quality of skeletal muscle regeneration, characterized by inhibition of neoangiogenesis, significant activation of fibroblasts and poor activity of progenitor cells.

Acknowledgements. The work is a part of the research “Molecular-genetic and morphological features of lower extremity tissues regeneration under chronic hyperglycaemia conditions” (state registration number 0117U003926).

Metaplastic breast carcinoma in Latvia: a pilot study

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Background. Metaplastic breast carcinoma (MBC) is a rare but aggressive subtype of breast cancer, represented in about 0.2 % of the invasive breast carcinomas (McKinnon et al., 2015). MBC represents a group of unrelated invasive breast cancers displaying differentiation of the tumour cells into squamous or mesenchymal elements. This includes, but is not limited to, spindle, chondroid, osseous, and rhabdoid cells, and these elements may be mixed with carcinoma of usual type.

Objective. The aim of this study was to investigate the number of a breast metaplastic carcinomas in Latvia in a 5-year (2019–2023) period, as well as to explore the survival and treatment effectiveness.

Methods. Archive search was carried out to identify all the breast cancer patients surgically treated in 2019 in the Riga Eastern Clinical Hospital. In total, 2 cases were diagnosed as metaplastic carcinoma.

Results. At present, the study shows that from all the breast carcinomas a metaplastic breast carcinoma occurs in less than 1 % of cases. Our study reveals the great morphological differences in both diagnosed cases. The first case had a short anamnesis of a breast lump, and in a core-needle biopsy a *low-grade* carcinoma with multinucleated giant cells and mesenchymal component was found. At this stage, the patient underwent checkpoint lymph node extraction and a further 5 lymph nodes were examined in a frozen ward procedure. Glandular structures, such as metastases, were found in four lymph nodes. Mastectomy and lymphadenectomy were performed and revealed irregular breast mass. The second case showed a *high-grade* carcinoma with a squamous cell differentiation in a core-needle biopsy. At this point, the tumour was diagnosed as inoperable. After 8 courses of neoadjuvant therapy, which had a positive effect, a mastectomy was carried out and a further analysis of an operation material was done. In both cases, an extensive immunohistochemical examination was performed. Based on immunohistochemistry and histological features in the operation material, a diagnosis of breast metaplastic carcinoma was made.

Conclusions. MBC is a very rare neoplasm. It is very important to differentiate it from a ductal carcinoma, as the prognosis for MBC is poor and the survival rate is low. MBC shows a great morphological variability and even similarities to other breast carcinomas. It could make diagnostic complicated, especially in core-needle biopsies.

Acknowledgements. The authors declare the absence of conflict of interest.

Development of pancreatic insufficiency in patients with pancreatic tumours and chronic pancreatitis, depending on the operation

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Background. Chronic inflammation of the pancreas and pancreatic tumours can affect both functional systems of the pancreas. In addition, surgical resection may induce or exacerbate these dysfunctions. However, the prevalence of Exocrine Pancreatic Insufficiency (EPI) and type 3c diabetes mellitus is unknown.

Objective. To estimate the functional state of the pancreas in patients with Chronic Pancreatitis (CP), Pancreatic Ductal Adenocarcinoma (PDAC) and Benign Tumours of the Pancreas (BTsP); to determine the degree of decreased function of the pancreas before and after surgical treatment.

Methods. The study included 89 patients: 17 patients had resectable and 25 had unresectable PDAC, 19 had BTsP, and 28 had CP. Clinical manifestations and instrumental studies were used for diagnosis. Functional status of the pancreas was determined before and after surgery using C-peptide, fasting glucose, glycated haemoglobin and pancreatic elastase. All the patients with CP had severe pain and underwent Frey, Beger, or Whipple procedures. Resectable patients underwent Whipple procedures or distal pancreatectomy, depending on the location of tumours. The patients with BTsP underwent the same surgical treatment.

Results. 64 % ($n = 18$) of the patients with CP had endocrine insufficiency of the pancreas, in 82 % ($n = 23$) of the cases there was a severe EPI before surgery, and both worsened after surgical treatment.

Patients with resectable PDAC, a decrease in endocrine function noted in 35 % ($n = 6$) and in 17 % ($n = 3$) of the cases – a severe EPI. There were no significant differences in meanings regardless of the tumour location.

The patients with unresectable PDAC had a severe EPI more frequently ($n = 11$). Lower levels of C-peptide ($n = 4$) and elastase-1 ($n = 2$) before surgical treatment were more common with PDAC of the head ($n = 11$) than with PDAC of the body/tail ($n = 6$).

Likewise, pancreatic insufficiency increased after surgery in more than 50 % of the cases. Normal levels of C-peptide were observed in 94 % ($n = 18$) of the patients with BTsP before surgery, however, in 15 % ($n = 3$) of the cases they had a severe pancreatic insufficiency. After surgical treatment, the amount of endocrine and exocrine insufficiency increased, and it was noted in 26 % and 21 % of the patients, respectively.

Conclusions. In patients with CP, there was a pancreatic insufficiency and it grew regardless of the volume of surgery. The patients with PDAC of the head had more frequent exocrine and endocrine insufficiencies, when compared with the patients with PDAC of the body/tail. Pancreatic function worsened after the surgery regardless of the procedure and underlying pathology. In patients with BTsP, pancreatic function was not significantly different before and after surgery.

Acknowledgements. The authors declare the absence of conflict of interest.

Breast cancer incidence trends in Kyrgyzstan

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Background. Breast cancer (BC) occupies a leading position in the structure of cancer morbidity and mortality in women, and according to IARC forecasts, about 3 million new cases are expected in 2040. WHO (IARC) recommends screening for breast cancer along with screening for colorectal cancer and cervical cancer.

Objective. To study the dynamics of BC incidence in Kyrgyzstan.

Methods. Retrospective study (2003–2017) the sources of information included the data from the National Centre of Oncology under the Ministry of Health of the Kyrgyz Republic on new cases of BC. Extensive, crude (CR), age-specific incidence rate (ASIR) and age-standardized rate (ASR, world standard) of morbidity were calculated using generally accepted methods of medical and biological statistics.

Results. In 2003–2017, 7 861 new cases of BC were registered. The average age of the patients was 57.5 ± 0.3 years (95 % CI = 56.8–58.1).

In dynamics, crude incidence rate tended to increase from 17.6 ± 0.8 ‰ (in 2003) to 19.0 ± 0.8 ‰ in 2017, but the established differences are not statistically significant ($t = 1.24$, $p = 0.216$), and the average annual growth rate of the equalized indicator was $T = +0.5$ % ($R^2 = 0.2646$).

Age-specific incidence rate of BC incidence in Kyrgyzstan had a unimodal increase with a peak incidence in 60–64 years – 83.9 ± 4.2 ‰ (95 % CI = 75.6–92.3 ‰). If we look at the dynamics, age-related indicators of breast cancer incidence had a different tendency. Decreasing in date was observed in the age groups of 40–44 years ($T = -0.1$ %, $R^2 = 0.0003$), 45–49 years ($T = -1.1$ %, $R^2 = 0.1443$), 50–54 years ($T = -1.4$ %, $R^2 = 0.3538$) and 55–59 years ($T = -0.7$ %, $R^2 = 0.035$). In the other studied age groups, growth was observed: up to 30 years ($T = +4.5$ %, $R^2 = 0.1805$); 30–34 years – ($T = +3.8$ %, $R^2 = 0.2403$); 35–39 years old ($T = +0.8$ %, $R^2 = 0.0372$) and in 60–64 years old ($T = +1.4$ %, $R^2 = 0.1111$).

ASR of BC during the study period was 23.9 ± 0.6 ‰ (95 % CI = 22.8–25.0 ‰), and the average annual growth rate of the equalized indicator was $T = +0.4$ % ($R^2 = 0.0365$). It should be noted that standardized indicators of breast cancer incidence were statistically significantly higher than the crude incidence rate ($t = 6.53$, $p = 0.000$).

Conclusions. Generally, a very slight upward tendency was observed in Kyrgyzstan. The study results must be taken into account for monitoring and evaluation of antitumor activities, as well as used in the organization of mammalogical screening.

Acknowledgments. The authors declare the absence of conflict of interest and wish to express their gratitude to the Ministry of Health of the Kyrgyz Republic for the provided primary material.

Prostate cancer in Kazakhstan: component analysis of incidence dynamics

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Background. Prostate cancer is a malignant cancer that is one of the most prevalent diseases for years is characterized by a progressive increase in the incidence. According to WHO estimations, about 1 280 000 new cases of prostate cancer are registered annually in the world, and about 2 300 000 cases are expected in 2040.

Objective. To research changes in the incidence of prostate cancer in Kazakhstan using component analysis.

Methods. The incidence of prostate cancer (ICD 10–C61) in 2009 and 2018 was retrospectively studied, mainly using Dvoirin and Aksel guidelines. The component method in this study was used to divide the increase in the number of cases that belonged to the same population, but in different periods of time.

Results. In 2018, the number of prostate cancer cases (1 202 new cases) was by 90.5 % higher than in 2009 (631 new cases).

Incidence rate of prostate cancer in 2009 was 8.2 ‰ vs 13.7 ‰ in 2018, with a total growth of $T = +5.5 \text{‰}$. At that, the increase of $T = +0.9 \text{‰}$ was age-related and $T = +4.6 \text{‰}$ was due to the risk of contracting the illness.

According to the study results, the increase in the number of new prostate cancer cases in Kazakhstan could be mainly associated with the following components:

1. Population growth ($\Delta_p = +15.7 \%$).
2. Changes in the age structure of the population ($\Delta_A = +11.9 \%$).
3. The combined effect of changes in the population and its age structure ($\Delta_{pA} = +1.7$).
4. Changes in the risk of contracting the illness ($\Delta_R = +61.9 \%$).
5. The combined effect of changes in the risk of contracting the illness and changes in the population ($\Delta_{Rp} = +8.8 \%$).
6. The combined effect of changes in the risk of contracting the illness and changes in the population's age structure ($\Delta_{RA} = 0.0 \%$).
7. The combined effect of changes in the risk of the population to contract the illness and the population's age structure ($\Delta_{RPA} = 0.0 \%$).

Conclusions. Thus, the number of patients with prostate cancer in the entire country increases dramatically. The rise is mainly due to population growth and the risk of contracting the illness. The results of the component analysis of Kazakhstani prostate cancer incidence dynamics are recommended for usage in planning anti-cancer measures for cancer of this anatomical localization.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the Ministry of Healthcare of the Republic of Kazakhstan for the provided data and for supporting the public association “Central Asian Cancer Institute”.

Patient-centred oncology care at Masaryk Memorial Cancer Institute, Czech Republic

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Background. Patient-centred care entails providing multiple aspects for optimal cancer care; however, healthcare system frequently has a difficulty to meet the needs of oncology patients. Therefore, assessing the efficiency of overall care-centeredness is necessary in order to improve the delivery of cancer care.

Objective. The study aimed to investigate patient-centred oncology care at Masaryk Memorial Cancer Institute (MMCI), Czech-Republic as seen by foreign nationals.

Methods. A questionnaire of patient-centred cancer care was proposed to non-Czech citizens treated at MMCI. The questionnaire was designed by an INTENT group as a part of Interreg Central Europe project INTENT. Questionnaires included basic demographic data and 5 sections of questions: communication; shared decision making; accessibility to services; psychological support; participation in clinical trials. The survey was conducted from April to June 2019. Data was processed using SPSS 22.0.

Results. Overall, 25 of 138 questionnaires were completed, the respondents included 76 % females, 16 % males, while 8 % did not indicate their sex. Age distribution – 18–34-year olds (8 %); 35–49-year olds (32 %); 50–64-year olds (16 %); 65 and older (44 %). The most common cancer sites included breast (23 %), colorectal (13 %) and prostate (10 %). Overall, 54 % of the respondents marked meeting in person with healthcare professional as the most important channel on receiving disease-related information. More than a half (52 %) of the surveyed preferred to be informed on all the available treatment alternatives, 20 % needed more support from doctors when evaluating different treatment options. Only 28 % of the respondents did not want to participate in shared decision making. Regarding the accessibility of services, more time dedicated during doctor's visits was reported as necessary by 48 % of the respondents. Top three services respondents claimed to benefit from the most at home (as opposite to in-hospital care) were nursing support (20 %), physical therapy (18 %) and pain control care (17 %). Psychological support was reported as beneficial at any stage of disease by 48 % respondents. Lastly, 96 % marked research as necessary condition to improve cancer care and 92 % were willing to donate tumour tissue samples to Biobank.

Conclusions. The majority of oncology patients prefer receiving disease-related information from the healthcare professional in person, and being involved in shared decision making regarding selection of medical treatment. More time dedicated by the doctor, as well as availability not only of medical, but also psychological services are important in order to improve patient-centred cancer care.

Acknowledgements. The study was supported by INTENT project within the framework of Interreg Central Europe. The authors declare the absence of conflict of interest regarding the publication of this article.

INTERNAL MEDICINE

Qualitative and quantitative analysis of tear and eye surface in dry eye syndrome patients before and after increased visual load

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Background. Dry eye is a multifactorial disease that is a common condition in general ophthalmology, it can manifest itself as a discomfort and lead to visual disfunctions. Based on National Health and Wellness Survey data, the prevalence of dry eye disease ranges around 5 to 30 percent in persons over 50 years of age. Visual load increases due to everyday activities, such as reading. Dry eye patients' diagnostic parameters can be changed by simulating increased visual load.

Objective. To evaluate qualitative and quantitative changes of tear composition and eye surface in patients with dry eye disease before and after increased visual load.

Methods. A study group – the patients with pre-established diagnosis of dry eye disease and a control group – the patients without a diagnosis of dry eye disease. Dry eye disease diagnostic parameters were performed: tear break up time, corneal staining using fluorescein, conjunctive staining using lissamine green, Schirmer's test, meibography, interferometry, blinking count. Patients were asked to read a book for 30 minutes as an imitation of increased visual load. After the imitation, the diagnostic parameters were taken again. Diagnostic parameters were compared before and after the increased visual load, and results were compared between dry eye disease patients and control group.

Results. Study group ($n = 70$) and control group ($n = 50$) before and after increased visual load showed statistically significant differences in: NIBUT study group ($p < 0.001$). NIBUT control group ($p = 0.003$). Meniscus height study group ($p < 0.001$). Meniscus height control group ($p = 0.005$). Blinking count study group ($p < 0.001$). Blinking count control group ($p < 0.001$). Meibography study group ($p = 0.041$). Schirmer's test study group ($p = 0.001$). Schirmer's test control group ($p = 0.003$). Interferometry study group ($p < 0.001$). Interferometry control group ($p = 0.002$).

Conclusions. After increased visual load, in dry eye disease patients tear film stability, meniscus height, Meibomian gland percentage decrease more than in the control group. A single diagnostic parameter cannot indicate diagnosis, more methods are required to evaluate dry eye disease, and they would also help to indicate the prevailing pathogenetic mechanism.

Acknowledgements. The authors are pleased to acknowledge the assistance of Riga East Clinical University Hospital Ophthalmology Clinic Bīķernieki and private practice of Dr. Žanna Kudiņa.

Serum proteasome concentration in patients with different stages of diabetic retinopathy

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Background. Visual impairment as a result of diabetic retinopathy has a significant negative impact on the patient's quality of life. There are multiple risk factors and markers for the onset and progression of diabetic retinopathy. Proteasome concentration has been indicated to be a useful marker for some pathologies including diabetic nephropathy (Luo et al. 2011), as well as for tissue damage and dysfunction (Dutaud et al. 2002). Altered proteasome concentration may contribute to the development of diabetic retinopathy. A better understanding of the nature of proteasome concentration under normal and diabetic conditions may be important for development of novel strategies treating diabetic retinopathy.

Objective. The aim of this work was to investigate whether there were any differences between proliferative or nonproliferative/no retinopathy and whether proteasome concentration depended of the stage of retinopathy.

Methods. Altogether, 179 patients with type 1 diabetes were enrolled in the study. The patients were divided into two groups according to stage of diabetic retinopathy – proliferative retinopathy against non-proliferative/no retinopathy. Proteasome concentration was measured by ELISA method.

Results. Group of patients with proliferative retinopathy ($n = 76$) was compared with “no retinopathy” ($n = 103$) and there was a significant difference in age (47 ± 19 vs 32 ± 18 years), duration of diabetes (32 ± 14 vs 18 ± 7 years), glomerular filtration rate (98.6 ± 39.9 vs 118.9 ± 18.6 ml/min/1.73 m²), diabetic polyneuropathy (75 % vs 51 %), diabetic nephropathy (43 % vs 18 %), hypertension (83 % vs 45 %), vascular event (32 % vs 2 %), metabolic syndrome (63 % vs 32 %) and smoking (16 % vs 35 %) [median \pm interquartile range, $p = 0.000$]. There was no statistically significant difference between the groups in proteasome concentration, HbA1c, body mass index, albuminuria. Median proteasome concentration in all the studied patients was 120 ± 120 ng/ml. Proteasome concentration did not show correlation with other diabetes-associated markers (HbA1c, lipids, duration of diabetes etc.), when analysed by correlation and regression analysis.

Conclusions. In this study, we have demonstrated that there are several clinical differences depending on stage of retinopathy. Older age, longer duration of diabetes, frequency of diabetic polyneuropathy and nephropathy, vascular diseases and metabolic syndrome were more frequent in patients with proliferative retinopathy. Proteasome concentration was not significantly increased in any group, it means there should be further investigations like the measurement of proteasome activity.

Acknowledgements. The study has been supported by fundamental research grant in biomedicine and pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” by the Faculty of Medicine, University of Latvia and Genome Database of Latvian population.

Kidney survival analysis in Immunoglobulin A Nephropathy patients

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Background. Immunoglobulin A nephropathy (IgAN) is the most common form of glomerulonephritis. The disease can affect patients of any age, but the highest incidence is in the second and third decades of life. IgAN earlier was thought to carry a relatively benign prognosis, however, 1–2 % of all the patients annually develop an end-stage kidney disease.

Objective. The aim of the current study was to determine kidney survival in patients with IgAN, identifying potential risk factors.

Methods. A retrospective cohort study at Pauls Stradiņš Clinical University Hospital (PSCUH) Nephrology Centre included patients with a histologically confirmed diagnosis of IgAN from January 1, 2013 to November 1, 2019. Data were collected from medical records: GFR (glomerular filtration rate) was calculated according to CKD-EPI formula, daily proteinuria at the time of renal biopsy. The correlations were analysed by Spearman's Correlation. Kidney survival was defined as remained renal function with GFR > 15 ml/min/1.73 m² within 5 years after the biopsy. It was assessed by Kaplan-Meier method.

Results. 105 patients (59 men, median age 37 years (age range 18–72)) were included in the study. Most of the patients (38 %) were in the age group of 30–39 years. The overall median kidney survival time was 49 (95 % CI 26.81–71.19) months. In participants with proteinuria < 1 g, the median kidney survival time was longer than the follow-up period. It was longer than in patients with proteinuria 1–3 g or > 3.5 g, which was 40 (95 % CI 7.63–72.37) and 18 (95 % CI 5.81–30.19) months, respectively. A logrank test was conducted to determine if there were differences in survival distributions for the different daily proteinuria levels, $\chi^2(2) = 7.115$, $p = 0.029$. The survival distributions for the gender were not significantly different, $\chi^2(1) = 1.682$, $p = 0.195$. 75 % of the patients with daily proteinuria > 3.5 g renal survival time was 2 months, 1–3 g it was 8 months and for patients with proteinuria < 1 g – 60 months.

22 % (18/82) of the patients had daily proteinuria > 3.5 g, 39 % (32/82) had < 1 g and 1–3 g/day each. Median GFR was 51 (GFR range 3–130) ml/min/1.73 m². A moderate negative correlation was observed between patients age and GFR, $r_s = -0.339$; $p = 0.001$.

Conclusions. IgAN is more common in young adults. Daily proteinuria is an important risk factor for kidney survival. The patients with daily proteinuria > 3.5 g had the shortest renal survival time compared to the patients with daily proteinuria 1–3 g and < 1 g. There was a statistical correlation between age and GFR level.

Association of achievement of guideline-defined treatment targets with diabetic nephropathy and retinopathy in type 1 diabetes patients in Latvia

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Background. Good control of glycemia, blood pressure and blood lipids are associated with lower rates of diabetic complications in large prospective studies. In Latvia, these data are not analysed due to lack of instrumental diabetes registry and lag in progress of electronic medical records. “LatDiane” is a longitudinal study initiated in 2013, which aims to study clinical, environmental and genetic factors of complications in type 1 diabetes.

Objective. To assess the rate of achievement of treatment targets on HbA1c, low-density lipoproteins (LDL) and blood pressure in Latvian type 1 diabetic patients. To assess association between achievement of treatment targets with diabetic nephropathy and retinopathy.

Methods. Data of 334 “LatDiane” study patients with diabetes duration > 1 year were included. Patients were aged 18 – 86, median age – 35 years, 45 % male (n=151). Treatment targets were defined according to ESC/EASD guidelines and Standards of Medical Care in Diabetes 2018: HbA1c < 7 %, blood pressure < 140/85 mmHg, LDL < 2,6 mmol/L. Presence of nephropathy was defined as presence of micro-/macroalbuminuria, ESRD or eGFR < 60 mL/min. Albuminuria was assessed using albumin/creatinine in morning spot urine. Blood pressure was evaluated in sitting position twice after 5 rest. Retinopathy was evaluated based on ophthalmologists’ findings.

Results. Only 3,6 % (n=12) of patients achieve all defined treatment targets versus 96,4 % (n=322) who fail to achieve. 10,6 % achieve HbA1c target, 28,8 % – blood pressure target, 48,2 % – LDL target. Patient group that achieves all targets has 25 % (n=3) prevalence of nephropathy, 2 patients – microalbuminuria, 1 – ESRD and 33,3 % (n=4) prevalence of retinopathy, 1 patient – non-proliferative, 3 patients – proliferative or history of laser photocoagulation (LP). Group that fails to achieve targets – 30,4 % (n=98) nephropathy prevalence, 16,1 % as microalbuminuria, 8,1 % as macroalbuminuria, 4,7 % as ESRD, 1,5 % as eGFR < 60 mL/min and 50,9 % (n=162) retinopathy prevalence, 17,9 % as non-proliferative and 33 % as proliferative/LP.

Conclusions. Treatment target achievement in Latvian type 1 diabetes is quite low. Patient group that achieves targets shows better results on microvascular complications – nephropathy and retinopathy. However, study is under significance level it might be valuable to continue study with greater number of participants.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” by the Faculty of Medicine, University of Latvia and Genome Database of Latvian population.

New onset of diabetes mellitus after kidney transplantation: analysis of modifiable and non-modifiable risk factors

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Background. New onset of diabetes mellitus (NODAT) has been recognized as an increasing problem in kidney transplantation (KT), with an impact on patient morbidity and transplant function. NODAT usually occurs early after transplantation, and is diagnosed according to general population guidelines. There is a number of modifiable and non-modifiable risk factors for NODAT development.

Objective. The aim of the study is to analyse the association of the most frequent modifiable and non-modifiable risk factors with development of NODAT.

Materials and methods. A retrospective study involved 216 patients undergoing KT between 2014 and 2017. The patients were divided into two groups: NODAT group and control group (without NODAT). Risk factors influencing the development of NODAT were studied. Shapiro-Wilk, Kolmogorov-Smirnov, Cramer's V, Chi-square, Fisher exact, Mann-Whitney and T-tests were used to determinate risk factors.

Results. A total of 191 patients were analysed (25 were excluded due to death or insufficient information), of which 13 or 6.81 % developed NODAT. Statistical analysis showed that there was a weak correlation ($V = 0.15$) between C-hepatitis infection and the development of NODAT, as the differences were not statistically significant but limited (23.08 % vs 6.78 %, $p = 0.07$).

None of the remaining risk factors affected the possibility to develop NODAT, as the results were similar to both of the groups: glucose intolerance (7.69 % vs 5.65 %, $p = 1.00$), deceased donor (100 % vs 80.23 %, $p = 0.13$), re-transplantation (23.08 % vs 14.69 %, $p = 0.70$), acute CMV infection (15.38 % vs 14.69 %, $p = 1.00$), vitamin D deficiency (76.92 %, vs 64.00 %, $p = 0.55$), acute rejection (15.38 % vs 20.34 %, $p = 1.00$). Although the relative risk for autosomal dominant polycystic kidney disease was 0.14, and 95 % CI 1.38 ± 0.98 , the incidence was 46.15 % vs 17.51 %, $p = 0.08$ which means that statistical significance is limited and by increasing the population, the statistical significance with PTDM is likely to appear.

By analysing use of tacrolimus as a maintenance therapy over 3-year period, there were no statistically plausible differences in both groups: $(5.6 \pm 1.68 \text{ ng/dl vs } 6.35 \pm 1.37 \text{ ng/dl, } p = 0.40)$. There was also no data that higher doses of tacrolimus ($> 7 \text{ ng/dl}$) would affect the formation of NODAT.

Conclusions. According to the results, the prevalence of the studied population was relatively small (6, 81 %). By analysing risk factors, the association to NODAT was found only with regard to C-hepatitis infection, although it was a weak correlation. With the other known risk factors, the association was not proven. By including a higher number of patients, we could expect to obtain a greater statistical credibility.

Neuropeptide Y concentration in type 1 diabetes patients with different cardiovascular disease risk factors

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Background. Diabetes mellitus (DM) is associated with different cardiovascular disease (CVD) risk factors such as arterial hypertension, obesity, dyslipidaemia, microalbuminuria, metabolic syndrome (MS) and hypoglycaemia. Neuropeptide Y (NPY) is a neurotransmitter, which is involved in various homeostatic processes in central and peripheral nervous systems and was reported to be involved in the pathophysiology of CVD in DM.

Objective. To study the association of NPY concentration with different CVD risk factors, as well as its association with frequency of hypoglycaemic events in type 1 DM patients.

Methods. This was a cross-sectional study on data of 288 patients with type 1 DM from the longitudinal “LatDiane” study. Data about DM history and blood chemistry investigation were obtained from “LatDiane” research forms. Frequency of symptomatic hypoglycaemic events was classified based on hypoglycaemia frequency in the last 4 weeks: rare (1–4 events), frequent (≥ 5 events). NPY was measured in serum samples of patients *ELISA* method. The participants were divided in 2 groups, using the NPY mean = 13.23 ng/ml. All the data were analysed with SPSS programme.

Results. The mean NPY concentration in group with microalbuminuria was lower than in a group with macroalbuminuria (microalbuminuria: 14.53 ± 7.57 ng/ml; macroalbuminuria: 19.91 ± 7.14 ng/ml; $p = 0.000$). More than a half of patients with MS had elevated NPY concentration, compared to patients without MS (60 % vs 40 %; $p = 0.018$). Level of NPY positively correlated with metabolic syndrome ($R = 0.146$, $p = 0.013$). The mean NPY concentration was higher in a group with rarely occurring hypoglycaemia than in a group with more frequent hypoglycaemia (frequent hypoglycaemia: 15.46 ± 7.47 ng/ml; rare hypoglycaemia: 14.06 ± 8.08 ng/ml; $p = 0.033$). The group with elevated NPY level had an increased serum total cholesterol (5.06 ± 1.13 mmol/l, $p = 0.034$). In the group with hypertension, more than a half of participants had a higher NPY concentration in plasma (59.7 % vs 40.3 %; $p = 0.004$).

Conclusions. NPY was associated with CVD risk factors in type 1 DM. More frequent hypoglycaemia is associated with a lower NPY serum level that can indicate the presence of autonomic dysfunction in DM patients.

Acknowledgements. The study has been supported by fundamental research grant in biomedicine and pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” by the Faculty of Medicine, University of Latvia and State Genome Database project. We thank Gita Gersone for measurement of NPY concentrations.

Comparison of the prevalence of tick-borne pathogens in field-collected ticks in Latvia in two time periods, 2005–2007 and 2017–2019

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Background. Ticks are globally important arthropod vectors that can transmit the most diverse array of infectious agents to human and animals. They are unique organisms that have both vector and reservoir properties. Ticks are exposed to biotic (host) or abiotic (climate, habitat) factors, whose changes affect the tick population itself, distribution and abundance, with the following influence on tick-borne disease epidemiology.

Objective. To compare the prevalence of tick-borne pathogens, *Borrelia* spp., *Anaplasma phagocytophilum*, *Rickettsia* spp. and *Babesia* spp. in ticks collected in Latvia during two time periods, 2005–2007 and 2017–2019.

Methods. In the present study, the total of 6066 ticks were analysed. These ticks were collected by flagging method in 2005–2007 (1471 ticks) and 2017–2019 (4595 ticks) in Latvia. DNA was extracted from all the samples and the presence of pathogens was analysed by PCR methods and sequencing.

Results. In 2005–2007, in Latvian habitats only two epidemiologically significant tick species, *Ixodes ricinus* and *I. persulcatus*, were found, while in 2017–2019 the third species, *Dermacentor reticulatus*, was also present. The following pathogens were identified: *Borrelia afzelii*, *Bo. bavariensis*, *Bo. burgdorferi*, *Bo. garinii*, *Bo. lusitaniae*, *Bo. valaisiana*, *Bo. miyamotoi*, *A. phagocytophilum*, *Rickettsia helvetica*, *R. monacensis*, *R. raoultii*, *Babesia canis*, *Ba. capreoli*, *Ba. microti* and *Ba. sp. venatorum*. Single-pathogen infection in ticks collected in 2005–2007 was, as follows: *Borrelia* spp. 30.4 %, *A. phagocytophilum* 0.5 %, *Rickettsia* spp. 4.9 % and *Babesia* spp. 0.7 %. Also, 7.3 % of the samples had multiple-pathogen coinfection with 26 different pathogen combination variants. Single-pathogen infection in ticks collected in 2017–2019 was, as follows: *Borrelia* spp. 10.9 %, *A. phagocytophilum* 0.7 %, *Rickettsia* spp. 15.1 % and *Babesia* spp. 1.1 %. Also, 5.3 % of the samples had multiple-pathogen coinfection with 49 different pathogen combination variants.

Conclusions. Between two time periods, several significant changes were observed: (1) emerging of a new tick species (*D. reticulatus*); (2) new pathogens were identified (*R. raoultii* and *Ba. canis*); (3) tick infection rate with *Rickettsia* spp. pathogens increased, but with *Borrelia* spp. – decreased; (4) the total multiple-pathogen coinfection diversity increased.

Acknowledgements. This work was supported by the ERDF project No. 1.1.1.1/16/A/044.

Eosinophilic granulomatosis with polyangiitis (EGPA), a study of 11 patients in Latvia

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Background. Eosinophilic granulomatosis with polyangiitis (EGPA) is an extremely rare autoimmune disease. In 1951, Jacob Churg and Lotte Strauss for the first time described this disease in 13 patients.

Objective. The aim of the current study was to make analysis of cases of this rare disease and partially to determine the situation of the EGPA cases in Latvia.

Methods. Altogether, 11 patients were enrolled in this study and statistical methods were used.

Results. All 11 patients (100 %) were with this disease. The age of these patients (6 of them females, 5 males) was from 26 – 78 years, 64 percent of these patients were aged 30 – 60 years. All patients met at least one of the EGPA diagnostic criteria, 8 patients met more than three EGPA diagnostic criteria. The suggestions are given for further good formulation and clarification of diagnosis of EGPA.

Conclusions. This study included the comparison of the obtained data. EGPA is a rare systemic vasculitis, which also is present in Latvia.

Acknowledgements.

I, Silvija Kaugere, as the author of this study, submitting the abstract, clearly state below that there are no conflicts of interest regarding the submission and publication of the manuscript and its potential implications.

Relationship between biofilm forming potential and types of bacterial species isolated from patients with chronic tonsillitis

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Background. Microorganisms in tonsillar crypts have an opportunity for long-time interactions with immune system. Biofilm production is an important characteristic of bacteria and it can affect treatment results and facilitate chronicization of the tonsillopathy.

Objective. The aim of the current study was to assess relationship between biofilm-forming capacity and types of bacterial species isolated from tonsillar crypts of patients with chronic tonsillitis.

Methods. During prospective controlled study, punch biopsy samples from tonsillar crypts of patients with chronic tonsillitis were taken for microbiological testing. Identification of microorganisms was performed with MALDI-TOF mass spectrometry. Microtitre plate method was used for the in vitro cultivation and quantification of bacterial biofilms. The optical density (OD) of each well was measured using micro-titre plate reader. Cut-off value (OD_c) was defined as three standard deviations above the mean OD of the negative control. The strains were divided, as follows: $OD \leq OD_c$ = no biofilm producer, $OD_c < OD \leq 2 \times OD_c$ = weak biofilm producer, $2 \times OD_c < OD \leq 4 \times OD_c$ = moderate biofilm producer, $4 \times OD_c < OD$ = strong biofilm producer. Fisher's exact test was used to determine associations between the variables.

Results. From tonsillar crypts of 40 patients with chronic tonsillitis, the following 59 pathogenic bacteria were identified: 30 gram-negative (*K. pneumoniae* – 19/30, *E. coli* – 5/30, *N. subflava* – 1/30, *A. ewoffii* – 2/30, *M. morganii* – 1/30, *H. influenzae* – 1/30, *K. oxytoca* – 1/30) and 29 gram-positive (*S. aureus* – 21/30, *S. pyogenes* – 1/30, *S. pneumoniae* – 5/30, *S. anginosus* – 2/30). Using micro-titre plate method, 40.6 % (24/59) of strains were shown to be weak biofilm producers, 44.1 % (26/59) of strains – moderate biofilm producers, 6.8 % (4/59) of strains – strong biofilm producers, and 8.5 % (5/59) of strains did not produce biofilm. There was no significant association between gram-positive or gram-negative bacteria and biofilm production ability ($p = 0.741$). There was no statistically significant association between the identified types of bacterial species and biofilm production ability ($p = 0.087$).

Conclusions. Our study indicated a high rate of biofilm-producing bacteria. No statistically significant association between identified species and biofilm-forming capacity was identified. The biofilm production capacity has to be assessed for each isolated pathogen, regardless of bacterial species.

Acknowledgements. The authors declare the absence of conflict of interest. This study was supported by the research grant from Rīga Stradiņš University.

A retrospective analysis of risk factors for secondary vasospasm leading to delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage

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Background. Approximately 10 % of strokes are caused by aneurysmal subarachnoid haemorrhage (aSAH). Among the patients who survive after ruptured aneurysms, cerebral vasospasm (CV) is a major cause of delayed cerebral ischemia (DCI), causing increased mortality and poor neurological outcome.

Objective. Retrospectively to identify the main risk factors for cerebral vasospasm and delayed cerebral ischemia.

Methods. The total of 121 patients after aSAH who had been hospitalised at Riga Eastern University Hospital, Riga, Latvia in the time period of 1 year from January 2018 were retrospectively analysed. 74 patients were admitted to Intensive Care Unit. According to inclusion criteria, 48 were enrolled in further analysis. The average age of these patients was 59 ± 15 years, 24 were male and 24 – female. We analysed the influence of age, gender, arterial hypertension, smoking, chronic alcohol intake, body mass index, diabetes mellitus, severity of aSAH according Fisher's classification and Glasgow Coma Scale (GCS) to CV and DCI development. Statistical significance $p < 0.05$.

Results. Of 48 patients, CV was detected in 9 (18.7 %) patients by using digital subtraction angiography ($n = 7$) and computer tomography angiography ($n = 2$) in average on 8.11 ± 4.5 day. Overall, DCI developed in 10 (20.8 %) patients, generally, on 7.5 ± 3.9 day, and only 3 of those had confirmed CV. When comparing the patients with and without CV, the first presented more severe status at admission in hospital with a lower Glasgow Coma Scale, i.e., 10.8 ± 3.5 vs 13.4 ± 2.6 ; $p < 0.0001$ and a higher Fisher's scale, i.e. 4 ± 0 vs 3.46 ± 0.82 ; $p = < 0.0001$. Additionally, we found a statistically significantly higher risk of CV in males ($\chi^2 = 4.3$; $p = 0.038$) and smokers ($\chi^2 = 7.28$; $p = 0.007$). Parallely, more risk factors increase the risk for DCI ($p = 0.04$). A statistically significant correlation was found between age and development of DCI ($r = -0.34$; $p = 0.017$), demonstrating that younger patients have an increased risk for DCI.

Conclusions. A greater risk for development of CV was observed in patients with larger scores on Fisher's scale and lower scores on GCS at the admission to hospital, those of male gender and smokers. Younger patients have a higher risk to develop DCI.

Acknowledgements. The author declared the absence of the conflict of interest.

Newly diagnosed amyloidosis in Rheumatology Centre, Latvia

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Background. There is an increased risk to develop AA amyloidosis in patients with autoimmune diseases, like rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis. These patients almost always have a renal involvement. Although frequency of AA amyloidosis development in patients with rheumatic diseases is decreasing due to better treatment options, the referral of undiagnosed amyloidosis patients to rheumatologist may have other causes.

Objective. The aim of the current study was to evaluate the causes and type of amyloidosis in newly diagnosed cases referred to rheumatology centre in 2019.

Methods. Data was collected from medical documents of patients newly diagnosed with amyloidosis (with histological confirmation) collected in 2019 at Rheumatology Department, Unit 9 of Pauls Stradiņš University Hospital.

Results. 5 patients were diagnosed with amyloidosis in 2019. 2 of them had AA amyloidosis due to autoimmune diseases – one with juvenile idiopathic arthritis, and one with rheumatoid arthritis. In both cases, arthritis was long-standing with a duration of more than 10 years. Both patients were treated with biological disease-modifying antirheumatic drugs. Both patients had kidney amyloidosis with significant proteinuria. 2 patients had AA amyloidosis due to hematologic malignancies – one with non-Hodgkin's disease, and one with multiple myeloma. Both had kidney amyloidosis with proteinuria. The main complaint of the patient with non-Hodgkin's disease was orthostatic hypotension, but heart MRI did not show amyloid accumulation. One patient had AL amyloidosis, with the main complaints of tongue enlargement and pain in shoulders, cervical stiffness. The patient was found to have macroglossia, racoon eyes and shoulder pad sign. Biopsy was taken from tongue, and AL amyloidosis was confirmed. In sonography, amyloid accumulation was seen on shoulder tendons and joint space. There was no kidney involvement.

Conclusions. Although the frequency of AA amyloidosis is decreasing due to larger variety of treatment options, there still are patients with a very high disease activity despite available medication, and they develop amyloidosis.

Typical triade of symptoms for AL amyloidosis is rarely seen. Patients presenting with cervical stiffness and pain in shoulders can be referred to rheumatologist with suspicion of seronegative spondylarthritis. Sonography is a valuable tool for diagnosing shoulder pad sign with rarely observed findings of homogenous mass depositions on tendons, bursas, synovium.

Acknowledgements. The author declares the absence of conflict of interest.

Adherence to medication among patients with chronic diseases

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Background. According to the World Health Organization (WHO), adherence to long-term therapy for chronic illnesses in developed countries averages 50 %. Furthermore, about 50 % of prescriptions filled for chronic diseases in developed countries are not taken correctly, and 40 % of patients do not adhere to their treatment regimens. Poor adherence to long-term therapies negatively impacts the effectiveness of treatment and increases health care costs.

Objective. The aim of the current study was to find out the level of adherence to medication among the patients with chronic diseases and the factors influencing it.

Methods. The study included 100 patients with chronic diseases using medication for at least one year. Patients were asked to complete an anonymous questionnaire about their age, education, occupation, number of daily medication doses, duration of medication and hospitalization times during the last year. Morisky Medication Adherence Scale (MMAS-8) was used to assess patients' adherence to medication. Data were processed using MS Excel and IBM SPSS software. The data were analysed using descriptive statistical method.

Results. 100 questionnaires were analysed for this study, which involved 58 females (58%) and 42 males (42%) aged 22 to 89. The study shows that 52 % of the patients had a low adherence to therapy, 36 % of the patients had a medium adherence to therapy, and only 12 % of the patients were highly adherent to therapy. According to the study data, 47 % of the patients did not use all the prescribed medication. The reasons for nonadherence were equally distributed – “expensive” (36 %), “fear of side effects” (30 %) and “doctor does not convince” (34 %). Retirees were statistically less (9.8 %) likely to forget to take medication than the working patients (27.1 %) ($p = 0.038$). The patients with higher education are statistically more likely to continue to use medication (87.5 %) in case of improvement ($p = 0.033$). There was no statistically significant association between gender, age, number of daily doses, duration of medication on adherence rates.

Conclusions. More than a half of the patients with chronic diseases showed an extremely low adherence to medication. The cost of medication, fear of side effects and disbelief in doctors were equally common reasons for not taking the prescribed medication. Age, gender, number of daily doses of medication, duration of medication did not impact adherence rates. Medication adherence had no impact on hospitalization times. To achieve the goals of treatment, it is worthwhile to make sure at each visit that the patient with chronic diseases is taking the medication as prescribed.

Anti-nociceptive actions of adipose-derived mesenchymal stem cells administered locally in different regiment at experimental model of peripheral trauma-induced neuropathy

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Background. Neuropathic pain (NP) is caused by a primary lesion in the nervous system. Its treatment is very difficult. Current available therapeutic drugs in addition to their potential side effects are at times mitigating only the temporal pain properties rather than targeting the several mechanisms underlying the generation and propagation of NP. Cell-based therapies using mesenchymal stem cells provide hopeful results.

Objective. The aim of the current study was to evaluate anti-nociceptive actions of locally administered adipose-derived mesenchymal stem cells (ADMSCs) investigated in experimental model of peripheral neuropathy caused by nerve trauma.

Methods. We used axotomy (complete sciatic nerve transection) model of NP in the Wistar rats (group 1). Allogenic (from other rats of same breed) ADMSCs were transplanted into the projection of nerve trauma via 4 injections according to imaginary clock face (on 3, 6, 9 and 12 o'clock). Such stem cell transplantation was performed in doses of 1 or 2 million cells per kilogram of animal weight and with 2 different regimens: once (on day 7) or twice (on days 7 and 14) after sciatic nerve transection. Other rats were daily receiving pregabalin (13 mg/kg, intragastric) for 8 weeks in a row as a drug of comparison. All the neuropathic rats were monitored starting from day 7 from the surgery until 180 days after it. On days 21, 90 and 180 some animals were sacrificed for histological studies.

Results. Complete sciatic nerve transection lead to decrease in pain thresholds and development of pain-like behaviours, such as mechanical allodynia and thermal hyperalgesia. ADMSCs were able to reduce pain behaviour both administered once or twice into the area of trauma. An anti-nociceptive effect was detectable from day 21 post-surgery (14 days after the first cell transplantation or 7 days after the second one), and was comparable with that of pregabalin. ADMSCS abolished pain most effectively while being transplanted once in a dose of 1 million cells per kilo. Histological data support findings obtained with physiological tests.

Conclusions. This study could provide novel findings in ADMSCs therapeutic potential in regenerative medicine.

Acknowledgments. The authors declare that they have no conflict of interest. The study was funded by state programme "Fundamental and applied sciences for medicine".

RAD51B rs8017304 association with exudative AMD treatment

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Background. The leading cause of irreversible vision loss among elderly people in developed countries is described as age-related macular degeneration (AMD). Although the *intravitreal anti-vascular* endothelial growth factor (VEGF) therapy for patients with exudative AMD has been found, the response to this treatment varies and suggests genetic factor effect on treatment outcome in patients with exudative AMD.

Objective. Our aim was to determine the impact of rs8017304 at RAD51B gene on exudative AMD treatment.

Methods. The study enrolled $n = 57$ patients with exudative AMD who were treated with anti-VEGF intravitreal injections. The DNA extraction was carried out from samples of whole blood using a DNA salting-out method. The genotyping of RAD51B rs8017304 was carried out by the real-time polymerase chain reaction (RT-PCR) method using TaqMan SNP Genotyping Assay (*ThermoFisherScientific*). Central macular thickness (CMT) measurements were performed before Anti-VEGF therapy after 3 months and 6 months during therapy, using optical coherence tomography (OCT). The best-corrected visual acuity (BCVA) was also measured before and during the therapy. According to these data, we divided patients into “responders” and “poor-responders”. Statistical analysis was performed using the SPSS/W20.0 software (Statistical Package for the Social Sciences for Windows, Inc., Chicago, Illinois, USA).

Results. Our study results showed that “poor-responders” were likely to have the risk allele G at RAD51B rs8017304 than “responders”. The analysis also revealed that carriers of at least one risk allele at *RAD51B* rs8017304 (GA+GG vs AA) had thicker macular before treatment using anti-VEGF injections (median (IQR): 353 (57) vs 304 (93.5), $p = 0.004$, respectively). The same tendency was found after 3 and 6 months during the treatment, unfortunately, the differences did not reach statistical significance. No statistically significant associations between RAD51B rs8017304 and BCVA were found.

Conclusions. RAD51B rs8017304 gene polymorphism plays a role in exudative AMD development and may have an association with central macular thickness.

Acknowledgements. None of the authors have any proprietary interests or conflicts of interest related to this submission. This work was funded by a grant No. SEN-11/2015 from the Research Council of Lithuania.

Hereditary angioedema – treatment possibilities and its responsiveness in Latvia

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Background. Hereditary angioedema (HAE) is a rare autosomal dominant disease with recurrent attacks of severe life-threatening swelling and a prevalence of about 1 in 30,000 people worldwide. It is caused mostly by mutations in the *SERPINE1*, plasminogen or in the factor XII genes and results in enhanced activation of the plasma contact system and generation of bradykinin. HAE has 3 types: type 1 with reduced C1-INH protein and C1-INH functional levels, type 2 with normal C1-INH protein levels, but reduced C1-INH functional levels, and type 3 with normal C1-INH Ag and function (there are several subtypes in the new classification).

Objective. To assess treatment possibilities and responsiveness in patients with hereditary angioedema in Latvia.

Methods. Retrospective study was performed. Seven HAE patients were diagnosed in Latvia (according to the WAO/EAACI definition 2017) during the period from 2006 to 2019 and included in the study. We analysed clinical histories, immunological blood tests of these patients, as well as treatments and responsivity to these.

Results. All 7 patients were female. The diagnosis was most commonly made in adults between the ages of 31 and 63 years. All the patients had a delay between the onset of first symptoms and diagnosis of HAE (more than 12 years). 70 % (5/7) of our patients had a positive family history. 6 patients were diagnosed with HAE type I and one patient – with HAE type III. Patients were treated with C1q inhibitors replacement therapy – in 100 % (7/7), by tranexamic acid – in 57 % (4/7), fresh frozen plasma – in 42 % (3/7) and bradykinin antagonist – in 28 % (2/7), androgens – in 57 % (4/7). Only 30 % (2) of the patients had uncontrolled relapses of disease despite the specific treatment.

Conclusions. HAE is often poorly recognized because of its nonspecific signs. Appropriate therapy is delayed, putting patients at an increased risk of morbidity and mortality. Early diagnosis and treatment can improve the quality of life of patients. Replacement treatment provides a significant reduction in hereditary angioedema attacks.

Acknowledgements. The authors declare the absence of conflict of interest.

Factors affecting achievement of HbA1c goals in patients with type 1 diabetes in Latvia

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Background. Glycated haemoglobin is essential in diabetic metabolic compensation associated with the risk of late diabetic complications. However, a lot of type 1 diabetes patients do not reach the HbA1c level recommended by the international guidelines.

Objective. The aim of the study was to analyse the aspects of clinical care related to the achievement of the HbA1c target in type 1 patients in Latvia using the data of the LatDiane study.

Methods. The study was based on the analysis of 336 questionnaires completed by type 1 diabetes patients about the quality of diabetes care and the patient's knowledge related to diabetes self-control. The association of these factors with the achievement of therapeutic goals of HbA1c was consequently assessed. The analysis was carried out regarding questions about patients understanding of HbA1c goals and satisfaction with it, number of visits to medical staff during the last year. Some questions focused on nutritional issues, comprehension of hypoglycaemia symptoms and fear of it. All the participants were divided into 3 groups based on HbA1c index (1 – less than 7 %, 2 – 7–8 %, 3 – more than 8 %). The study included adults of all ages and both genders with type 1 diabetes of at least 1-year duration.

Results. 81 % of the study participants had an average HbA1c above the target. The mean was HbA1c 8.9 ± 1.9 %. 157 participants (50.5 %) do not know or cannot correctly name the last HbA1c. Only a half of the participants in all groups (48.5 %, 51.5 %, 48.5 %) visit the doctor at least 3–4 times a year. The frequency of visits does not statistically correlate with achievement of the goal HbA1c ($p = 0.82$). 35.3 % and 29.4 % of the participants in groups with HbA1c ≥ 7 had discussed nutritional issues more than 3 years ago. Each group also included participants with whom nutrition issues were never discussed (17.9 %, 8.8 %, 5.4 %). Participants have a poor ability to recognize the symptoms of hypoglycaemia, although the frequency of hypoglycaemia did not differ in groups with different HbA1c ($p = 0.059$). The higher HbA1c participant had, the more often he or she had a fear of hypoglycaemia ($p = 0.005$) and had a bite to eat ($p = 0.058$).

Conclusions. The aspects of medical care of patients with type 1 diabetes in Latvia are associated with non-achieving targets of glycaemic control.

Acknowledgements. The study was supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases diagnostics and personalized treatment”, the Faculty of Medicine, University of Latvia. The authors thank State Genome database project and Sanita Kalva-Vaivode for assistance in recruitment of patients.

Cortex changes after electrical stimulation in experimental rodent model of partial seizures

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Background. The problem is of outstanding importance since to date the issues of epileptogenesis remain unrevealed. Most of the previous studies described changes in the limbic structures of animal after epileptic seizures or status.

Objective. The aim of the current study was to evaluate the cortex changes after electrical stimulation in experimental rodent model of partial seizures.

Methods. 36 adult Wistar rats (average weight 289 ± 1.2 g) were used in experiments. Stimulating red electrode was implanted into frontal cortex of the right hemisphere. Reference black electrode was fixed to rats' skull aponeurosis on the left side. Electrical stimulation during 4 weeks was carried out with the following parameters: pulse rate – 80 Hz, pulse width – 800 msec, pulse amplitude – from 1.0 to 2.5 V. The stimulus duration was 20 seconds. The experimental rats were stimulated once a day for 5 stimuli. Developmental seizures were only partial (grading by Racine's scale). On day 1, 7, 14 and 21 some animals were sacrificed for histological studies.

Results. Histologically, after electrode implantation in the right hemisphere, foci of frontal cortex destruction were revealed with minimal haemorrhage. On day 7 after the operation, formed "channels" were revealed in rats' brain at the place of intracerebral electrode locations. Astrocytes and microglia cell proliferation was also found. Focal neurons' loss, nuclei hyperchromia of neurons, signs of neuronophagy, gliosis were noted on day 14 in the right frontal cortex. On day 21, impaired cortex layering, several gliosis, neurons' loss were detected in the right frontal cortex. Small foci of neuronal damage and gliosis were also found in the left frontal cortex.

Conclusions. Brain damage in the place of electrode implantation was previously described. In our study, we revealed "mirror" changes in right and left frontal cortexes of rats after chronic electrical stimulation in an experimental model of partial seizures.

Acknowledgements. The authors declare the absence of conflict of interest. The study was funded by state programme "Fundamental and applied sciences for medicine".

Comparison of virulence factors and antibiotic resistance of *Staphylococcus epidermidis* between strains isolated from patients and healthy volunteers

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Background. Methicillin-resistant *Staphylococcus epidermidis* often causes nosocomial infections worldwide, most commonly affecting intravenous catheters and prosthetics with subsequent complications. The main virulence factor of *S. epidermidis* is the ability to produce a biofilm that creates antibiotic resistance and protects the bacteria against the immune response. Around 90 % of clinical *S. epidermidis* are multidrug-resistant (including methicillin). As a result, treatment of patients becomes challenging.

Objective. To compare antibacterial resistance, beta-hemolysis and biofilm production between *S. epidermidis* isolates of medical students and clinical isolates.

Methods. Samples were taken from the buccal and nape skin of healthy volunteers and from the intravenous catheters of clinical patients. Antibacterial sensitivity was determined by using the BBL Disk Diffusion test. The microtiter plate method was used to determine bacterial biofilm formation. Differences in beta-hemolysis, biofilm production and antibacterial resistance, were investigated using Chi-square test. PCR was used to detect *mecA* gene. Statistical significance was considered at $p < 0.05$.

Results. Out of all *S. epidermidis* isolates ($n = 24$) of the student group, 62.5 % were working in ICU.

Out of all the participants, 21 (43.8 %) isolates were beta-hemolysis-negative, 18 (37.5 %) were erythromycin sensitive, 16 (33.3 %) were ceftiofur sensitive, and 29 (60.4 %) produced biofilm. Out of all ($n = 24$) clinical isolates, 18 (75.0 %) were beta-hemolysis positive, 3 (12 %) were erythromycin sensitive, 1 (4.2 %) was ceftiofur sensitive, and 13 (54 %) produced biofilm. Out of all student isolates, 9 (38 %) formed beta-hemolysis, 9 (38 %) were sensitive to ceftiofur and erythromycin, and 6 (25 %) were able to produce biofilm.

There was a statistically significant difference between the student group and patient group in beta-hemolysin production ($\chi^2 = 6.85$; $p < 0.01$), erythromycin resistance ($\chi^2 = 12.80$; $p < 0.01$), ceftiofur resistance ($\chi^2 = 18.38$; $p < 0.01$), and biofilm formation ($\chi^2 = 4.27$; $p < 0.04$). Also, there was a statistically significant difference ($\chi^2 = 4.80$; $p < 0.04$) between bacterial biofilm-producing isolates of students working in ICU.

Conclusions:

1. There is a statistically significant association indicating that *S. epidermidis* resistance to ceftiofur and erythromycin is characteristic to students working in ICU ($p = 0.03$).
2. Haemolytic activity was demonstrated in 9 (38 %) of bacteria identified in healthy subjects and in material of 18 (75 %) patients
3. The presence of biofilm was more characteristic in 13 (54%) of the analysed material obtained from clinical isolates than for the control group 6 (25%).
4. Ceftiofur resistance was shown in 23 (96 %) isolates obtained from patients' clinical material and in 9 (38 %) isolates obtained from healthy volunteers.
5. The *mecA* gene is positive for all isolates in the clinical group.

Acknowledgements. To the authors thank all the employees of the RAKUS TPSC Laboratory of Mycobacteriology for supporting them during this research.

Assessment of the frequency of headache and quality of life of patients with migraine

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Background. Migraine is one of the leading causes of disability worldwide. Migraine attacks vary in frequency and severity among patients.

Objective. To evaluate the frequency of headache in study group and establish possible associations with other chronic diseases, and to assess the quality of life, comparing study group and control group.

Methods. A prospective study was conducted in Health Centre 4, at a headache specialist's office. 100 patients with migraine (study group, SG) and 100 people without migraine (control group, CG) completed questionnaires, and kept diaries for the duration of one month, where they daily noted their headaches (SG) or pain of other localization (CG), and indicated the quality of life (QoL). Statistical analysis was performed for 82 (SG) and 80 (CG) participants using Excel, IBM SPSS.

Results. An independent T-test showed that there was no statistically significant difference ($p = 0.03$) in age between SG ($M = 42.6$; $SD = 13.3$) and CG ($M = 44.8$; $SD = 13.4$).

53.6 % ($n = 44$) of the patients (SG) had a headache more often than 4 times a month (frequent migraine attacks), 36 % ($n = 16$) of them had taken preventive therapy, most often – tricyclic antidepressants ($n = 8$; 50 %). The people with frequent migraine attacks more often suffer from high intensity headaches ($p = 0.043$) and feeling of brain fog ($p = 0.025$) than the people with less frequent migraine attacks. Mental diseases ($p = 0.003$) and skin diseases ($p = 0.03$) prevail in SG. During a month, SG more often marked their quality of life as very poor compared to CG ($M = 1.29$, $M = 0.73$; $p = 0.04$).

Conclusions. Many patients had frequent migraine attacks and a higher pain intensity and a feeling of brain fog, despite the prophylactic therapy. Migraine attacks had a negative impact on the quality of life.

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Lyme disease presenting as Bannwarth syndrome

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Introduction. Lyme disease is caused by spirochete *Borrelia burgdorferi* and transmitted by a tick bite. It is a multisystem and multistage infection. One of the disease's manifestations can be lymphocytic meningoradiculoneuritis, also known as Bannwarth syndrome.

Objective. In this study, we aimed to evaluate the prevalence of Bannwarth syndrome in our clinic, as well as determine the clinical features and laboratory data of the respective patients.

Materials and methods. We used a retrospective study design. Information was obtained from medical records of patients who were diagnosed with Lyme disease at Department of Neurology in Riga East Clinical University Hospital from 2014 to 2019. Data was analysed using IBM SPSS Statistics 22.

Results. In total, 77 patients with confirmed Lyme disease were enrolled in the study. Among these patients, 15.6 % ($n = 12/77$) were diagnosed with Bannwarth syndrome at an early stage of the disease. These patients were included for further analysis, between which 41.7 % ($n = 5/12$) were women and 58.3 % ($n = 7/12$) were men. The average age was 51 (SD 13.5) years. The patients were admitted to the hospital with the following complaints: unilateral facial weakness (16.7 %, $n = 2$), backache with radiculopathy (50 %, $n = 6$), bilateral facial weakness and backache with or without radiculopathy (33.3 %, $n = 4$). Almost a half of the patients (41.7 %, $n = 5$) had had a known tick bite in history, and a quarter of patients (25.0 %, $n = 3$) previously had noted a skin lesion. Lumbar puncture was performed and further cerebrospinal fluid analysis in all cases revealed lymphocytic pleocytosis; the average data showed 194.5 (SD 153.9) cells per microlitre and elevated protein concentration – 1.76 (SD 0.69) grams per litre. Borrelial immunoglobulin G in cerebrospinal fluid was analysed in 58.3 % ($n = 7/12$) of the patients. In all these cases, intrathecally produced borrelial antibodies were confirmed with high antibody indices ($AI > 1.5$). The median length of hospital stay was 15.5 (SD 5.9) days. All the patients received intravenous antibacterial therapy with Ceftriaxone for 14, 21 and even for 28 days with clinically significant improvement (less pain and improvement in facial muscle strength).

Conclusions. The clinical presentation of Lyme disease may vary widely. A small part of patients can recall tick bite or a rash (*erythema migrans*). It is crucial to recognise symptoms of meningoradiculoneuritis as a possible Lyme disease's neurological manifestation because it might mimic other diseases. Additional investigations and tests are needed to make a correct diagnosis. Specific and effective treatment for Bannwarth syndrome is available.

Acknowledgements. The authors declare the absence of conflict of interest.

Regenerative actions of adipose-derived mesenchymal stem cells administered locally in different regiment within experimental model of peripheral neuropathy

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Background. Mesenchymal stem cells are attractive candidates for application in regenerative medicine with hopeful results of cell-based therapies.

Objective. The aim of current study was to evaluate regenerative actions of locally administered adipose-derived mesenchymal stem cells (ADMSCs) in different regiment investigated in experimental model of peripheral neuropathy (NP) caused by nerve trauma.

Methods. We used axotomy (complete sciatic nerve transection) model of NP in the Wistar rats ($n = 20$). Allogenic ADMSCs were transplanted into the projection of nerve trauma via 4 injections according to imaginary clock face (on 3, 6, 9 and 12 o'clock). Such stem cell transplantation was performed in doses of 1 or 2 million cells per kilogram of rodent weight and with 2 different regimens: once (on day 7) or twice (on days 7 and 14) after sciatic nerve transection. On days 21 and 90 after surgery some animals were sacrificed for histological studies.

Results. Histologically, on days 21 and 90 after surgery. in group ($n = 5$) with one-time ADMSCs injection (1 mln cells/kg) the following conditions were noted: a minimal fibrosis of surface and intramuscular fascia, an absence of diffuse inflammation, a minimal muscle atrophy and neovascularization of neurovascular bundles with minimal fibrosis of perineurium. In group ($n = 5$) with two-time ADMSCs injection (1 mln cells/kg) and group ($n = 5$) with one-time ADMSCs injection (2 mln cells/kg) on days 21 and 90 revealed a diffuse inflammatory process and mild fibrosis of superficial, intermuscular fascia and neurovascular bundles perineurium. Foci of atrophy and hypertrophy of muscle cells and intermuscular lipomatosis were noted. In group ($n = 5$) with twice administered ADMSCs injection (2 mln cells/kg) on day 21 several muscle necrosis foci with strong diffuse inflammation were detected. On day 90, the observations included a severe fibrosis of superficial fascia with mild diffuse inflammation, an atrophy of muscle, an intermuscular fibrosis and a lipomatosis. We did not find regeneration of nerve trunk after surgical transection in all groups.

Conclusions. This study revealed that ADMSCs regenerative potential depends on dose and frequency of injections.

Acknowledgments. The authors declare that they have no conflict of interest. The study was funding by state programme "Fundamental and applied sciences for medicine".

Level of vitamin D in acne patients and its correlation with severity index

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Background. Vitamin D deficiency has been extensively studied worldwide, therefore, in recent years, dermatologists have become increasingly interested in understanding the role of vitamin D in skin diseases. There is an increasing number of publications related to vitamin D deficiency in diseases such as atopic dermatitis, psoriasis and acne. The results of worldwide epidemiological studies on the relationship between vitamin D and severity of acne are contradictory.

Objective. The purpose of our research was to identify serum vitamin D level in patients with acne and to evaluate its correlation with acne severity index.

Materials and methods. This retrospective study included 100 patients with acne and 98 healthy controls. The database of private dermatology clinic in Riga was used. The severity of acne was assessed according to the global acne grading system (GAGS) score. Laboratory data with serum 25 (OH)D was collected. Vitamin D deficiency is considered to be < 10 ng/ml, inadequate 10–30 ng/ml, sufficient 30–100 ng/ml and toxic > 100 ng/ml. SPSS version 25.0 was used for analysis.

Results. The mean age of the patient group was 23.22 ± 6.78 (range 14–46) years and 38.27 ± 11.50 (range 15–70) years of controls. The average 25 (OH)D level was 24.12 ± 8.55 ng/ml (range 4.00–50.00) in patients and 32.29 ± 10.91 ng/ml (range 3.00–60.91) in healthy controls, with statistically significant difference ($PT = 2.30 \times 10^{-8}$). Serum 25 (OH)D was significantly lower in patients and more respondents have vitamin D deficiency than in controls ($P = 2.10 \times 10^{-5}$). In the patient group, 14 % had mild, 14 % very severe, 33 % moderate and 39 % severe acne. The correlation between the 25 (OH)D level and the acne vulgaris is inverted and the average close or correlation coefficient is -0.50 ($P_r = 1.48 \times 10^{-7}$). It can be concluded that as the level of vitamin D decreases, the level of acne increases statistically.

Conclusions. Vitamin D is significantly lower in acne patients. Vitamin D is inversely proportional to the severity of acne. Although our hypothesis is supported by contradictory data in the literature, it is necessary to investigate this relationship more extensively, with a larger number of patients, excluding factors that may influence the outcomes.

Acknowledgements. This study has not received funding, the authors declare the absence of conflict of interest.

MENTAL HEALTH

Suicide attempts by using psychotropic medications: relationship with psychiatry consultations and diagnosed mental disorders

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Background. Suicide is one of the most relevant issues in Lithuania, and the numbers of deaths by suicide are among the highest in the world and in Europe. In 2018, 24.4 in 100 000 inhabitants committed suicide in Lithuania. Meanwhile, the number of suicide attempts remains unclear – according to different sources, it may be 30 times greater than the number of committed suicides. Various scientific studies show that psychotropic drug poisoning is the most frequent method of suicide in suicide attempts.

Objective. To determine the relationship between suicide attempts using psychotropic medications and psychiatry consultations, as well as diagnosed mental disorders.

Methods. This clinical study was performed in the Psychiatry Department of the Hospital of Lithuanian University of Health Sciences. The study included all cases of inpatients following a suicide attempt during the period from June 2015 to May 2018 ($n = 632$). The data provided in this presentation is a part of the overall project. Individuals needed to be ≥ 18 years of age, and hospitalized in the Psychiatry Department due to a suicide attempt. Diagnosis and suicidal behaviour were assessed according to ICD-10-AM criteria and using self-administered questionnaire (including the nature of suicide attempt, history of psychiatry consultation). The statistical analysis conducted using SPSS 20.0 (License No. 9582494), p -value ≤ 5 . The study protocol was approved by the Regional Medical Research Ethics Committee (N: BE-2-29/2015). The study was supported by the Research Council of Lithuania (N: MIP-047/2015).

Results. We estimate that 52.37 % of all the subjects ($n = 331/632$) attempted to commit suicide by using medications (ICD-10: X60,61,63,64), 82.8 % of them selected psychotropic drugs ($n = 274/331$; X61; OR=4.81, $p < 0.0001$), and 37.23 % ($n = 102/274$) of them had stress-related, 26.64 % ($n = 73/274$) – affective, 17.15 % ($n = 47/274$) – psychotic, 10.95 % ($n = 30/274$) – psychoactive substance-related, 8.03 % ($n = 22/274$) – other mental disorders. Women attempted to commit suicide by using psychotropic medications more often than men (71.0 % vs 29.0 %; $p < 0.0001$). We estimated that 75.5 % ($n = 207/274$) of all the subjects, who attempted to suicide using psychotropic medication, had been receiving psychiatric consultations: 91.49 % with psychotic, 90.41 % – affective, 77.27 % – other mental disorders, 65.69 % – with stress-related issues, 46.67 % – with use of psychoactive substances.

Conclusions. The possibility of selecting psychotropic medications in case of suicide attempt by using medications is 4.81 times higher. Women attempted to commit suicide by using psychotropic medications more frequently than men. 75.5 % of all the people attempting suicide by using psychotropic medications, had been receiving psychiatric consultations, and 37.23 % of them had stress-related, 26.64 % – affective, 17.15 % – psychotic disorders, while 10.95 % had been using psychoactive substances.

Acknowledgements. The authors declare the absence of a conflict of interests.

Attitudes of health care professionals toward looking after their own backs

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Background. Low back pain (LBP) is the leading cause of disability worldwide (GBD, 2017). Some studies suggest that sedentary lifestyle increases the incidence of LBP. Currently there are very few studies about health care professionals' (HCP) attitudes toward their own back and the possible impact of these attitudes on their choice of exercises and treatment of patients with LBP.

Objective. To investigate beliefs of HCP regarding looking after their own backs.

Methods. During the cross-sectional study, HCP were interviewed during their educational events. The questionnaire inquired into demographic data, pain characteristics, and contained the Back-Pain Attitudes Questionnaire developed by Darlow et al. in 2014. Questions regarding beliefs about looking after one's back were further explored.

Results. The survey brought sixty-five responses. The average age of the participants was 65 (SD = 11.37) years, the respondents were predominantly female (81.5 %; $n = 53$), while 18.5 % ($n = 12$) were male. At the time of survey, 20 % ($n = 13$) of the participants experienced LBP, 60 % ($n = 39$) had had LBP episodes during their lifetime, and 20 % ($n = 13$) had not experienced LBP episodes themselves. All the participants agreed that good posture is important to protect one's back. The majority of the participants (96.9 %; $n = 63$) agreed that it was important to have strong muscles to support one's back, and only 3.1 % ($n = 2$) were unsure about it. Most participants (93.8 %; $n = 61$) agreed that if one overuses his or her back, it will wear out, while 3.1 % ($n = 2$) were unsure and 3.1 % ($n = 2$) did not agree with this statement; 81.6 % ($n = 53$) agreed that if an activity or movement causes back pain, one should avoid it in the future, 9.2 % ($n = 6$) were unsure about it and 9.2 % ($n = 6$) did not agree. The greatest part (87.7 %; $n = 57$) thought that one could injure one's back if one is not careful, 4.6 % ($n = 3$) were unsure about it and 7.7 % ($n = 5$) did not agree. More than a half of the participants (73.8 %, $n = 48$) agreed that one can injure one's back and only become aware of the injury at a later time, 7.7 % ($n = 5$) were unsure about it and 18.5 % ($n = 12$) did not agree.

Conclusions. The vast majority of HCP agreed that strong muscles and good posture is important for the back. This indicates that HCP acknowledge that exercise and physical activity is important for the back. However, a part of HCP also believed that their back was vulnerable and could be overused or damaged by the movement. These beliefs could affect the type and amount of prescribed physical activity, as well as the treatment recommendations given to the patients with LBP.

Anxiety and depressive disorders in patients with diabetes

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Background. Diabetes mellitus (DM) is one of the most pressing problems of modern medicine. The number of DM cases is increasing rapidly. Prolonged illness and chronic complications of diabetes cause early disruption in the function of various organs, leading to early impairments and premature disability, which undoubtedly affect the emotional state of patients.

Objective. To evaluate the psycho emotional state (anxiety and depressive states) of the patients with the 1st and 2nd-type diabetes.

Methods. Hospital Anxiety and Depression (HAD) scale was used to measure depressive state and anxiety. The study included 397 (257 female and 140 male) diabetic patients: 75 had type 1 and 322 – type 2 DM, the mean age of the patients – 53.5 years.

Results. The survey showed that 25.0 percent of men and 23.6 percent of women, i.e., a quarter of patients with type 1 diabetes were reported to be in a depressive state. The depressive state is more often determined in older subjects, i.e., 66.7 percent; those with secondary education (34.4 percent), 50.0 percent of pensioners, 28.6 percent of single people. The anxiety was higher in women (52.7 percent), in the age groups of women of 40–49 and 60–69 years of age (66.7 percent); in those with incomplete secondary education (80.0 percent), unemployed (100 percent), disabled people (70.0 percent), single people (60.7 percent). The depressive state has been diagnosed in 37.6 percent of the patients with type 2 diabetes, while anxiety accounted for 55.0 percent. The depressive and anxiety states were more frequent in women and depended on the level of education, social and marital ($p < 0.05$) status, the depressive state also depended on the patient's age ($p = 0.0001$). The depressive and anxiety states of the patients with type 1 diabetes often had a longer duration and complications of diabetes, was found to be present in the overweight patients, the ones with AH and the ones underestimating their health. The frequency of depressive states was dependent on the duration of the disease and complications. The depressive and anxiety states depended on the duration of the disease, BMI, complications and health assessment of the patients with type 2 diabetes.

Conclusions. Emotional (anxiety and depression) disorders are a common problem in DM patients. It is more common in women, depending on age, social status, medical condition, duration of illness and complications.

Acknowledgments. The authors confirm the absence of conflict of interests.

Assessing fulfilment of service recipients' and providers' environmental needs in inpatient mental health care institutions

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Background. With growing number of people suffering from mental disorders, the need for inpatient mental health care services is also increasing. It is therefore important to ensure that inpatient mental health care institutions have an appropriate infrastructure and that the environment is adapted to the needs of both service recipients and providers.

Objective. To assess the fulfilment of environmental needs of service recipients and providers in inpatient mental health care institutions.

Methods. A prospective study was performed during the period from 04.11.2019 to 01.01.2020 in The Hospital of Lithuanian University of Health Sciences *Kauno Klinikos*, Department of Psychiatry. The participants included service recipients (psychiatry patients) and service providers (psychiatrists, residents in psychiatry, mental health nurses, nursing assistants and other staff). Data collection was based on an original questionnaire containing sociodemographic information and questions about seven main fields of the environment of an inpatient mental health care institution: movement/orientation, comfort/security, nature/open spaces, ability to communicate/private space availability, external and internal factors, aesthetics/accessibility. The questionnaire answers were rated using the Likert scale choosing from 1 (“strongly disagree”) to 5 (“strongly agree”) to the given questions. General rating of the fulfilment of environmental needs was evaluated using the scale from 0 to 10. MS Excel was used for data collection and IBM SPSS for data analysis.

Results. The study population consisted of 112 participants: 53.4 % service providers ($n = 62$; mean age 40.89 ± 15.23 years) and 46.6 % service recipients ($n = 50$; mean age 39.24 ± 14.47 years). General rating of the fulfilment of environmental needs in the service recipient group was $7.9 \pm 2.15 / 10.0$ points ($p = 0.06$). Service recipients rated the comfort/security, orientation, nature and open spaces, ability to communicate and cosiness of inpatient mental health care institutions significantly higher than service providers ($p = 0.0001$).

Conclusions. 1. The general rating of the fulfilment of environmental needs in service recipients was creditable. 2. In most of the main fields of the environment of an inpatient mental health care institution, service recipients rated the conditions higher than service providers. The only three subfields that were rated higher by service providers, comparing with service recipients, were the patient's ability to choose a single-bed ward, the opportunity to watch TV and the opportunity to communicate with animals. 3. When designing infrastructure, it is important to pay attention to the design of service providers' work environment.

Acknowledgements. The authors confirm the absence of conflict of interest. The study has not received any funding.

Substance use disorders among men in Latvian prisons

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Background. The relationship between substance use and criminal behaviour is closely related. Substance use tends to amplify participation in crime and is more common among repeat offenders (Fazel et al., 2015). Little is known about the prevalence of specific substance use disorders among the first-time prisoners.

Objective. To examine prevalence of alcohol and drug use disorders among the first-time prisoners and repeat offenders.

Methods. The retrospective study was performed in Riga Centre of Psychiatry and Addiction Disorders. The data on prisoners were obtained from the study "Risk and needs evaluation in Latvian prisons", which was implemented with participation of the authors, and analysed. Examination using ICD-10 criteria measures of substance dependence and abuse, AUDIT (Alcohol Use Disorders Identification Test) and DAST (Drug Abuse Screening Test) were used for substance use disorder evaluation.

Results. 242 prisoners were included in the study, both the first-time prisoners ($n = 120$) and repeat offenders ($n = 122$). The mean age of the prisoners was 35.03 years ($SD = 10.27$). Most of the prisoners – 65.7 % ($n = 159$) reported that they had used alcohol within the past 12 months before incarceration with no statistical difference among groups. 26 % ($n = 63$) were found to have alcohol dependence, and 19 % ($n = 46$) had yielded to alcohol abuse. Alcohol use despite of problems were found in 47.8 % ($n = 107$), with a higher prevalence among repeat offenders ($p = 0.011$). 65.3 % of prisoners ($n = 158$) had used drugs once a month or less, while 27.3 % ($n = 66$) – almost every day. Within both groups, 23.6 % ($n = 57$) had polysubstance dependence and 5.4 % ($n = 4$) were found to have polysubstance abuse. Stimulant use despite of problems was found in 61.4 % ($n = 43$), with a higher prevalence among the repeat offenders ($p = 0.016$).

Conclusions. Most of the prisoners had used at least one substance within the past 12 months. Substance use disorders were found in both prisoner groups. Alcohol and stimulant use despite of problems was more common among the repeat offenders with statistical significance. No significant differences between groups were found among rest of ICD-10 criteria. Knowledge about the substance use disorders in lifetime and before imprisonment could benefit in rising awareness for rehabilitation needs in prisons and can be used to explore behaviours which lead to incarceration.

Associations between psychosocial work environment factors and self-rated health among physicians

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Background. According to research, psychosocial risk factors are important occupational factors impacting job satisfaction, job quality and quality of life. There are numerous psychosocial risk factors, such as strain, job schedule, high job demands, inadequate relationship between efforts and reward, in physicians' work environment.

Objective. The aim of this study was to evaluate the psychosocial work environment factors and their association with life quality of the physicians.

Methods. The study design was cross-sectional. The population ($n = 340$) included all the physicians working in 5 hospitals of Kaunas district and was conducted during March–February 2018. The participants filled in the anonymous questionnaire; the sample size was 230 physicians (response rate 79.4 %). Copenhagen Burnout Inventory was used for measuring burnout assessment, Job Content Questionnaire – for assessing psychosocial risk factors, self-rated health was estimated by SF-36 questionnaire, Copenhagen Psychosocial Questionnaire provided the stress rating scale. Statistical data analysis was performed using the SPSS (version 20.0) software package. Hypotheses about dependence of symptoms were checked using chi square criteria (χ^2) and z tests were performed. Associations were tested by using a multifactor linear regression analysis.

Results. Psychosocial risk factors among physicians: very high work-specific skills at work – 41.3 %, low influence on decision making – 5.6 %, high demands at work – 19.1 %, lack of freedom in decision making – 54.8 %, low supervisor support 11.3 %. Good self-rated health was estimated by 73.5 % physicians, excellent subjective health was found in 24.4 %, while only 2.1 % of the respondents complained about poor health. 32 % of physicians suffered from occupational burnout. It was found that burnout at work was significantly related to self-related health. Multifactor linear regression analysis showed that: psychological stress (behavioural ($\beta -0.242$, $p = 0.000$), somatic ($\beta -0.254$, $p = 0.000$), cognitive stress ($\beta -0.135$, $p = 0.027$), occupational burnout ($\beta -0.190$, $p = 0.003$) and the need for work-specific skills ($\beta 0.138$, $p = 0.008$) had statistically significant values in predicting physicians' self-rated health.

Conclusions. It was found that psychological stress (behavioural, somatic, cognitive stress), occupational burnout and the need for work-specific skills are statistically significantly predicting physicians' subjective health.

Acknowledgements. The authors declare the absence of conflict of interest.

Exposure to total 36-h sleep deprivation reduces physiological and psychological thermal strain to whole-body uncompensable passive heat stress in young adult men

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Background. Exposure to total sleep deprivation (TSD) has been reported to strongly alter control of body thermoregulation. In real-life situations, subjects such as soldiers and athletes can be subjected to prolonged wakefulness and acute heat stress repeatedly for several consecutive days on a regular basis. However, no previous study has explored the effects of partial sleep deprivation (PSD) and TSD on the thermoregulatory effector responses to daily passively induced severe whole-body hyperthermia.

Objective. The aim of the current study was to investigate heat-unacclimated young adult men to determine whether 36 h of TSD would suppress the responses of the autonomic system to whole-body uncompensable passive heat stress in a traditional Finnish sauna heat.

Methods. Sixteen healthy male subjects were recruited for the study. The study comprised a control (normal 8 h sleep per night) experiment and experiments with 4 h PSD and 36 h TSD. After completing resting measurements, the participants were asked to enter a sauna room. The sauna bathing protocol comprised four sets with the first set for 15 min. and three sets for 10 min., with a rest interval of 15 min. between each set, where the participants remained in a semirecumbent posture at $T_a = 25^\circ\text{C}$. Every 5 min. in the sauna and during the rest interval between and after the sauna we assessed and recorded body temperature, heart rate, blood pressure and subjective ratings.

Results. Sauna bathing that induced whole-body hyperthermia had a residual effect on reducing peripheral vascular resistance (PVR) in the 8 h and 4 h of sleep per night conditions according to blood pressure measurements. By contrast, 36 h of total wakefulness led to an increase in PVR. These observed sleep deprivation-dependent differences in PVR modifications were not accompanied by changes in the blood plasma epinephrine and norepinephrine concentrations. However, during sauna bathing, an increase in PVR following 36 h of TSD was accompanied by significant decreases in body temperature, heart rate and physiological strain together with a diminished sweating capacity, enhanced vagus-mediated autonomic control of heart rate variability, and improved thermal perception by the subjects.

Conclusions. Our results suggest the impaired ability of the body to accumulate heat externally under uncompensable passive heat condition following 36 h of TSD because of the TSD-attenuated autonomic system response to acute heat stress.

Acknowledgements. The authors acknowledge the contribution of the subjects who took part in the study and Danute Juciene for collecting the blood samples.

Prophylaxis of posttraumatic delirium in orthopaedic surgery ward, using haloperidol. Prospective, comparative study

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Background. Posttraumatic delirium is a common complication in elderly population. It can cause patients to increase their fracture dislocations, or interfere with wound healing, or rehabilitation. Delirium can provoke decompensation of other diseases, and increase mortality.

Objective. The aim of this study is to investigate prophylactic use of haloperidol in selected population and to find out other factors that increase the incidence.

Methods. The prospective study was conducted during the period of 2019–2020 in Vidzeme Hospital. The patients older than 70 years of age, who corresponded to the criteria of the study, were randomised in two groups. Group H ($n = 22$) was given 0.35 mg of haloperidol 3 times a day, from day 1 until the 4th postoperative day. Group K ($n = 33$) was the control group. Patients were observed and their confusion status was recorded. Confusion was measured using NEECHAM scoring tool. Incidence and severity of confusion was compared between the groups. Other factors such as age, gender, pathology, blood loss, type of operation were accounted for.

Results. Study sample consists of 55 patients (46 – female, 9 – male) with the mean age of 82.1. Inclusion criteria – > 70 years of age, proximal femur fractures or hip arthroplasty, not suffering from mental illnesses. Incidence of delirium in Group K – 24.24 % and Group H – 18.18 %. Other significant factors were pathology and operation type, age, gender, blood transfusion. When looking at operation type (cervicocapital endoprosthesis – CKEP, intramedullary nailing – PFN, total hip arthroplasty – EP) in Group H incidence of delirium was CKEP – 27.3 %; PFN – 16.7 %; EP – 0 %, while in Group K, CKEP – 35.7 %; PFN – 25 %; EP – 12.5 %. Comparing the overall incidence between genders provided the following results: men – 44.4 %, women – 17.4 %. The mean age for men with delirium – 82.2, for women – 86. In case of blood transfusion, delirium incidence was 14.3 %, whereas in cases with no blood transfusion the incidence was 22.9 %. In Group H, the mean lowest NEECHAM score was 15.7, while in Group K – 21.3, measured in scale 0–30 where < 19 is severe delirium and 27–30 means absence of delirium.

Conclusions. The incidence of delirium in studied population is very high. Prophylactic use of haloperidol in small and safe dosages can lower the incidence of delirium. There should be early recognition and treatment of acute posthemorrhagic anemia with blood transfusion. Age and gender also have an influence in development of delirium. A higher incidence in EP and CKEP groups could suggest bone cement influence on patient's mental state. Differences in severity of delirium between groups have to be studied additionally to investigate whether the problem is dosage-dependant or concerns drug safety.

Acknowledgements. The authors would like to acknowledge the institutional contribution of the University of Latvia.

CARDIOVASCULAR MEDICINE

Factors influencing outcome in patients with acute pulmonary embolism: the experience at one clinical centre in 2018

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Background. Acute pulmonary embolism (PE) is the third most common cause of death in hospitalized patients. The prognosis of patients with PE depends on various factors including patients' general condition and presence of co-morbidities.

Objective. To evaluate the presence of co-morbidities, which could affect the outcome in patients admitted with acute PE.

Methods. A retrospective study was implemented to evaluate co-morbidities found in medical records among patients admitted to Riga East University Hospital with an acute pulmonary embolism in January – December 2018. A total of 108 patients were included in the study, out of these, 69 (63.9 %) female participants, the mean age – 74 years (11.9 %). The patients were divided into two groups according to hospital outcome – survivors and non-survivors. Data were presented as mean (SD) and number (%), and processed by IBM SPSS Statistics 22. The *p*-value below 0.05 was considered statistically significant.

Results. Nineteen (17 %) of 108 study patients died. In non-survivor patients' group, a statistically significant association was established between hospital outcome and presence of chronic heart failure of functional class III-IV (NYHA) (*p* < 0.05), chronic kidney disease in the stage above II (*p* < 0.05) and old myocardial infarction (*p* < 0.05). No statistically significant association was found between the outcome and the radiologist's assessment of PE by computed tomography (massive vs non massive PE).

Conclusions. The presence of chronic heart failure of functional class III-IV (NYHA), chronic kidney disease in stage above II and old myocardial infarction were important comorbidities, impacting hospital outcome in acute PE patients' study group.

Acknowledgements. The authors have no conflict of interest to disclose. No funding was received for the study.

Tendencies and regularity of medication usage in patients with atrial fibrillation in Pauls Stradiņš Clinical University Hospital

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Background. Medications for atrial fibrillation patients have an important role in preventing arrhythmia side-effects, such as thromboembolic events and progression of heart failure. However, a worldwide problem is the choice of patients to discontinue or interrupt the usage of medication.

Objective. The aim of the study is to compare and analyse the regularity and habits of medication usage in patients with atrial fibrillation.

Methods. This is prospective study included 141 patients in 2019 with confirmed atrial fibrillation hospitalized in Pauls Stradiņš Clinical University Hospital. The study was based on voluntary participation, and all the participants provided a written informed consent. Data were collected from interviews and medical records. We inspected pharmacological groups: antiarrhythmics, beta blockers, sodium channel blockers, anticoagulants, antiplatelets, angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers, aldosterone antagonists, diuretics and statins.

Results. This study included 49.6 % (n = 70) males, 50.4 % (n = 71) females. They were divided according to types of atrial fibrillation: paroxysmal 48.9 % (n = 69), persistent 36.9 % (n = 52) and permanent 14.2 % (n = 20). 12 of them could not name the medications they were taking. Irregular usage of medications was reported in 25 % of persistent, 24.6 % of paroxysmal, 20 % of permanent type of atrial fibrillation. The most-used medicines were anticoagulants 68.1 % (n = 96), beta blockers 61.7 % (n = 87) and statins 46.1 % (n = 65), other of pharmacological groups were used far less frequently. The count of electrocardioversions was 44 % (n = 66), electrocardiostimulator was found in 19.9 % (n = 28) cases. Most of them had NYHA II-III class of heart failure (75.9 %, n = 107, p = 0.006), and C class (76.6 %, n = 108) of ACC/AHA classification of heart failure. A part of the patients (13.5 %) have already had a stroke.

Conclusions. Overall, 24.1 % (n = 34) of patients do not use drugs regularly. There is no statistically significant difference in usage of medications according to the type of atrial fibrillation. This study shows a low compliance of pharmacological treatment.

Acknowledgements. There is no conflict of interest regarding the publication of this article.

Prevalence of chronic kidney disease among patients with confirmed pulmonary artery thromboembolism

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Background. Pulmonary artery thromboembolism is the third most common cardiovascular disease. Chronic kidney disease can affect procoagulant and anticoagulant systems that can be associated with increased risk of thromboembolic events. It is believed that pulmonary artery thromboembolism can affect kidneys and their functions through alterations in hemodynamics.

Objective. The aim of this research is to find an association between pulmonary artery thromboembolism and chronic kidney disease (CKD).

Methods. This is a retrospective study of pulmonary artery thromboembolism patients in year 2018, at Pauls Stradiņš Clinical University Hospital, Latvian Centre of Cardiology and Intensive Care unit. This study analysed 177 patients (70 males, 107 females).

Results. 64.4 % ($n = 114$) had massive PATE and 81.9 % ($n = 145$) bilateral involvement. 4.5 % ($n = 8$) of all the patients had an acute kidney failure, but 18.1 % ($n = 32$) had chronic kidney disease. Of those, the biggest part 14.7 % ($n = 26$) had the 3rd to 4th stage of chronic kidney disease, $p = 0.011$. Other types of kidney-related complaints did not have any statistical significance. In this research, the 3rd stage of chronic kidney disease was not divided into stages 3a and 3b due to the lack of information in patients' medical records. An end stage renal disease was found only in 1.1 % ($n = 2$) of all patients, the first stage of chronic kidney disease was detected in 0.6 %.

Conclusions. Although thromboembolic events should rise with the stage of chronic kidney disease, this study highlights that there is a greater association with CKD stage 3 that could be considered a potential risk factor for pulmonary artery thromboembolism.

Acknowledgements. There is no conflict of interest regarding the publication of this article.

Association of Arg389Gly polymorphism of ADRβ1 gene and T393C of GNAS1 gene with risk of development of acute coronary syndrome in patients with arterial hypertension

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Background. According to the observations in recent years, arterial hypertension in patients is often accompanied by obesity, diabetes, and hypercholesterolemia. The risk of development of hypertension and the severity of its clinical manifestations, including the occurrence of complications in the form of acute coronary syndrome (ACS), depends on many circumstances, such as genetic factors, lifestyle, and environmental factors.

Objective. The aim of the study is to determine the role of Arg389Gly polymorphisms of the ADRβ1 gene and T393C polymorphisms of the GNAS1 gene in the risk of developing ACS.

Methods. The study encompassed 550 patients undergoing treatment for hypertension in the Sumy region (Ukraine) within a period of 7 years. In the process of observing the included subjects, 211 of them were diagnosed with ACS with/without the elevation of the ST segment. Other 334 patients with hypertension were in the control group; five patients were excluded from the study early, because they could not be reached. The T393C polymorphisms of the GNAS1 gene (rs7121) and Arg389Gly of the ADRβ1 gene (rs1801253) were determined by the polymerase chain reaction (PCR) method. To determine the risk of ACS, we calculated the odds ratio (OR) with a 95 % confidence interval (95 % CI), using polynomial logistic regression.

Results. In the analysis of the dominant model with adjustments for age, sex, and excess body weight, the risk of developing ACS was 1.49-fold higher in Arg/Arg genotype carriers than in Arg/Gly and Gly/Gly genotype carriers (OR = 1.49 (1.04–2.14); $p = 0.028$). Upon a further calculation, this tendency persisted in the recessive model (OR = 2.06 (1.28–3.31); $p = 0.001$) and homozygous model (OR = 2.53 (1.52–4.20); $p < 0.001$). Subsequent analysis showed the following associations: increased risk of ACS development in carriers of the C/C genotype compared with the carriers of T/T and T/C genotypes based on the recessive model (OR = 3.39 (2.00–5.74); $p < 0.001$); increased risk in carriers of the C/C genotype compared with the carriers of the T/T genotype based on the homozygous model (OR = 3.42 (1.89–6.17); $p < 0.001$).

Conclusions. In our study, we discovered the relationship of the Arg389Gly polymorphism of the ADRβ1 gene and the T393C polymorphism of the GNAS1 gene with the risk of ACS development in the Ukrainian population. Carriers of the Arg389 allele of the polymorphism of the ADRβ1 gene and the C393 allele of the polymorphism of the GNAS1 gene showed a higher risk of ACS development relative to the opposite alleles in these gene polymorphisms.

Characteristics of the use of antihypertensive medication prescribed to older people

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Background. Arterial hypertension is one of the most common cardiovascular diseases amongst older patients. It is a chronic disease that is treated with medications. People of older age face the problem of medication use.

Objective. The aim of the study is to identify the drug therapy problems, which occur to patients using medications to treat arterial hypertension.

Methods. Participants of the research – patients over the age of 65 who were diagnosed with arterial hypertension. The sample of the research consisted of 100 respondents. The analysis of the collected data was conducted using Microsoft Office Excel 2010 and SPSS 22.0 statistical data analysis software. The permission of the Centre for Bioethics was granted to conduct the survey. The results of the research were published only in a summary form.

Results. According to the collected data (sample size – 100 respondents), the participants were divided, as follows: 73 % female and 27 % male; 73 % of participants living in villages and 27 % living in towns; only 15 % of the respondents had a higher education (university diploma); only 23 % (71.5 % of women and 28.5 % of men) of the respondents follow the doctor's instructions on how to use antihypertensive medications; 46 % (91.5 % of women and 8.5 % of men) partly follow the instructions, while 31 % (45 % of women and 55 % of men) do not follow the instructions at all. The problems that occur while using medications were evaluated. The results revealed that 42 % of the respondents tended to forget using antihypertensive medications, 38 % did not remember when and which medications should be used, 33% took many different medications simultaneously, 26 % were fearful of the medications because of their addictive qualities, 19% avoided using prescribed medication because it was hard to swallow.

Conclusions. The obtained results showed that only a minority of respondents follow the doctor's instructions. Blood pressure control depends on patients' sex, age and education ($p < 0.05$). According to the collected data, following the doctor's instructions on medication use and recalling which drugs should be used are significant problems.

Evaluation of psycho-emotional state and sleep quality in patients with ischemic heart disease

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Background. Cardiovascular diseases are the leading cause of mortality, morbidity and disability worldwide, and they often affect young people. According to the studies, psychosocial risk factors such as depression, anxiety, and lack of rest play a significant role in the development of the disease.

Objective. To assess the psycho-emotional state and sleep quality in patients suffering from ischemic heart disease.

Methods. Sleep quality was subjectively assessed by the use of Pittsburgh Sleep Quality Questionnaire (PSQI); Hospital anxiety and depression scale (HAD scale) was employed to assess the psycho-emotional state of the respondents. 150 patients suffering from coronary heart disease were examined through random selection. Data analysis was conducted using the statistical SPSS Windows (v. 17.0) and Excel programs.

Results. Depressive state was determined in 27.3 %, while anxiety – in 42.0 % of the respondents. Depressive state ($p = 0.004$) and anxiety ($p = 0.003$) were more frequently observed among the female patients. Frequency of depressive states was determined by the presence of other conditions ($p = 0.047$), health assessment ($p < 0.001$). Respondents who had poor valuation of their health showed more frequent cases of depressive state and anxiety. It was discovered that emotional state among female patients was more often impacted by fears regarding upcoming surgery, heart-beat and family problems than in men ($p < 0.005$). Bad sleep quality was diagnosed in 78 % of the respondents. It was established during the research that a good quality of sleep was observed more commonly among male rather than female patients ($p = 0.005$). Based on the research results, health assessment was determined by sleep quality – the respondents who assessed their health as good, also more frequently had good sleep quality ($p = 0.001$). The respondents who had a low assessment of their health more often showed bad sleep quality ($p = 0.001$). The results demonstrated a dependence of sleep quality in patients suffering from ischemic heart disease on emotional state: increasing frequency of depressive ($p = 0.001$) and anxious ($p = 0.001$) states were followed by worsening of the sleep quality ($p = 0.001$).

Conclusions. Depressive state and anxiety more often affected female, elderly, disabled, retired and widowed patients. It depended on self-assessment and other conditions, and did not depend on duration and frequency of exacerbations of illness. Bad sleep quality was diagnosed in 78 % of the respondents. Sleep quality was impacted by emotional state and gender, and it was not affected by the respondents' age, BMI, educational background, social, marital state, nor duration of illness.

Prognosis of the course of coronary artery disease after revascularization

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Background. Over the past 10 years, the incidence rate of cardiovascular diseases in the Republic of Kazakhstan has grown 1.7 times. Out of 13 million adults, 350 thousand people have been diagnosed with chronic heart failure.

Objective. The purpose of this study is to evaluate the prognosis and characteristics of the clinical course of coronary heart disease after revascularization.

Methods. 28 people were examined. Of these, the larger proportion was male. 60 % of the examined were over 60 years old. 82 % of those surveyed had a sedentary lifestyle and high BMI. 57 % of the patients continued smoking after PCI or bypass surgery.

Results. Overall, 60 % of the patients were overweight. Concomitant arterial hypertension was detected in all the patients, concomitant diabetes was detected in 36 % of the examined patients. In 68 % of patients, PCI was previously performed, 22 % had had a bypass surgery, and 10 % had had a bypass surgery after PCI. Most often, a lesion of the LAD and PKA was revealed. In patients with bypass surgery, LV ejection fraction was lower than in the group with PCI. 92 % of the patients had had a heart attack without ST segment elevation. A retrospective analysis of delivery time and type of surgical intervention made possible to determine ischemia time, in 44 % of patients the myocardial ischemia time was 2 hours, in 36 % of patients ischemia time was 5 hours, in 20 % of the patients – ischemia time was more than 72 hours. At 54 %, survival was more than 5 years after surgical treatment. In 2 patients, the probability of restenosis was 16 %.

Conclusions. Over the past 10 years, the incidence of cardio-vascular diseases has increased in the Republic of Kazakhstan. In the study group smoking men prevailed. This group was characterised by concomitant hypertension and diabetes, a sedentary lifestyle, excess weight and obesity. PCI was performed for younger patients; bypass surgery was performed in the older group with damage of multiple arteries and concomitant diabetes mellitus with numerous complications. In this group, ejection fraction was below normal. In most patients, ischemia time was 2 hours. Most of the patients achieved 5 year survival after re-vascularization. A prognostic model of re-stenosis suggested that 2 patients had a higher risk of re-stenosis than others.

Exercise stress test in patient with persistent atrial fibrillation receiving treatment with Class Ic antiarrhythmic drugs

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Background. Propafenone and flecainide are Class Ic antiarrhythmic medications used for rhythm control in the management of persistent atrial fibrillation. Currently, the data regarding the use of bicycle exercise testing in patients with normal ejection fractions testing to screen for proarrhythmia is limited.

Objective. The purpose of our study is to determine the efficacy and utility of bicycle exercise stress test in evaluating outcomes of initiation and chronic therapy with Class Ic agents.

Methods. This is a one-centre prospective study. At Latvian Centre of Cardiology between October 2019 and December 2019 patients with persistent atrial fibrillation were selected, who were initiated on a Class Ic agent during current hospitalization. The patients were asked to perform a stress test before and after receiving therapy. In order to analyse the safety blood tests and electrocardiogram were controlled.

Results. The study population included 25 patients (40 % male, mean age 61; mean ejection fraction, 55 %) started on aethacizinium (n = 14; 56 %) and propafenone (n = 11; 44 %). All the patients underwent evaluation with a transthoracic echocardiogram before the stress test. The mean ejection fraction was 55.0 ± 5.2 %. No proarrhythmic events were observed during the study. There were no important changes in electrocardiogram and performed blood tests. The primary reason for not being discharged on Ic agent was due to detection of ischemia (n = 1; 4 %) with bicycle exercise testing. The bicycle ergometer test time increased from a mean of 5.52 minutes to 6.04 minutes ($p = 0.005$).

Conclusions. With screening, initiation of Class Ic agent is associated with very low rate of proarrhythmia. Bicycle exercise testing has an escalating value and should be completed in all patients after initiated Class Ic antiarrhythmic drugs. The bicycle ergometer test is an effective, safe and widely available additional method in patients with atrial fibrillation that can be used to evaluate physical activity level changes while treated with negative inotropic agents. Further studies in larger populations are needed.

Acknowledgements. The authors confirm the absence of conflict of interests. No funding or other acknowledgements.

Do platelet and inflammatory readings differ between chronic heart failure patients' groups according to NYHA functional classes?

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Background. It is stated in the literature that thrombosis in the chronic heart failure (CHF) patients may be caused by interaction of inflammation and platelets. The incidence of venous thromboembolism in heart failure patients is found to be the highest in the patients classified as NYHA IV.

Objective. We aimed to test whether platelet and inflammatory readings differ between chronic heart failure (CHF) patient's groups according to NYHA.

Methods. We have compared the C-reactive protein (CRP), fibrinogen concentration, platelet count (PLT), mean platelet volume (MPV), and NT-proBNP in CHF patients' groups according to New York Heart Association (NYHA). 203 patients with CHF with reduced ejection fraction (systolic heart failure classes I–IV according to NYHA) were included in the study.

Results. There were no statistically significant differences in fibrinogen concentration, CRP and PLT between the groups according to NYHA. The MPV was statistically significant higher in NYHA IV group than in NYHA III, NYHA II and NYHA I groups (10.86 ± 1.14 and 9.78 ± 1.21 and 9.65 ± 1.22 and 9.21 ± 0.59 respectively, $p = 0.006$). There was a weak correlation between CRP and PLT ($r = 0.293$, $p = 0.010$), and between MPV and fibrinogen concentration ($r = 0.205$, $p = 0.012$). There was a moderate correlation between MPV and NYHA ($r = 0.361$, $p < 0.001$) and between fibrinogen concentration and CRP ($r = 0.381$, $p < 0.001$). MPV rising in the patients' groups and correlation between MPV and NYHA class, and plasma fibrinogen concentration, correlation between PLT and CRP, correlation between CRP and NT-proBNP concentration confirm, that low inflammation can take place in the MPV rising.

Conclusions. There were no statistically significant differences in fibrinogen concentration, CRP and PLT between the groups according to NYHA. The MPV was statistically significantly highest in NYHA IV group.

Acknowledgements. This work was funded by the Lithuanian University of Health Sciences. The authors declare no conflict of interest. The authors alone are responsible for the content and writing of the paper.

The effect of oxidant on platelet aggregation and dityrosine concentration in chronic heart failure patients and healthy controls

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Background. According to the statement in the literature, one of the reasons for thrombosis in chronic heart failure (CHF) patients might be reactive forms of oxygen activating platelets.

Objective. The aim of this study was to evaluate the effect of oxidant hypochlorous acid (HOCl) on platelet aggregation and dityrosine concentration in CHF patients and healthy controls.

Methods. CHF patients (n = 67) and healthy (n = 31) were investigated, performing heart echoscopy, six minute walking test, complete blood count, platelet aggregation, dityrosine concentration. Platelet aggregation and dityrosine concentration were measured in plasma samples after 10 min. incubation at 37 °C temperature with different HOCl concentrations (0.15, 0.0778, and 0.0389 mmol/L).

Results. No reliable differences in platelet aggregation induced with ADP in samples with saline added were obtained between the CHF and control groups. Dityrosine concentration was higher in CHF patients' samples with saline (1.54 ± 0.48 in CHF and 1.27 ± 0.53 in control, $p = 0.032$). The spontaneous platelet aggregation with oxidant added was higher in CHF patients (6.49 ± 3.85 in CHF, 4.94 ± 3.17 in control, $p = 0.004$). With the increase of oxidant concentration, dityrosine concentration increased in samples from CHF patients and healthy controls in samples with highest and lowest oxidant concentration (in CHF 1.56 ± 0.49 , in control 1.34 ± 0.40 and in CHF 1.73 ± 0.54 , in control 1.82 ± 0.48 respectively, $p = 0.05$). With the increase of oxidant concentration, platelet aggregation increased in both groups with the exception of the average HOCl concentration ($p = 0.05$). Platelet aggregation was the highest in samples with the highest oxidant concentration in both healthy controls (81.61 ± 13.26 , $p = 0.0006$) and in CHF patients (69.10 ± 21.06 , $p = 0.036$). Platelet aggregation was higher in NYHA III group in comparison to NYHA II group (61.75 ± 22.44 and 56.13 ± 12.57 respectively, $p = 0.0014$). The highest concentration of dityrosine was obtained in NYHA IV group samples (with saline 1.71 ± 0.46 , with the highest oxidant added 2.11 ± 0.43 , with the middle oxidant added 1.63 ± 0.52 , with lowest oxidant added 1.09 ± 0.65 , $p = 0.05$). Platelet aggregation, induced with ADP, correlated with LV EF ($r = 0.42$, $p = 0.007$). Dityrosine concentration correlated with NYHA functional class ($r = 0.27$, $p = 0.05$).

Conclusions. The increase in platelet aggregation in CHF and healthy controls shows the oxidant effect on platelets. The increase in dityrosine concentration in higher NYHA functional classes shows the bigger oxidative stress in patients with worse condition.

Acknowledgements. This work was funded by the Lithuanian University of Health Sciences. The authors declare no conflict of interest. The authors alone are responsible for the content and writing of the paper.

The impact of telomere shortening on determining a higher risk for cardiovascular diseases

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Background. Throughout the years, cardiovascular diseases have been associated with the highest mortality and morbidity. For this reason, the ability to identify a higher risk of an illness remains the key to managing cardiovascular diseases. Despite observation of risk factors, it is useful to apply other prognostic values. According to other scientists, because of influence on biological ageing, telomere length can be a useful biomarker to suspect cardiovascular diseases (CVD).

Objective. The aim of the current study was to determine the impact of telomere shortening on the development of CVD.

Methods. A prospective observational study evaluating manifestation of cardiovascular disorders on 17 women was performed. All participants had similar demographic, professional, familial and medical aspects. Only women were enrolled due to the differences in cardiovascular risk compared between genders, furthermore, all of them were younger than 65 years old, with the aim to avoid a naturally increased cardiovascular risk.

The blood samples were taken in *InMedica Clinic*, Vilnius, Lithuania, then sent to Life Length in Spain, where telomere length was measured. The level of cholesterol concentration was assessed as well, and all the participants filled the questionnaires.

The data was analysed by the IBM SPSS statistics 25. The value $p < 0.05$ was considered as statistically significant.

Results. The average chronological age of participants was 41.2 years; $s = 10.4$, biological age – 43.9 years; $s = 9.9$. The mean value of BMI – 22 kg/m²; $s = 3.03$, 6 participants were smokers, 14 occasionally (not exceeding the recommendations) used alcohol, 7 (41 %) had a positive family history for CVD. 8 participants (47 %) visited a cardiologist, 7 (41 %) suffered from an increased concentration of cholesterol. A statistically significant negative correlation was determined between the telomere length and differences between chronological and biological age ($p < 0.05$, $r = -0.7$). Nevertheless, there was no statistically significant shortening of telomere depending on cholesterol level, risk factors, family anamnesis or visiting a cardiologist ($p > 0.05$).

Conclusions. Telomere shortening is related to faster biological ageing, although we did not discovered any relation between telomere shortening and development of CVD or non-modifiable cardiovascular risk factors. This result may be due to the low sample size of this study. For this reason, we are planning to repeat this research with a greater number of subjects.

Acknowledgements. Nothing to disclose: ID, PS, DS, MML – no conflict of interest.

SURGERY, ANAESTHESIOLOGY & INTENSIVE CARE

Clinical update on bariatric surgery in Latvia

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Background. Bariatric surgery as a method of morbid obesity treatment is slowly gaining popularity in Latvia, but there is lack of data and publications about it. There are two major surgery types applied for patients – gastric bypass (or Roux-en-Y gastric bypass) and sleeve gastrectomy.

Objective. The aim of the study is to clarify the data characterising bariatric patients' demographics and comorbidities in Latvia.

Methods. This was a quantitative cohort prospective study carried out in three clinics in Latvia. Participation of all patients was random and voluntary. The data of patient histories and information from follow-up visits after 3 months was used in this study.

Results. During consecutive 9 months of 2019, we collected data from 46 patients (34 women, 12 men, average age – 43 years). In 50 % (16 women and 7 men) of all the patients BMI was higher than 40 kg/m². Almost 1/5 (19.6 %) of all the patients were superobese with BMI over 50 kg/m².

More than 2/3 (71.7 %) of all the implemented surgeries were gastric bypass ($n = 33$; 23 women), and only 28.3 % ($n = 13$; 11 women) had sleeve gastrectomy. The median BMI prior to gastric bypass surgery was 44.7 kg/m², but before sleeve gastrectomy – 41.8 kg/m². 87 % of the patients had gastrointestinal problems, 33 % had endocrine complaints, 50 % – lung problems, 50 % – cardiovascular problems, and 37 % had musculoskeletal problems.

Patients lost 41 % of their excess weight during 3-month post-surgery period. There was no statistical difference of weight loss regarding comorbidities. However, patients lost more weight (-51 %), if they had no respiratory disease, and lost less (-39 %), if they had musculoskeletal problems.

Conclusions. Bariatric surgery patients in Latvia mostly were middle-aged women with multiple comorbidities. Gastric bypass surgery was more popular than sleeve gastrectomy and was performed mostly in patients with higher BMI. The impact of comorbidities on weight loss is still unclear.

Acknowledgements. The authors declare the absence of conflict of interest.

Optimal osteosynthesis of II–V metacarpal extra articular distal meta-epiphyseal fractures

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Background. Metacarpal fractures are the most common hand fractures in the population – they make up almost a half of all hand fractures, in most cases affecting the right hand and young people of working age. The performance of osteosynthesis of metacarpal bone fractures is one of the factors that determine the functional results of the operative hand, therefore it is important to evaluate and choose the optimal method of surgery, which ensures the best postoperative results in the treatment of patients.

Objective. To find a justification for choosing intramedullary osteosynthesis or conventional method for treating distant metacarpal bone fractures.

Methods. The study included and evaluated 48 patients who underwent II–V metacarpals' distal meta-epiphysal fracture OS with wires. Information was gathered on trauma mechanism, anatomical localization of the fracture, duration from trauma to surgery, operation method and the existence of complications, as well as the functional indicators of the patients' operated hands were evaluated. The resulting data were processed in the *IBM Statistics 22* program.

Results. 44 men and 4 women participated in the study. Their average age was 33.96 years; SD = 11.35. In 36 patients, the operation method was conventional OS, while in 12 patients intramedullary OS. In the intramedullary OS group, complications were observed in 3/12 cases, in the conventional OS group – in 4/36 cases. qDASH survey data did not show a statistically significant difference between the two patient groups. The average grip strength of the left hand was 24.00 kg; SD = 3.38 kg, while the mean grip strength of contralateral arms was 27.00 kg; SD = 3.85 kg. The average grip strength on the right hand was 24.80 kg; SD = 6.40 kg, but the mean force of the contralateral arms was 22.18 kg; SD = 7.37 kg. There was no statistically significant difference between the grip strength measurements. There was also no statistically significant difference between active flexion and extinction measurements. Subjective complaints during the visit noted 3/12 intramedullary OS patients and 9/36 conventional OS patients.

Conclusions. There were no statistically significant differences in the results of both methods with the methods chosen for the study, but it was observed that in the conventional OS group, metal structures tend to move, with no similar complications observed in the second group of patients, therefore intramedullary OS is considered as an optional method.

Acknowledgements. The authors declare the absence of the conflict of interest in this study.

A prospective comparison of frequency of postoperative neuropathies after different types of treatment methods for varicose veins

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Background. Varicose veins are a frequently encountered medical condition, and the extraction is associated with some complications. *N. saphenous* injury is the most common complication after surgical treatment of varicose veins. It has been associated with a risk factor of *v. saphena magna* (VSM) stripping, but sometimes it can occur during ablation. Injury happens because of the anatomical relationship between *n. saphenous* and VSM. New treatment methods have been developed within the last years. The risk of nerve injury is cited as a reason to avoid stripping and use minimal invasive techniques.

Objective. The aim of our study is to share our experience of frequency of postoperative neuropathies after different types of surgical treatment of varicose veins.

Methods. A retrospective study of patients with chronic venous disease who had undergone primary extirpation or ablation of varicose veins. Patients were divided into 4 groups depending on the treatment method – phlebectomy, endovenous laser ablation (EVLA) with 1470 nm or 1940 nm wavelength laser, or the newest method with *n-butyl cyanoacrylate* adhesive. Neurography of *n. saphenous*, *n. suralis*, *n. peroneus superficialis* and *n. tibialis* were done before the surgery and one month after the surgery. The study continues since November 2018. The data was analysed using IBM SPSS 22.0.

Results. Altogether 64 patients were included in the study. The mean age was 49.03 (SD 14.125, range 21–80). 16 patients underwent phlebectomy, 15 had EVLA 1470 nm laser, 17–EVLA 1940 nm laser, and 16 patients had a treatment with cyanoacrylate glue. In one patient, nerve transmission abnormalities were detected before surgery and he was excluded from the study. In 20 patients, a statistically significant ($p < 0.05$) *n. saphenous* or *n. suralis* lesion was identified one month after surgery. Out of those who underwent phlebectomy, injury of nerve was caused in 62.5% of patients, 40 % of patients who underwent EVLA 1470 nm and 23.5 % – EVLA 1940 nm had nerve injury, however, none of the patients who underwent the procedure with cyanoacrylate adhesive had neuropathy.

Conclusions. Neuropathy can be caused not only by phlebectomy, but also during EVLA. However, the frequency of damage does not only depend on the treatment method, but the wavelength of diode laser might also be the determining factor. Neurography findings may suggest that treatment with cyanoacrylate glue closure system gives the best results. Injury to nerve during this procedure seems unlikely to happen. The risk of nerve injury should be considered as a reason to choose, if possible, the minimal invasive treatment of varicose veins.

Different microsurgical approaches in cervical disc disease

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Background. Outcomes of cervical spine surgery are most favourable in radicular pain, spinal instability, progressive myelopathy, or upper extremity weakness. The anterior cervical discectomy and fusion (ACDF) continues to be the gold standard for the treatment of radicular pain triggered by cervical disc herniation, however, other surgical approaches have been developed. In contrast to anterior procedures, which usually do require fusion across the disc space, posterior cervical microdiscectomy (PMCD) does not.

Objective. The purpose of this study was to determine the optimal surgical approaches depending on clinical and radiological findings.

Methods. In total of 34 preoperative and postoperative patients, magnetic resonance imaging (MRI) and plain x-ray data were obtained, and were operated by one spinal surgeon by using microsurgical technique in one medical centre. 26 (76.5 %) patients with 'hard' disc herniation (1–3 levels) on MRI and bilateral radicular pain or progressive myelopathy were operated via ACDF by using a titan implant cage technique. 8 (23.5 %) patients with 'soft' disc herniation (one level) on MRI and monoradicular pain were operated via PMCD approach. All the patients were followed-up within 3 years after surgery. No complications and lethal outcomes had occurred. Pain assessment was performed by using visual analogue pain scale, which was applied in order to compare the outcomes of both groups.

Results. Comparable clinical improvements were observed in both groups, associated with rapid relief of arm/neck pain; with addition of physical therapy, improved resolution of muscle weakness in certain muscles and increased sensory function. Compared to PMCD approach, when it was necessary to implement cervical collar immobilization for 2–3 months, ACDF approach required only 2–3 weeks of immobilization.

Conclusions. Anterior cervical discectomy (ACDF) and posterior cervical microdiscectomy (PCMD) may improve cervical radicular symptoms. PCMD is a method of choice in one cervical unilateral disc herniation with monoradicular pain.

Acknowledgements. The authors declare the absence of the conflict of interest regarding the publication of this article.

Early results of endoscopic microdiscectomy via interlaminar approach

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Background. Conventional open posterior interlaminar microdiscectomy (MDE) is the gold standard method for treatment of lumbar disc herniation, however, it can traumatize the spinal structures (muscles, ligaments, bones), and leaves symptomatic epidural scarring in more than 10 % of the cases.

Objective. Compare the early clinical results of percutaneous endoscopic and conventional microdiscectomy.

Methods. In total, 28 patients with L5–S1 disc herniation underwent surgery by one surgeon, using microsurgical technique, in one medical centre, from 2017 to 2019. Conventional MDE in disc herniation of L5–S1 was performed on 16 patients. 12 patients with disc herniation of L5–S1 underwent endoscopic interlaminar lumbar microdiscectomy (EMDE). Visual analogy scale (VAS) scores for back pain and leg pain were recorded preoperatively, on the first day after surgery and 1–3 months postoperatively. The results were compared to evaluate the feasibility, safety, and efficacy of this technique.

Results. VAS scores for back pain and leg pain revealed statistically significant improvement when they were compared with preoperative values. The mean hospital stay was statistically shorter in the endoscopic group (1.5 days), and less postoperative pain was observed. Complications included one case of dural tear with rootlet injury and three cases of recurrence of disc herniation within 1 month, which subsequently required open MDE. There were no neurological or infectious complications. No lethal complications were observed.

Conclusions. Disc herniation at the L5–S1 level can be adequately treated endoscopically. In comparison to conventional approach, percutaneous endoscopic discectomy is less invasive. However, the endoscopic technique requires previous surgical experience and proper patient selection, which might improve clinical outcomes.

Acknowledgements. The authors declare the absence of conflict of interest regarding the publication of this article.

New treatment of postburn sluggish wounds

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Background. Treatment of burn wounds is one of the most pressing issues in combustiology and has a long history. Burn injuries result in development of cicatricial deformities, motor dysfunction and a high level of disability of the patients. Therefore, medical and socio-economic importance remain relevant in solving this problem.

Objective. The aim of the study is to explore the features of the course of the wound process with the external use of liquorice root oil extract.

Methods. The study is based on data from examination and treatment of 29 patients of both sexes aged 18 to 65 years with flaccid healing burns. The area of burn wounds ranged from 1 to 9 % of the body surface. The main study group consisted of 15 patients (6 women, 9 men) aged 18 to 65 years (the mean age – 40.5 years). The comparison group consisted of 14 persons with burn wounds (1 woman, 13 men), aged 22 to 63 years (the mean age – 38.5 years).

The treatment of burn wounds in patients of the control group was carried out on days 3–21 from the moment of injury (on average 10.71), using gauze dressings with ointment on a water-soluble basis.

Results. In patients of the main group, a complete wound cleansing took place on days 5–11, granulation tissue formation occurred on days 6–12, and wound epithelization was completed on days 8–15. Wounds were cleaned in the control group on days 5–12, granulation was formed on days 6–13, epithelization occurred on days 9–17.

It was found that in cases when an oil extract was used, the wounds healed 3–5 days sooner, compared with those in the control group, and the regeneration process accelerated by 1–2 days compared with the control group.

The clinical study confirmed effectiveness of liquorice root oil extract in healing of burn wounds. In the treatment of post-burn sluggish wounds, the stimulating effect on the regeneration processes was observed.

Conclusions. Thus, our new method for local treatment of burn wounds with liquorice root oil extract has been shown to be effective in treating patients with flaccid healing burns of various localization at all stages of the wound healing process, which allows us to recommend it in the clinical use at burn and trauma departments.

Acknowledgements. The authors would like to extend special regards to the staff of Traumatology Department of Aktobe Emergency Hospital for their assistance.

Differential approach in injection sclerotherapy techniques for treatment of chronic venous disease CEAP 1-2

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Background. Treatment of the early stages of chronic venous disease (CVD) is aimed at restoring of the aesthetic comfort, in particular – at the elimination of the existing cosmetic defects and prevention of new ones. The current treatment involves the use of minimally invasive techniques such as liquid sclerotherapy and foam sclerotherapy. Each of them has its advantages and disadvantages, creating a need for a differential approach, which would maximally prevent the complications of each of the methods and obtain stable clinical and aesthetic results.

Objective. To improve the effectiveness of the treatment of CVD at stages C1–C2 according to the CEAP classification with differential approach in the choice of treatment method: liquid or foam sclerotherapy.

Methods. The study randomly included 88 patients with telangiectasia and small varicose veins of less than 5 mm in diameter. The patients were divided into 2 groups according to treatment regimens: the first group ($n = 42$) was treated with liquid sclerotherapy; the second group ($n = 46$) – with modified Tessari foam sclerotherapy method. Based on the diameter of the vessels ($d < 1$ mm, 1–2 mm, 2–5 mm), the groups were divided into 3 subgroups. They were comparable in age (46 ± 8), gender (mostly women in all groups – 90–92 %) and clinical status. The following methods were applied: objective examination of the local status; subjective evaluation of the results of treatment by the patient, ultrasound monitoring with SonoScape S6 with linear sensor L741, statistical analysis.

Results. Maximum of complications (hyperpigmentation, local oedema, haemorrhages) in the treatment of veins with $d < 2$ mm was demonstrated after performing of the foam sclerotherapy. At the same time, the best subjective result (87.5 %) followed by complete disappearance of veins in 75 % of the patients after foam sclerotherapy, were obtained in the treatment of 2–5 mm veins. Liquid sclerotherapy results in plenty of complications (incomplete disappearance of vessels, relapse) in the treatment of veins $d > 2$ mm. The best subjective (90.9 %) and objective liquid sclerotherapy outcomes were achieved in treatment of veins $d < 2$ mm.

Conclusions. The study demonstrated the following clinical approach for the management of early stages of CVD: the treatment of veins with $d < 2.0$ mm basically requires the use of liquid sclerotherapy, whereas that of the vessels with a diameter in the range of 2–5 mm – foam sclerotherapy.

Acknowledgements. The authors declare the absence of the conflict of interest.

Acute traumatic extra-axial intracranial haemorrhages in Riga East Clinical University Hospital

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Background. Subdural (SDH) and epidural hematomas (EDH) are common neurosurgical emergencies associated with long hospitalization and disability. To our knowledge, statistics about prevalence of these disorders and factors affecting the hospitalization length and effect of alcohol intoxication on clinical course had not yet been made in Riga East Clinical University Hospital.

Objective. To determine the prevalence of SDH and EDH, the factors affecting the hospitalization length and the effect of alcohol intoxication on clinical course.

Methods. Data on patients hospitalized with acute SDH and EDH in Riga East Clinical University Hospital from 2012–2014 were collected. The patients who had also developed intra-axial hematomas were excluded from the study. The data was then statistically analysed using descriptive statistics and non-parametric tests due to the non-normal distribution of the data.

Results. 141 patients were included in statistical analysis (117 males, 24 females). The mean average age of patients was 55 years (SD = 18 years). 121 patients had SDH and 20 – EDH. 52.1 % of patients were treated surgically, while 47.9 % – conservatively. 6.4 % of the patients died during hospitalization. The mean average hospitalization length was 11 days [IQR 8 – 20]. The length of hospitalization strongly correlated with maximum width of hematoma ($r_s = 0.441$; $p < 0.001$), midline shift ($r_s = 0.594$; $p < 0.001$), the admission Glasgow Coma Scale (GCS) score ($r_s = -0.440$ $p < 0.001$). A weak but significant correlation was also found between the hospitalization length and admission haemoglobin ($r_s = -0.264$; $p = 0.002$), and the time CT scan was performed since the patient had been admitted ($r_s = -0.188$; $p = 0.028$). A positive blood alcohol test was found in 59 out of 141 patients (41.84 %), the mean average blood alcohol concentration (BAC) was 1.06 % (IQR 1.74–3.32). The mean average BAC was higher among patients with skull base fracture (1.57 % [IQR 0.00–3.165]), compared to the patients without skull base fracture (1.27 % [IQR 0.00–1.64]), $p = 0.002$. A positive BAC was also related to lower admission GCS Scores ($u = 1527.00$; $p = 0.001$). The mean average age of the patients with skull base fracture was lower (50 [IQR 35–64]) compared to the patients without skull base fracture (57 [IQR 45–72]), $u = 1794$, $p = 0.038$. The admission GCS score correlated with the width of hematoma ($r_s = -0.441$, $p < 0.001$) and midline shift ($r_s = -0.594$, $p < 0.001$).

Conclusions. This study shows that dramatic amount of acute traumatic intracranial haemorrhages are related to consumption of alcohol. Hospitalization length correlates with width of hematoma, midline shift and GCS.

Carolina Comfort Scale analysis of hernia patients before and after operation with polypropylene implant

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Background. Numerous studies have been published about pain spectrum analysis after hernia repair by prosthetic implant, but there is a lack of information regarding pain spectrum before hernia surgeries with mesh.

Objective. The aim of the current study is to establish and analyse hernia patients pain spectrum before and after the surgery with polypropylene implant.

Methods. In a prospective study we enrolled the patients with abdominal wall hernia who were operated by applying a polypropylene mesh. Caroline Comfort Scale (CCS) was used to assess pain spectrum, as well as quality of life before and after hernia operation with mesh. CCS contains eight questions, under every question, the scale includes sensation of mesh, pain, movement limitations, which are evaluated from 0–5 points and the total score (maximum – 115 points). These subscores were defined as: 0 – no symptoms, 5 – severe symptoms. The questionnaire was completed before the operation and a telephone survey was carried out 3 months or more after the operation.

Results. 71 patients were enrolled in the study, and 31 patients were analysed. The total of CCS points differs significantly pre and postoperatively. 18 patients reported that preoperatively they felt pain when walking or standing, but after the operation only 2 patients reported pain in that position. The survey showed that, 14 feel pain while they sit, but postoperatively there are no patients who feel pain when they sit up. Preoperatively, 23 patients described pain while performing routine activities (getting dressed, bathing), whereas after operation only 2 patients reported pain. Before the surgery, 10 patients felt pain while exercising, while postoperatively only 2 reported pain. Comparing pain after deep breathing and coughing, there was a statistically significant difference between pre- and post- operation groups ($\chi^2 = 15,915$, $p=0,044$). The comparison of pain when patients exercise, between groups ($\chi^2 = 40,621$, $p<0,01$), and pain when they bend over ($\chi^2 = 31,817$, $p<0,01$). Other results showed no statistically significant difference between groups.

Conclusions. The study results indicate that the CCS questionnaire is a useful tool to measure and analyse the pain spectrum in patients before and after hernia repair with mesh. The small cohort of study patients does not permit to formulate definitive conclusions and further research is needed.

Acknowledgements. The study did not receive any funding.

Effect of transcutaneous electric nerve stimulation on postoperative pain relief following inguinal hernia repair: first data from randomised, double blinded, placebo-controlled trial

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Background. Inguinal hernia repair can lead to postoperative acute and chronic pain. Multimodal access to analgesia, using a variety of analgesics and techniques combined with non-pharmacological interventions is recommended for postoperative pain treatment. Transcutaneous electrical nerve stimulation (TENS) is one of non-pharmacological methods used to control different types of pain.

Objective. The aim of the study was to evaluate the analgesic effect of TENS in patients following open inguinal hernia repair.

Methods. 80 male patients admitted to Kaunas Clinical Hospital for elective primary unilateral open hernia repair (Lichtenstein modification) in a period from August 2018 to November 2019 were enrolled in a randomised, double blinded, placebo-controlled trial. The participants were randomly allocated into TENS and placebo-TENS groups. TENS group received local and segmental conventional high frequency TENS on the first and second postoperative days, twice a day for 30 min. In placebo-TENS group, the self-adhering electrodes were placed, but no current was supplied. All the patients received standard postoperative pain medication at 6:00 and at 20:00 on the first and second postoperative days. At any time, they were able to ask for additional dose of analgesics, if needed. The pain was measured by using the 10 cm visual analogue scale (VAS) when lying down, standing up from the bed and walking. The hand-held electronic pressure algometer was used for assessment of pressure pain. The pain relief and the need of analgesic medication intake, as well as changes in pressure algometry parameters were of interest.

Results. The decreases in VAS were observed in TENS group, as well as in placebo-TENS group ($p < 0.01$), but the pain relief was higher in TENS group vs placebo-TENS group ($p < 0.001$) when lying down (0.08 ± 0.13 vs 0.55 ± 0.29), standing up from bed (0.98 ± 0.56 vs 0.19 ± 0.30) and walking (0.74 ± 0.40 vs 0.08 ± 0.13). Meanwhile, analgesic requirements were lower in TENS group compared with placebo-TENS group on the first and second postoperative days ($p < 0.001$). Pressure pain threshold (PPT) and maximal tolerable pressure (MTP) in hernia side were equal before intervention in both groups ($p = 0.84$), but higher in TENS group compared with placebo-TENS group (PPT 17.36 ± 6.64 vs 13.54 ± 7.27 ; and MPT 24.92 ± 10.50 vs 19.30 ± 10.41 ; $p < 0.001$) after intervention.

Conclusions. TENS has an analgesic effect in multimodal pain treatment after inguinal hernia repair.

Acknowledgements. Project was funded by Lithuanian University of Health Sciences. The authors declare the absence of conflict of interest.

Ultrasound measurements of the lower uterine segment during the III trimester in pregnant women with scars on the uterine following caesarean surgery

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Introduction. The number of caesarean deliveries in the world has been steadily increasing during the last decade, while the number of vaginal births after a caesarean section has been decreasing. There are not many studies in Latvia on the ultrasound measurements of the LUS during the 3rd trimester in pregnant women with a uterine scar following a caesarean surgery.

Objective. To collect information on perinatal outcomes in pregnant women with a uterine scar, as well as to determine the correlation between ultrasound measurements performed by an ultrasound expert and a resident of obstetrics and gynaecologist between October 2019 and February 2020 at the Prenatal Diagnostic Centre of the Riga Maternity Hospital.

Method. The study involved pregnant women during the 30th to the 32nd weeks of pregnancy with and without a uterine scar due to a previous caesarean section. During the ultrasound, LUS was measured transabdominally and transvaginally.

Results. Between October 2019 and January 2020, 33 pregnant women participated in the study, 15 of whom had a caesarean scar due to a previous section, while 18 of them had none. The measurements of the LUS carried out by both the resident and the expert showed statistically significant differences in women with and without a caesarean scar – LUS in women with a caesarean scar was thinner. Namely, the transabdominal measurements recorded by the resident were 3.2 mm and 4.6 mm, respectively ($p = 0.01$), while the transvaginal measurements recorded by the resident were 2.7 mm and 4.0 mm ($p = 0.01$); the transabdominal measurements recorded by the USG expert were 3.1 mm and 4.4 mm ($p = 0.02$) the transvaginal measurements recorded by the expert were 2.6 mm and 3.9 mm ($p = 0.01$). There is no statistically significant difference between the LUS measurements recorded by the resident and the USG expert, neither transabdominally ($p = 0.6$), nor transvaginally ($p = 0.7$).

Conclusions. The lower uterine segment in pregnant women with a uterine scar is thinner compared to the lower uterine segment in pregnant women without a scar of caesarean section during the third trimester of pregnancy. The resident doctor can independently perform measurements of the lower uterine segment during the third trimester of pregnancy. The analysis of the study data is still ongoing.

Cartogram of the lower limbs varicose incidence in Kazakhstan

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Background. Varicose disease of the lower limbs (LL) is one of the most common vascular pathologies. The disease has frequent relapses, a large number of complications leading to disability of the population. Consequently, new ways to assist this category of patients are sought worldwide.

Objective. To study the regional features of incidence of varicose veins of the LL in Kazakhstan by compiling cartograms.

Methods. To compile cartograms, we used the incidence rates for 10 years (2009–2018) and applied the method of compiling cartograms based on the determination of the standard deviation (σ) from the mean (x).

Results. During the study period, over 158 203 cases of varicose veins of LL were registered in Kazakhstan. The average annual incidence of varicose veins was 91.6 ± 9.6 per 100 000 population. In dynamics, the incidence rates tended to increase from 69.2 ± 0.7 ‰ in (2009) to 138.7 ± 0.9 ‰ in 2018, the established difference is statistically significant ($t = 60.96$, $p = 0.000$). The average annual growth rate of the equalized indicator was $T = +11.0\%$ ($R^2 = 0.7828$). To compile cartograms, at the outset the levels of varicose disease were determined, which meet the following criteria: low – up to 67.4 ‰, average – from 67.4 to 105.1 ‰, high – above 105.1 ‰. On this basis, the following groups of areas were defined:

1. Regions with low indicators (up to 67.4 ‰) included Aktobe (28.1 ± 1.4 ‰), Mangistau (37.5 ± 8.6 ‰), West Kazakhstan (47.0 ± 4.4 ‰), Kostanay (50.3 ± 3.4 ‰), and Akmola (66.1 ± 3.0 ‰) regions.

2. Regions with average indicators (from 67.4 to 105.1 ‰) involved Kyzylorda (69.5 ± 14.6 ‰), East Kazakhstan (70.0 ± 9.3 ‰), Zhambyl (86.6 ± 11.0 ‰), Almaty (87.2 ± 8.3 ‰), Atyrau (88.0 ± 19.8 ‰), Pavlodar (97.6 ± 5.2 ‰) and South Kazakhstan (102.8 ± 20.7 ‰) regions.

3. Regions with high indicators (105.1 ‰ and above) included Karaganda (128.3 ± 19.5 ‰) and North Kazakhstan (130.5 ± 7.6 ‰) regions, as well as the cities of Almaty (128.1 ± 19.5 ‰) and Astana (163.0 ± 16.5 ‰).

Conclusions. The established regional features of the incidence of varicose veins indicate variability with territorial differentiation of “loci” with low and high rates. The results will allow healthcare providers to have a clear spatial picture regarding the frequency of varicose veins of the LL and its incidence rate, which must be used to monitor and evaluate the treatment and preventive measures.

Acknowledgments. The authors declare the absence of conflict of interests and express their appreciation to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

Use of demographic and clinical parameters to predict postoperative complications and adverse events in patients with high risk of obstructive sleep apnoea

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Background. Obstructive sleep apnoea (OSA) is a sleep disorder associated with cessation or significant decrease of airflow despite the respiratory effort. Patients with OSA develop postoperative complications significantly more frequently than those without OSA.

Objective. The aim of the present study was to determine demographic and clinical predictors for postoperative complications and adverse events in patients with a high risk of OSA.

Methods. An observational prospective study was conducted with approval of ethics committee. A total of 400 patients scheduled for elective surgery were enrolled in the study. The Berlin questionnaire was used for screening patients at high risk for OSA. Complications and adverse events were recorded in postoperative period before discharge from hospital. Statistical analyses were carried out using SPSS version 22.0 for Windows. A series of multiple regression analysis were performed to examine the relationship of demographic and clinical parameters with complications and adverse events in patients with a high risk of OSA.

Results. According to the Berlin questionnaire, 309 patients were identified as having a high risk for OSA. Multiple regression analysis showed that age > 50 years ($p = 0.025$), preoperative hypertension ($p = 0.0001$), and body mass index (BMI) > 35 kg/m² ($p = 0.002$) were associated with the occurrence of cardiovascular complications. The probability of cardiovascular complications in patients with a high risk of OSA aged > 50 years with preoperative hypertension, and BMI > 35 kg/m² was 80.2 %. Neck circumference > 40 cm ($p = 0.026$) and BMI > 35 kg/m² ($p = 0.050$) were statistically significant predictors of respiratory complications. The probability of respiratory complications in patients with OSA, neck circumference > 40 cm and BMI > 35 kg/m² was 13 %. Only the preoperative forced expiratory volume in one second less than 320 ml ($p = 0.035$) was predictive of the development of adverse events in patients with a high risk for OSA.

Conclusions. The developed probabilistic model incorporating the presence of high risk for OSA, age > 50 years, preoperative hypertension, body mass index > 35 kg/m² predicts cardiovascular complications in 80.2 % of patients. The neck circumference > 40 cm and BMI > 35 kg/m² were identified as predictors of respiratory complications; preoperative forced expiratory volume in one second less than 320 ml can be used to predict adverse events in patients with a high risk of OSA.

Acknowledgements. None. No funding to declare.

Effects of opiates on the early postoperative period

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Background. One of the main tasks in postoperative period is to provide good pain management. Poorly controlled acute postoperative pain is associated with increased morbidity, functional impairment and decreased quality of life, delayed recovery time, prolonged duration of opioid use, and higher health-care costs. Common side effects of opioid administration include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression.

Objective. The aim of the study is to investigate the effect of opiates on patients after cardiac surgery in the postoperative period.

Methods. Data were collected prospectively during the period from 03.01.2020 to 31.01.2020, the patients, who were prepared for cardiac surgery were interviewed at Pauls Stradiņš Clinical University Hospital. The patients were interviewed before surgery, and the vital data, medication use, pain history, gastrointestinal diseases, VAS (visual analogue scale) were collected. After the surgery, the data were collected about opiate dosage and side effects. Statistical analysis was performed using IBM SPSS Statistics Version 21.

Results. The study involved 25 participants, 12 women, 13 men, the average age was 68.6 years, the average body weight – 79.5 kg. All the patients received opioids in dosage 20 mcg/kg/h. In the 2nd hour ($p = 0.14$) after the surgery there was no correlation between opioid dosage and VAS scale, nor was there in the 4th ($p = 0.14$), and the 6th ($p = 0.63$) hour. The average opioid dosage and nausea in the 2nd, 4th, and 6th hour after surgery had no correlation ($p = 0.23$). 20 % of the participants reached more than 4 on VAS scale in the 2nd hour after surgery, whereas 36 % of the participants in the 4th hour reached more than 4 on the VAS scale, and 16 % of the participants reached more than 4 on VAS scale in the 6th hour. Three patients in the 2nd hour, six patients in the 4th hour, four patients in the 6th hour experienced a breakthrough pain of more than 6 on VAS scale.

Conclusions. All the patients were treated with a similar dose of opioid that was clinically low and there was no demonstrable credible adverse reaction arising directly from the opioid. Data show that opiates are effective painkillers, but dose titration is required to achieve an ideal result. The highest VAS score was observed at the 4th hour after surgery, which could be explained by the fact that at the 3rd hour the extubation is usually carried out and sedation dose reduced. These factors can cause agitation, increased movement, which can provoke additional pain. Almost a half of the patients had breakthrough pain episodes, with moderate to severe pain and other painkillers were required, which means that opioids in monotherapy in dosage that does not cause side effects, do not provide adequate pain management.

Vivostat Fibrin Sealant effect on blood volume loss during revision total hip joint replacement surgery and post-surgery recovery

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Background. Revision total hip joint replacement is a complex and long surgery which is usually performed for elderly people. Large volume surgeries are known to cause a large blood volume loss which negatively affects person's physical health and recovery process. Small capillaries located in periost, bone tissue and soft tissue blood vessels are the main cause of bleeding during and after the surgery.

Objective. Comparison of blood volume loss during revision total hip joint replacement surgeries and post-surgery blood loss through drain with and without using Fibrin Sealant. Research and analysis took place in The Hospital of Traumatology and Orthopaedics in Riga. The timeframe of this research: February 17–December 31, 2020.

Methods. Prospective study includes 24 patients of revision total hip joint replacement surgery. These patients are divided into 2 subgroups. Group A patients received revision total hip joint replacement surgery without Fibrin Sealant, while group B patients received surgery with Fibrin Sealant used intraoperatively. Post-surgery blood volume loss is determined by accumulating blood in blood bag through drain.

Results. Group A consisting of 23 patients received revision total hip joint replacement surgery without Fibrin Sealant. According to analysis of lost blood volume during and post-surgery, it was determined that the average blood loss during the surgery was 1051 millilitres, the smallest blood loss was 400 millilitres, while the largest loss was 2700 millilitres. 12 hours post-surgery, the average blood volume loss was 405 millilitres, the smallest blood loss was 45 millilitres, while the largest loss was 1100 millilitres of blood. During the first post-operative day, the average loss of blood was determined to be 279 millilitres.

To date, only one hip revision surgery has been performed with Fibrin Sealant, the patient of research group B lost 360 millilitres of blood during the surgery and 300 millilitres of blood during the first 12 hours after the surgery. Drain was removed 12 hours post-surgery, because no blood was found in blood bag. During the first part of the research, only one patient received surgery with Fibrin Sealant due to limited technological possibilities, for further research the number of patients in group B will be increased.

Conclusions. The research data displays the positive effect of Fibrin Sealant usage during hip joint revision surgery. Use of Fibrin Sealant reduces intraoperative wound bleeding and post-surgery risk of possible complications due to blood loss. For further research, more surgeries with Fibrin Sealant are needed to produce results of a greater precision.

PEDIATRICS

Bacillus clausii in treatment of rotavirus infection in children

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Background. Every year, 2 million patients are hospitalized with a severe form of rotavirus infection (RVI), 25 million need medical assistance of a doctor and 111 million cases are treated at home. The most severe illness occurs in children at the age of 4–36 months of life. Rotavirus infection still remains the cause of more than 215 000 deaths annually, especially in low-income countries. Probiotics are widely known to be used in acute diarrhoea in children and adults. Today, in clinical practice the use probiotic drugs that are normal residents of the intestinal tract, such as lactic acid bacteria and spore-forming, mainly representatives of the genus *Bacillus*.

Objective. The purpose of our research is to study the effectiveness of the use *Bacillus clausii* in children with rotavirus infection by assessing the duration of clinical symptoms.

Methods. We have studied 42 children with RVI between the ages of 1 and 5 years, group I consisted of 20 patients received standard treatment and group II – 22 patients received additional probiotic, which includes *Bacillus clausii*. The control group consisted of 15 healthy children, representative of age and gender. Diagnosis of rotavirus infection was verified according to results of the immuno-chromatographic test.

Results. In the examination of patients, DVF syndrome, characterized by diarrhoea, vomiting, and fever, was the leading symptom, in addition, the reduction of turgor of skin, pain in the epigastric and umbilical areas with palpation of the abdominal was determined. When comparing the duration of these symptoms, it was found that in children of group II the fever lasted for 0.61 days, vomiting for 0.65 days and diarrhoea for 1.09 days less than for the patients in group I ($p < 0.05$).

Conclusions. The inclusion of *Bacillus clausii* in the treatment of children with rotavirus infection reduced the duration of the main clinical symptoms. Furthermore, the use of a probiotic preparation containing *Bacillus clausii* in the complex treatment of rotavirus infection contributed to the improvement of treatment efficiency.

Acknowledgements. None declared.

Behavioural and mental health screening in children with type 1 diabetes mellitus

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Background. Research has proved that mental health problems, including emotional and behavioural disorders, as well as relationship and social functioning difficulties deteriorate the patients' compliance in treating the diabetes, which results in a worse metabolic control of the disease.

Objective. The aim of the current study was to report the results of behavioural and mental health screening for children with type 1 diabetes mellitus (T1D) seen in Children's Clinical University Hospital (Latvia).

Methods. This was a study of children with T1D in two groups, sorted by age – the participants of the first group were aged 2–4 years (N 24) and those of the second group – 5–18 years (N 77). For the purposes of screening, the Strengths and Difficulties Questionnaire (SDQ) (by Goodman) was used. SDQ scale and total difficulties scores were compared by age. The SDQ Parent Version is a brief, 25-item, behavioural screening questionnaire that assesses positive and negative attributes across 5 scales with 5 items on every scale: 1) emotional symptoms, 2) conduct problems, 3) hyperactivity – inattention, 4) peer relationship problems and 5) prosocial behaviour. A total difficulties score is calculated by summing the scores of the first four scales and ranges from 0 to 40 (every scale scored from 0 to 10). For all scales, except prosocial behaviour, higher scores were associated with worsening symptoms. Patient characteristics included age, gender, duration of T1D, glycosylated haemoglobin, acute complications and genetic background.

Results. From December 2019 to January 2020, 101 children were eligible for screening. In the age group of 2–4 years the borderline score was found on the scale of the emotional symptoms. The total difficulties' scores were within the norm. In the age group of 5–18 years, the borderline scores were found on the scales of emotional symptoms, behavioural problems and relationships with peers, as well as in the limiting value increased total difficulties score.

Conclusions

1. Children with T1D in the age group of 5–18 years are to greater extent subject to emotional, behavioural and relationship disorders than the children in the age group of 2–4 years;
2. Children with T1D (both groups) had borderline scores on the emotional symptoms scale, suggesting a risk of psychological disorders, such as depression, anxiety, eating disorders;
3. Further multiprofessional research is necessary not only for children with T1D, but also for their families, in order to avoid the development of stress-related mental health disorders.

Acknowledgements. None declared.

Breastfeeding problems and use of infant formula without medical indications

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Background. Each year formula-feeding becomes a more popular option among the new mothers, although there are only some indications for its use. A lot of new mothers are not qualitatively educated on breastfeeding procedure and lactation-inducing techniques, therefore they encounter difficulties that induce them to use baby milk, even though often there might not be any medical indications.

Objective. The aim of this study is to investigate the problems that bring mothers to apply formula feeding without confirmed medical indications.

Methods. This cross-sectional cohort study includes 534 new mothers that use infant formula to feed their infants (under 1 year old). The respondents filled in an anonymous questionnaire of 47 questions. The study was conducted from 1.12.19 to 31.01.20, in family doctors' offices, the Department of Obstetrics and Gynaecology of Jelgava Hospital, kindergartens and groups of new mums from Latvia in the Internet. Data were processed using «Excel» and «SPSS 2.0» programs.

Results. The series of questions that test correct application of the main principles for inducing lactation were correctly answered by 28 respondents (5.24 %). Correct breastfeeding technique expose 23 (4.3 %) of respondents, however, only 3 (0.6 %) of them fed their children for the necessary duration of time (30–45 min). The attempts of family doctors to find out problems that mothers encounter during breastfeeding, negatively correlate with the prevalence of weight deficiency among newborns (by 39.37 % lower prevalence). Lactose intolerance as a cause to use formula was selected by 11 % of respondents, but only 0.7 % had a weight deficiency after the first month (which is the main sign of lactose intolerance). Babies of women with flat nipples where unable to take breast (52.94 %), to hold breast (54.91 %) and to suck breast milk (16.34 %), but none of the respondents had tried the special nipple shields. 43 % of respondents counted weight gain from the birthday (19 % of them noted weight deficiency), however other 57 % of respondents counted weight gain from the day they left hospital (23 % of them noted weight deficiency).

Conclusions. Most of the women either do not try to apply lactation-inducing methods or use them incorrectly. Often, family doctors do not try to find out physiological causes of a decreasing breast milk supply before they prescribe a formula. There is no common method in Latvia to count weight gain during the first month. Most women are not qualitatively educated about breastfeeding procedure, essentials and lack advice to solve possible problems.

Acknowledgments. None declared.

Comparison in psychomotor function of children receiving Montessori therapy and children that do not receive any therapy

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Background. The Montessori Method fosters rigorous, self-motivated growth for children in all areas of their development – cognitive, emotional, social, physical. Montessori education is student-led and self-paced but guided, assessed, and enriched by knowledgeable and caring teachers, the leadership of their peers, and a nurturing environment. Within the community of a multi-age classroom designed to create natural opportunities for independence, citizenship, and accountability – children embrace multi-sensory learning and passionate inquiry. Individuals follow their own curiosity at their own pace, taking the time they need to fully understand each concept and meet individualized learning goals.

Objective. To evaluate the outcomes in psychomotor functions between children who received Montessori therapy and children who did not receive any therapy.

Methods. This study involved children aged 2 to 5 years, who were regularly visiting the Children Clinical University Hospital and the Social Paediatrics Centre of the University of Latvia from 2013 to 2015. The developmental state of children was evaluated by a physician using Denver functional test. After basic evaluation, children were indiscriminately separated in two groups, those who were taking part in Montessori therapy and those who were not. Over time of 6–8 months after the initial examination, the final evaluation was carried out by using Denver functional test. Numerous logistic regression models adapted for age, compliance of development to age norms, and initial diagnosis of a child were created to correlate between attendance the Montessori therapy and advancement in psychomotor functions.

Results. Our observation revealed that the psychomotor function in children who had been attending Montessori therapy had significantly improved. Montessori therapy was especially effective for speech development (Odds ratio, OR = 22.7 [95 % confidence interval 0.49;1044.1] and fine motor skills (OR = 46.14 [2.81;757.1]) (Table).

Table. Improvement of psychomotor function in children attended the Montessori therapy.

Psychomotor abilities	B	Standard error	OR	95 % confidence interval
Hearing	2.96	1.24	19.3	1.69; 221.1
Fine motor skills	3.83	1.43	46.14	2.81; 757.0
Gross motor skills	1.77	0.92	5.89	0.98; 35.3
Speech development	3.12	1.95	22.66	0.49; 1044.1

Conclusions. Taking part in Montessori therapy is beneficial for children for improvement of their psychomotor function. We propose that not only children with developmental issues, but also healthy children can benefit from therapies.

Acknowledgments. None declared.

Early diagnosis of diabetic nephropathy in children with type 1 diabetes mellitus using the VCAM-1 biomarker

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Background. Diabetes mellitus is a global epidemical problem. According to the International Diabetes Federation, in 2019 463 million adults lived with diabetes and more than 1.1 million children suffered from diabetes type 1. Diabetic nephropathy is one of the most common complications of diabetes. Biomarkers play an important role in early diagnosis and adequate treatment. Vascular cell adhesion molecule-1 (VCAM-1) – is a 90-kDa glycoprotein that is expressed in endothelial cells and is involved in the migration and recruitment of inflammatory cells. Recent studies have shown that urinary VCAM-1 levels were significantly increased in patients with kidney disease.

Objective. The aim of the current study was to investigate the features VCAM-1 levels in urine of children depending on the diabetes duration.

Methods. We analysed 3 groups of children with type 1 diabetes mellitus and comparison group of children without diabetes from Regional Children's Clinical Hospital in Sumy. VCAM-1 was measured by ELISA using a Proteome Profiler Human Kidney Biomarker Antibody Array (R&D Systems, Minneapolis, MN, USA). Results were detected with BioRad ChemiDoc Touch. The arrays were analysed semi-quantitatively, using BioRad Image Lab Software.

Results. Study included 47 children with diabetes and 8 children without diabetes. VCAM-1 in urine increased by 24 percent in children with the duration of diabetes below one year compared to the control group. VCAM-1 levels were elevated by 33 percent in children with the duration of diabetes from one to five years. The marker increased by 54 percent in children who lived with diabetes for more than five years.

Conclusions. Increase in urinary VCAM-1 was observed in the first year of diabetes in children. Measuring the level of VCAM-1 in urine may be useful for the early diagnosis of diabetic nephropathy.

Acknowledgements. We thank the research group of Thomas Boren (Department of Medical Biochemistry and Biophysics/MIMS, Umea University) for the opportunity to conduct research in framework of collaboration in Erasmus+ (KA1) programme, 2018/2019. The authors declare absence of potential conflicts of interest.

Measuring process of care in paediatric palliative care

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Background. Paediatric palliative care is defined as the prevention and relief of suffering of paediatric patients and their families facing the problems associated with life-threatening illness. These problems include the physical, psychological, social and spiritual suffering of patients, and psychological, social and spiritual suffering of family members. During the process of care, nurses should consider the needs of the patients and their families.

Objective. Previous studies show that important factors affecting the needs of palliative care patient's family are related to support of professionals in the areas of information and finances. The aim of this study is to measure process of care from the patient's perspective.

Methods. The quantitative research method was applied in cross sectional study, where *Measure of process of care* was used as an instrument. The survey consisted of 20 statements that were divided into 5 categories of family-centred care principles: encouragement and cooperation, provision of child-specific information, coordinated and comprehensive care, a respectful and supportive environment.

Results. Families were more positive about principles like respectful and supportive environment ($M = 4,84$, $SE = 1,27$) and coordinated and comprehensive care ($M = 4,65$, $SE = 1,8$). The lowest rating was given to provision of child-specific information category ($M = 3,43$, $SE = 1,24$).

Conclusions. A fundamental aspect of palliative care is the continuity of care, which involves availability and follow-up by healthcare specialists, access to information and other medical treatment and care-related resources. Currently, the services provided by palliative care professionals are partly oriented towards providing patient-centred care.

Acknowledgements. None declared.

Opinion of children with rheumatic diseases and their parents about their quality of life according to Kidscreen-52 questionnaire

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Background. In recent years, increasing attention is dedicated to the quality of life in children, including children with chronic diseases. It is important to appraise the quality of life in patients with chronic diseases in order to be able to assess the physical and psychoemotional well-being of children, including the welfare of entire families impacted by the diseases. It would also help to reveal and evaluate opinions and positions of children themselves regarding their health status, impact of the disease on him or her. The patients have joint pains in the active period of diseases, and, as a result, their quality of life is affected.

Objective. The objective of the study was to analyse quality of life in children with rheumatic diseases. The aim of this study was to find out opinions of children with rheumatic diseases about their health, physical and emotional well-being comparing to their parents' opinion.

Methods. In this study, children with rheumatic diseases aged 8 to 18 years and their parents were surveyed at the Children's Clinical University Hospital. The participants voluntarily filled out KIDSCREEN-52 questionnaire. The survey includes 10 Health Related Quality of Life (HRQoL) dimensions, encompassing physical, emotional, social life. The participants were divided into two groups – children's and parents' group. Statistical analysis was performed with SPSS statistics by using Mann-Whitney test. The level of statistical significance was set at $p < 0.05$.

Results. Overall, 88 participants were surveyed – 47 children and 41 parents of these children. The mean children's age was 13.61 ± 2.4 (8 – 17) years. 87.2 % ($n = 41$) of children had Juvenile idiopathic arthritis, 12.8 % ($n = 6$) – other rheumatic diseases. 40.9 % of children thought that his/her health was more than good. 53.8 % of children were satisfied with life, 10 % felt sad and 32.5% felt happy at school. Using Mann-Whitney test, it was found that the difference between children's and parents' views regarding the question whether the child and his friends are helping each other, was a statistically significant one ($p < 0.05$). In other questions, no statistically significant differences ($p > 0.05$) were found.

Conclusions. Opinions of children and their parents regarding the children's quality of life did not differ significantly, except in one question from the section "Friends". We need to continue studies about children's quality of life, increasing the sample size of patients.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment", the University of Latvia Faculty of Medicine.

The relationship between duration of breastfeeding and socio-demographic factors: age, education and number of children

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Background. Socio-demographic factors are found to be relevant to the duration of breastfeeding.

Objective. The aim of the study was to evaluate the relationship between age, education and number of children with the duration of breastfeeding (DB) in breastfeeding mothers (BFM).

Methods. 620 BFM were recruited via the Internet by using a breastfeeding questionnaire, developed by the authors. Mothers were asked for how long they had been breastfeeding, and 4 groups were defined: the 1st (< 6 months) – 33.7 % (n = 209), the 2nd (6–12 months) – 25.3 % (n = 157), the 3rd (12–24 months) – 31.1 % (n = 193), the 4th (24+ months) – 9.8 % (n = 61). Sociodemographic data and number of children were collected; 4 age groups were defined: A (18–25 years) – 8.9 % (n = 55), B (26–30 years) – 41.1 % (n = 255), C (31–35 years) – 39.0 % (n = 242) and D (36+ years) – 11.0 % (n = 68). The methods used in the study include Pearson correlation coefficient and chi-square test.

Results. Results showed that BFM of age group B were breastfeeding for a shorter period – 60.4 % (n = 154) were in the 1st group and 39.6 % (n = 101) – in the 2nd, compared to C group – 23.1 % (n = 56) were in the 2nd group and 76.9 % (n = 186) – in the 3rd, while BFM of D group were breastfeeding longer – 10.3 % (n = 7) were in the 3rd group and 89.7 % (n = 61) – in the 4th, $p = .0016$.

Education and DB relation was significant only in age group B: secondary education (9.8 %; n = 25) was more frequently related to shorter breastfeeding (40 % (n = 10) of BFM were in the 1st group and 60 % (n = 15) – in the 2nd), but less frequent in comparison to higher non-university education (20.8 % (n = 53) (64.2 % (n = 34) were in the 1st group and 35.8 % (n = 19) – in the 2nd), and similar to higher university education (66.3 %; n = 169) (36.3 % (n = 107) were in the 1st group and 36.7 % (n = 62) – in the 2nd), $p = .04$.

The number of children was related to shorter DB in age group B: 61.2 % (n = 156) had one child (48.7 % (n = 76) of BFM were in the 1st group and 51.3 % (n = 80) in the 2nd); 32.9 % (n = 84) of BFM had two children (76.2 % (n = 64) – in the 1st group and 23.8 % (n = 20) in the 2nd); 4.7 % (n = 12) of BFM had three children (91.7 % (n = 11) – in the 1st group and 8.3 % (n = 1) – in the 2nd); 1.2 % (n = 3) had 4 and more children, and all of these were in the 1st group, $p < .0001$.

Conclusions. Maternal age is related to DB. Education, number of children and duration of breastfeeding are related to the age 26–30 in BFM.

Acknowledgements. This study did not receive any funding. The authors would like to thank all participants of the study.

Analysis of attention indicators for children and young people with developmental disabilities

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Background. For children and young people with developmental disabilities it is essential to develop concentration and attention capacity, which promotes adaptation and integration into society. The use of these opportunities is important for the work of the interdisciplinary team, in which nurse plays an important role.

Objective. The aim of the current study was to analyse the dynamics of attention indicators for children and young people with intellectual disabilities (ID) and their use in an interdisciplinary team.

Methods. An authorisation by the Ethics Commission was obtained and a signed form of consent for the participation was submitted by parents. The study involved 35 children and young people with ID and 15 respondents (nurses, psychologists, etc.), working in specialised schools. The Vienna Test System, Cognitron Test, subform S7 and S11 were used for the analysis of the attention indicators. Attention rates were assessed twice with an annual interval. Interviews of special school employees were conducted. A qualitative method was used for analysis: a semi-structured interview, an average duration – 30 minutes.

Results. An increased rate of test performance (e.g., in children with mild to moderate mental development disabilities in 2017, an average of 17.12 min, as compared with an average of 12.77 min in 2018 was observed), and an increased level of attention sustainability was found, but the accuracy had not changed significantly. The results show that despite the positive dynamics of cognitive function, it is too weak, while the number of respondents is too small to conclude that attention rates are improving.

Cross-sectoral team members believe that objective measurements of cognitive function will help analyse progress for people with ID. The main problems are responsibility and communication of each member of the team with the parents. It was stressed that the nurse who was a member of the team needed additional expertise in psychology and pedagogy.

Conclusions. An objective analysis of the individual cognitive function indicators of a mutually agreed, targeted cross-disciplinary team helps to identify more precisely the tasks of the team in order to ensure optimal development and adaptation of children and young people with developmental disabilities.

Acknowledgments. None declared.

Clinical and electrophysiologic features of childhood Guillain-Barré syndrome in Latvia

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Background. Guillain-Barré syndrome (GBS) is a rare disease with an annual incidence of 0.34 to 1.34 among paediatric patients. Nevertheless, it is the most common cause of acute flaccid paralysis in otherwise healthy infants and children. Clinical presentation is indicative of GBS, but diagnosis usually requires supporting evidence. When diagnosing GBS, electrophysiological studies including nerve conduction studies and electromyography are the most specific and sensitive methods.

Objective. To evaluate clinical symptoms, nerve conduction and electromyography results among paediatric patients during their in-hospital stay.

Methods. 19 children and adolescents under 18 years diagnosed with GBS were enrolled in this retrospective study. All of them were admitted to Children's Clinical University hospital between 2008 and 2018. Clinical history, nerve conduction studies (NCS) and electromyography were used to analyse their symptoms. This study has been carried out with the approval of the Ethics Committee of the Children's Clinical University Hospital.

Results. The average age of patients was 10.8 ± 4.6 years. The patients were predominantly female ($n = 11$). 16 patients had motor dysfunction, 9 – sensory dysfunction, and 7 had neuropathic pain. The dysfunction of the autonomic nervous system was observed in 4 patients. 7 patients did not report any infection 2–4 weeks before diagnosis. 4 patients reported respiratory infections, 1 – gastrointestinal infection, while 7 patients reported other infections prior to Guillain-Barré syndrome. The GBS subtype distribution was, as follows: acute inflammatory demyelinating polyradiculoneuropathy (AIDP) in 8 patients, acute motor axonal neuropathy (AMAN) in 8 patients, acute motor-sensory axonal neuropathy (AMSAN) in 3 patients.

Conclusions. GBS is a rare disease that requires hospitalization. NCS, electromyography and clinical symptoms are crucial for GBS diagnostics.

Acknowledgments. None declared.

Infant mortality in relation to economic factors since the economic crisis in the Baltic states 2010–2016

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Background. Previous research (1996–2010) demonstrated a causal relationship between infant mortality (IM), gross domestic product (GDP) and healthcare expenditures (HCE), and pointed out concerning discrepancies between IM in Latvia and the other two Baltic states. The economic crisis of 2008 appeared to be the most damaging in Latvia, where IM rates remained high at a regional level.

Objective. To assess whether IM in the Baltic states is still associated with GDP and HCE post-economic crisis in order to draft proposals for specific action to be undertaken by government.

Methods. Data on IM, GDP and HCE-related rates (total and per capita GDP in international currency, local currency units (LCU) and purchasing power standards (PPS), HCE by purchasing power parity (PPP) as a share of GDP for total, public and out-of-pocket payments) for the Baltic states, Sweden, Germany and the USA was obtained for 2010–2016 from open source databases (Eurostat, WHO, OECD and the World Bank). Multivariate regression and Spearman's correlation analysis was performed, using IBM SPSS 20.0.

Results. GDP per capita in LCU was associated with IM ($r = -0.93$, $p = 0.003$) and PNM ($r = -0.85$, $p = 0.02$) in Latvia, and PNM in Estonia ($r = -0.82$, $p = 0.02$). GDP per capita in PPS was associated with IM ($r = -0.83$, $p = 0.02$) and PNM ($r = -0.81$; $p = 0.03$) in Latvia. HCE per capita by PPP was associated with IM in Latvia ($r = -0.821$; $p = 0.02$), and PNM in Estonia ($r = -0.821$; $p = 0.02$). A persistent significant association between infant mortality and GDP in LCU and PPS pinpointed by previous research remains after the economic crisis in Latvia, however, it has disappeared in the other Baltic countries. A highly significant association between perinatal mortality (PNM) and GDP per capita in LCU and PPS has been identified in Latvia and Estonia, but not Lithuania. A strong correlation between IM and HCE per capita by PPP still exists exceptionally in Latvia, however, a relationship has been discovered between HCE per capita and PNM in Estonia.

Conclusions. The difference in IM mortality rates linked to GDP per capita and HCE among the Baltic states persists and is most prominent in Latvia. Causal relationships between mortality and economic indicators should be foreseen and investigated in other vulnerable age groups and remains a topical healthcare issue at a regional level, still not receiving enough attention from the government from budgetary and health strategy perspective.

Acknowledgements. None declared.

Prevalence of antibody deficiencies in patients with primary immunodeficiencies in Latvia

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Background. Primary immunodeficiencies (PID) are a group of more than 200 distinct disorders caused by a genetic defect leading to malfunction of the immune system. Antibody deficiencies are the most common group of primary immunodeficiencies. Antibody deficiency can be a separate disease entity, or a feature of another primary immunodeficiency. The most common clinical manifestation of PID include recurrent bacterial infections of the respiratory, gastrointestinal or urogenital tract, and skin lesions. In some cases, antibody deficiencies are asymptomatic and do not become manifest until adulthood. In certain cases, autoimmune manifestations, lymphoproliferative disorders, and/or granulomatous inflammation are the only features of the disease and patients do not develop recurrent infections.

Objective. The aim of the study was to evaluate the prevalence of primary antibody deficiencies among other PID patients in Latvia.

Methods. We retrospectively analysed the data from Children's Clinical University Hospital and Pauls Stradiņš Clinical University Hospital during time period from 1994 to 2020.

Results. Approximately 280 cases of primary immunodeficiencies were diagnosed in this period of time in both children and adults in Latvia. Precise number of patients is unknown owing to the fact that there is no national registry of these syndromes in Latvia. Primary antibody deficiencies – common variable immunodeficiency (CVID), specific antibody deficiency (SAD) and selective IgA immunodeficiency were found in 197 of PID patients. 85 % (168/197) of these patients had selective IgA deficiency. CVID and SAD were less common. Antibody deficiency patients presented with variable clinical features – recurrent viral and bacterial infections, autoimmune diseases, few had a malignant disease, and there were also asymptomatic cases.

Conclusions. Primary antibody deficiencies were diagnosed in approximately 70 % of all primary immunodeficiency patients in Latvia. The most common form of antibody deficiency in Latvia was the selective IgA deficiency. Timely diagnosis of antibody deficiency is important for prognosis and monitoring of these patients in order to predict the possible complications.

Acknowledgements. None declared.

Prevalence of breastfeeding among Latvian infants: Initiation of breastfeeding within one hour of birth significantly influences duration of exclusive breastfeeding

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Background. Breastfeeding provides optimal nutrition for infants, as well as promotes emotional contact between the baby and its mother. However, prevalence of breastfed infants varies and is influenced by a variety of factors.

Objective. To detect the prevalence of breastfeeding among Latvian infants and identify factors influencing duration of breast feeding.

Material and methods. A prospective study was carried out via internet (*Facebook, Mom-life*) during April, 2018 to April, 2019. Mothers of children (aged six months to seven years) were asked to answer anonymous questionnaire (mothers' and children's age, pregnancy, delivery, mothers and infants' diseases, duration of breastfeeding in total (TB) and duration of exclusive breastfeeding (EB), introduction of supplementation, mother's education and knowledge about breastfeeding).

The statistical analysis methods of this study include descriptive statistic, Chi square test, T-test.

Results. The total patient sample included data about 500 children; the mean age of respondents was 29.26 years (SD \pm 5.04 years, median of age 29), the youngest mother was 17 years old, the oldest – 49 years of age. The mean age of children was 2.22 years (SD \pm 1.56, median – 1.83), out of them the youngest was six months old, while the oldest – seven years old.

After delivery, EB was received by 98.4 % (492/500) of neonates. Duration of EB only a few days was reported in 11.6 % (58/500), a few weeks – in 9.4 % (47/500), a few months – in 16.0 % (80/500) and until introduction of solid food – in 61.4 % (307/500) of cases.

Overall, during the first year of life, 55.8 % (279/500) were breastfed; 9.6 % – formula-fed (48/500) and 34.6 % (173/500) reported mixed feeding.

Breastfeeding during the first year of life was more often observed among infants with an early breastfeeding initiation compared to those without early breastfeeding (61.5 % vs 41.2 %, $p = 0.001$); among infants with early baby/mother contact compared to those without the contact (55.7 % vs 47.3 %, $p = 0.186$); and among infants whose mothers did not report advising formula by medical staff (63.9 % vs 40.5 %, $p < 0.001$).

Conclusions. Exclusive breastfeeding until introduction of solid food was reported by more than a half of the respondents. Since the use of formula during the first days of life significantly influences prevalence of breastfeeding, more attention to promotion of breastfeeding should be paid by medical staff in the delivery departments.

Acknowledgments. None declared.

INFECTIOUS DISEASES

Relapse or reinfection: application of whole genome sequencing to distinguish between two independent forms of recurrent tuberculosis

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Background. Tuberculosis (TB) is a major problem in the context of global health and it remains a leading cause of death from a single infectious agent. Whole genome sequencing (WGS) of *Mycobacterium tuberculosis* (Mtb) enabled high-resolution strain differentiation and provided new insights into its evolution, epidemiology and drug-susceptibility profile. Distinguishing endogenous reactivation from reinfection can be challenging, particularly when multiple active disease episodes were caused by strains belonging to similar genotypes. Differentiation of a possible development mechanism of recurrent TB can be achieved by detailed analysis of these isolates' SNP profile and phylogeny using WGS approach.

Objective. The aim of this research was to differentiate endogenous relapse from exogenous reinfection in Latvian patients with recurrent TB episodes.

Methods. In total, 8 cases of recurrent TB were studied. According to spoligotyping, all patients repeatedly developed active TB disease caused by the identical Mtb genotype. Paired Mtb culture DNA samples for WGS analysis were provided by Mycobacteriology laboratory of Riga East University Hospital. Single-end genomic libraries were prepared using Ion Plus Fragment Library Kit and sequenced on Ion Proton system. Bioinformatic analysis of raw sequencing data was performed on Galaxy web platform and SNP differences between sample pairs from each patient were detected manually. Phylogenetic tree was constructed using CSI Phylogeny v1.4.

Results. 4 patients' isolates revealed SIT1 spoligotype, other 4 had SIT254 corresponded pattern. 3 SIT1 and 3 SIT254 isolate DNA samples obtained from recurrent cases had 0–4 SNP difference compared to the corresponded initial episode. This finding indicates endogenous disease reactivation. Two other isolate pairs (SIT254 and SIT1) showed different SNP patterns between episodes, therefore, in these patients, recurrent TB most likely occurred due to reinfection. Interestingly, deeper analysis of two isolate pairs revealed a possibility of mixed strain infection due to relatively high (27) heterozygotic SNP content in one of each patients' sample. Phylogenetic analysis demonstrated most of the listed findings and revealed two additional genetic relations in a sample set which might signify a possible involvement in the same transmission network.

Conclusions. WGS provided essential information that allowed to differentiate TB relapse cases from reinfection, making further studies of mycobacteria-related relapse provoking factors possible.

Acknowledgements. The authors would like to thank BMC core facility Genome centre for their contribution in sequencing. This study was supported by Latvian National Research Programme VPP "BIOMEDICINE" and Rīga Stradiņš University grant No. 23030102. The authors declare the absence of conflict of interest.

Insights on senescence and therapy-related adverse effects in tuberculosis patients

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Background. Tuberculosis treatment, especially for multi-drug resistant tuberculosis (MDR-TB), is often accompanied by side effects such as nephrotoxicity, ototoxicity and vestibulotoxicity, which in some cases may be irreversible and lead to therapy intolerance. Also, tuberculosis and the associated long-term chemotherapy could have additional effects on human health including ageing process. On the other hand, immune senescence and age-related decline of immune competence impacts the risk of tuberculosis.

Objective. The aim of the study was to explore the possible relation of senescence biomarkers and risk factors of adverse reactions in tuberculosis patients.

Methods. We examined clinical information which was obtained for 52 MDR-TB patients in cooperation with the Centre of Tuberculosis and Lung Diseases, Latvia. As a control group, age-matching healthy individuals were used. DNA samples and complementary data were obtained from national biobank Genome Database of Latvian population. The study was approved by the Central Medical Committee of Ethics in Latvia (No. 01-29.1/1). Relative mitochondrial DNA (mtDNA) count and telomere length (TL) were measured using RT-PCR. Statistical analyses of the data were carried out using XLSAT by Addinsoft software. Quantitative and qualitative variables were compared using multivariate analysis of variance (ANOVA), logistic regression and the principal component method of Factor Analysis for Mixed Data (PCAmix).

Results. Tuberculosis patients had significantly shorter telomeres ($p < 0.0001$) and higher mtDNA count than healthy individuals ($p < 0.01$); of all the factors considered, only tuberculosis status was able to explain these changes. Duration of MDR-TB treatment slightly correlated with TL and mtDNA count ($p < 0.05$). Neither ANOVA nor PCAmix could adequately explain the occurrence of treatment adverse effects in all TB patients, as in best scenario first two factors (F1 and F2) of PCA model could explain only 22.9 % of the total variation. The duration of treatment, the number of doses received, and the age of the patient in this study had no effect on the onset of ototoxicity or nephrotoxicity. However, the onset of ototoxicity was more influenced by amikacin ($p < 0.05$) and alcohol or drug dependence increased the likelihood of nephrotoxicity. Also, comorbidities (hepatitis and HIV) showed association with side effects.

Conclusions. A possible association between tuberculosis infection and immune senescence has been found. The age, lifestyle and treatment parameters did not significantly influence the onset of adverse effects. Additional studies on the genetic background and ageing processes may help to clarify the connection between tuberculosis and immune senescence.

Features of clinical and biochemical changes and indicators of APRI and FIB-4 in patients with chronic viral hepatitis C

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Background. Chronic viral hepatitis C (CVHC) is a common and dangerous liver disease. Viral liver damage progresses from inflammation to the development of fibrosis and cirrhosis. The degree of liver fibrosis is important for determining therapeutic tactics and further observation.

Objective. Define the features of the clinical course, laboratory changes, APRI-test and FIB-4 scores in patients with CVHC.

Methods. 287 CVHC patients, divided into three groups by genotypes (1b, 2, 3a), and 55 healthy individuals were examined. The calculation of the APRI-test and FIB-4 scores was carried out using the Android application developed by us. Statistical processing was carried out in Microsoft Office Excel 2010 and IBM SPSS Statistical 23.

Results. The study showed that young people (47.74 %), men (66.20 %), those with genotype 1b (52.3 %), moderate liver fibrosis (F2 – 31.25 %) and minimal process activity (73.17 %) ($p < 0.05$) prevailed among the patients with CVHC. Asthenic-vegetative syndrome (81.88 %) and enlarged liver (76.26 %) ($p < 0.05$) were the most common diagnoses. An increase in the number of lymphocytes, ESR, ALT, AST and GGT levels relative to the indicators of the comparison group ($p < 0.05$) was also observed.

Patients with genotype 1b, as compared to the total sample, were more frequently diagnosed with telangiectasias, glomerulonephritis, those with genotype 2 – with ischemic heart disease (IHD) and cardiofibrosis, and less often – with an enlarged liver ($p < 0.05$), anaemia was not observed. The patients with genotypes 1b and 2 had higher protein levels, alkaline phosphatase levels were lower in patients with genotype 1b and 3, and creatinine levels – in those with genotypes 1b and 2 ($p < 0.05$).

In the total sample, the FibroTest for METAVIR correlated with the APRI test (0.71 (0.44–1.37); $P = 0.426$; $p = 0.000$) and FIB-4 (1.55 (0.98–2.65); $P = 0.558$; $p = 0.000$). The De Ritis ratio only correlated with FIB-4 ($P = 0.431$; $p = 0.000$).

Conclusions. Asthenic-vegetative syndrome, enlarged liver, increased number of lymphocytes and elevated ESR and transaminases were the most prevalent clinical and laboratory features. Telangiectasias and glomerulonephritis were more commonly observed in genotype 1b, IHD and cardiofibrosis – in genotype 2, whereas anaemia was not observed. Elevated blood protein levels were diagnosed in patients with genotypes 1b and 2, decreased alkaline phosphatase levels – in those with genotypes 1b and 3, and creatinine levels – in those with genotypes 1b and 2. All non-invasive methods for diagnosing liver fibrosis correlated with each other.

Acknowledgements. The authors declare the absence of conflict of interest. The current research was funded by a grant of the Scientific Society of Students and PhD students of Sumy State University.

Diagnosis of tick-borne infections by PCR

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Background. Lyme disease is a naturally-occurring disease mainly caused by *Borrelia burgdorferi*. The problem is of outstanding importance since 2017, as Western Ukraine, particularly Ternopil region, is a territory endemic of Lyme borreliosis.

Objective. To estimate the quantity of infected ticks removed from the skin of the bitten children.

Methods. Altogether, 736 patients were enrolled in the examination. The survey was conducted in the framework of the research work “ Study of epidemiology, pathogenesis and clinic Lyme borreliosis in endemic regions of Ukraine including Ternopil region and improvement of its diagnosis, therapy, rehabilitation measures and prevention” which is a part of the common Ukrainian-Polish project.

Examination was carried out in the Laboratory of the Centre for the Study of Lyme borreliosis and other ticks' infections of I. Horbachevsky Ternopil National Medical University.

Results. 267 infected ticks (36.6 %) were found on the children's skin. PCR test revealed that *B. burgdorferi sensu lato* – infected –130 (17, 6 % of all the ticks), *Anaplasma phagocytophilum* –120 (16.3 %), *B. miyamotoi* 11 (1.5 %) were infected. The carriers of *Borrelia Burgdorferi sensu lato* and *Anaplasma phagocytophilum* were, as follows:- 23 (3.1 %) insects, *Borrelia miyamotoi* and *Anaplasma phagocytophilum* – 4 (0.5 %) ticks.

Conclusions. The implemented approach to estimation of infected ticks helps to make prognosis of disease development in the future.

Lyme disease dissemination in Ukraine

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Background. The natural focus of Lyme disease (LD) in Ukraine are caused by *Borrelia burgdorferi sensu lato Spirochaeta* Complex and are spread all over the territory.

Objective. Define epidemiological peculiarities of Lyme disease in Ukraine and Sumy region.

Methods. Used materials of Sumy Region Laboratory Centre of Ministry of Health Care of Ukraine (State statistical reporting (ф. №1) from 2000 to 2018).

Results. Starting from 2002, an absolutely positive incidence of LD increase has been observed in Ukraine: in 2000 were registered 58 cases of LD (0.12 per 100 000 of the population), in 2018 – 5418 cases (12.78 per 100 000 of the population) with peaks of activity in 2009 (2.12 per 100 000), 2013 (4.25 per 100 000 of the population), 2015 (7.96 per 100 000 of the population), i.e. during this period, the index increased 93.4 times. A high incidence of disease is observed in city of Kyiv, as well as Chernihiv, Cherkassy, Sumy, Lviv regions.

The first case of Lyme disease in Sumy region was officially registered in 2002. In 1999 and 2001, the registration shows one case a year. The number of cases in Sumy region in 18 years increased 75.5 times – from 0.31 per 100 000 of the population in 2003 to 23.04 in 2018 – on the average for Ukraine – 12.78.

The highest incidence is in Krasnopillia region – 38.37 per 100 000 of the population; Trostianets region – 34.69; Krolevets region – 31.95; Sumy region – 30.21; Nedryhailiv region – 25.02.

Working-age women (57.6%) and city population prevail among the patients hospitalized with Lyme disease.

The peak of ticks' activity is in May and June in Sumy Region and all over Ukraine. The greatest number of medical consultations is in June, however, ixodic ticks remain active almost up to first decade of November all over the country.

Conclusions. LD incidence in Sumy region and Ukraine is on the rise. During 2000–2018, the incidence increased 93.4 times (Ukraine) and 75.5 times (Sumy region). A high incidence of disease is observed in Krasnopillia, Trostianets, Krolevets, Sumy, Nedryhailiv regions. Working-age women and city population prevail among the patients.

Prevalence of isoniazid mono-resistant TB in Latvia

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Background. Tuberculosis (TB) is still a global public health problem. Isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) are drugs for the treatment of drug-sensitive TB (DS-TB). Isoniazid is a core drug for the treatment of DS-TB, and has the highest bactericidal activity against *Mycobacterium tuberculosis* (Mtb). In case of mono-resistance to H treatment, the regimen should be changed and becomes more toxic and less effective. On average, 8 % of TB cases worldwide are H mono-resistant. Data on the prevalence of H mono-resistant TB are not summarized and reported in Latvia.

Objective. The aim of the study was to determine the prevalence of H mono-resistance in Latvian TB patients and to compare results with global data.

Methods. Retrospectively, the data on drug susceptibility pattern (DST) of Mtb isolates from Latvian TB patients diagnosed from January 2015 to December 2019 were obtained from Mycobacteriology Laboratory of Centre of Tuberculosis and Lung Diseases of Latvia. Resistance to H was defined as identification of Mtb genomic mutations responsible for resistance to high concentrations of H (katG gene) and responsible for resistance to low concentrations of H (inhA gene) and/or detection of phenotypic resistance to H using critical drug concentrations (on BACTEC culture media 0.1µg/ml, on Lowenstein-Jensen culture media 0.2µg/ml and 1µg/ml). For each patient, only one DST result confirming resistance to H was counted. Data were entered in MS Excel, and resistance to isoniazid was analysed by SPSS 26 and MS Excel.

Results. Overall, DST from 2372 patients Mtb isolates were included in analysis. Mono-resistance to H was detected in 78/626 (12 %) patients in 2015, in 68/575 (12 %) patients in 2016, in 66/469 (14 %) patients in 2017, in 51/352 (14 %) patients in 2018, and in 47/350 (13 %) patients in 2019 ($p = 0.080$). In those, mono-resistance to H mutations in katG gene were identified in 15/51 (29 %) in 2018, and in 24/47 (51 %) in 2019. Mutations in inhA gene were detected in 9/51 (18 %) in 2018 and in 5/47 (11 %) in 2019.

Conclusions

1. The prevalence of mono-resistance to H in Latvian TB patients is higher compared to the average in the world;
2. During last 5 years, mono-resistance to H in Latvia has not significantly increased;
3. Most of patients with genotypic DST available had mutations in katG gene responsible for resistance to high concentrations of H.

Variability of complications of liver cirrhosis associated with hepatitis B and C viruses

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Background. In Ukraine, viral hepatitis C (HCV) is dominant in the structure of infectious pathology in terms of its negative impact on public health. The course of the disease and its effects can be influenced by a number of factors, including the presence of concomitant liver damage. The number of diseases of this pathology is 5–6 times higher than the official statistics.

Objective. The study was aimed at exploring the peculiarities of cirrhosis associated with virus hepatitis

Methods. The study examined 54 patients treated in the Sumy regional infectious hospital during 2015–2019.

Results. Among the surveyed, 84% of cases were divided, as follows: viral hepatitis C, viral hepatitis B 7.4 % co-infection B+D 5.6 %. In the surveyed group prevailed men (62.9 %) and city residents (70.4 %), the average age of patients was 44.2 ± 0.2 years. Probable pathway of infection: during medical interventions (18.5 %); use of intravenous drugs, donation (7.4 % each); dental procedures (11.1 %); blood transfusion or its constituents (5.5 %); professional activity (medical workers) (1.8%); not found – in 48.3 % of the surveyed.

Patients with minimal activity (68.5 %) were 3.7 times less frequent – moderate (18.5 %), 6.2 times – expressed (11.1 %). Decompensated cirrhosis (according to Child Pugh's classification) is registered in 3.7 % of people, subcompensated – in 37 %, and compensated – in 59.3 % of the patients. Comorbidity was detected in all the patients, every third patient had metabolic cardiomyopathy (40.7 %), hypertension (35.1 %), gall-stone disease (31.5 %), whereas heart failure and encephalopathy were less common (respectively – 29.6 % and 14.8 %) in the patients.

Ultrasound examination of abdominal organs revealed the following: increase in liver size (29.6 %), increase in echogenicity (77.7 %), increase in portal vein size (31.4 %), vascular compaction (38.8 %), sealing of the gallbladder wall (57.4 %); enlargement of the spleen (53.7 %) and enlargement of the splenic vein (77.7 %); the signs of portal hypertension (70.4 %). Varicose veins of the oesophagus were diagnosed in 31.5 % of the patients, oedema-ascitic syndrome – in 24.1 %. Cirrhosis was accompanied by thrombocytopenia (33.3 %), anaemia (14.8 %) and leukopenia (9.3 %).

Conclusions. Among the patients with liver cirrhosis associated with hepatitis virus, prevailed middle-aged men living in city. The probable route of infection in most patients could not be established. Minimal activity and severity of cirrhosis (according to Child Pugh) A and B. Predominant metabolic cardiomyopathy, arterial hypertension, and gallstone disease were associated with the condition. Complications included enlargement of a splenic vein, seal of vessels of a liver, consolidation of a wall of a gall bladder, portal hypertension, splenomegaly and varicose veins of the oesophagus, thrombocytopenia.

What do medical professionals know about vaccination against shingles?

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Background. In the Shingles Prevention Study, a significant reduction in HZ (51 %) was observed among vaccinated adults ≥ 60 years of age. The zoster vaccine has demonstrated the ability to reduce the incidence of postherpetic neuralgia (66.5 %) (PHN), as well [1, 2, 3]. The population of Lithuania is aging and the risk of HZ and PHN is on the increase. Therefore, our physicians must have sufficient knowledge about vaccination and its benefits in the prevention of this infection.

Objective. The aim of our study was to evaluate the knowledge of medical specialists about vaccination against HZ and to establish a relation with the age of physicians.

Methods. An internet survey was conducted in 2019, December in Lithuania. In total, 331 medical specialists filled in the anonymous questionnaire. Statistical analysis was performed using IBM SPSS Statistics 24.0 software.

Results. We formulated some basic statements about vaccination. A response was a choice of a single option from the following: “yes”, “no” or “I don’t know”. The results are summarized in the table below. Correct answers are highlighted.

Table. The statements about vaccination and the results of poll

Statement	Yes	No	I don't know
1. Vaccination against shingles is effective in preventing severe complications of this infection	282 (85.2 %)	3 (0.9 %)	46 (13.9 %)
2. Vaccination against shingles is an effective treatment for acute shingles	55 (16.6 %)	215 (65.0 %)	61 (18.4 %)
3. Patients with acute shingles should wait at least 12 months in order to be vaccinated against HZ	38 (11.5 %)	78 (23.6 %)	215 (64.9 %)

We established a statistically significant ($p < 0.05$) relation between the age and the responses. Older physicians (≥ 55 years old) more rarely knew that vaccination against shingles is effective in preventing severe complications of HZ. In addition, they less frequently realised that vaccination against shingles is not an effective treatment for acute infection.

Conclusions. We have to acknowledge that there are medical specialists who do not know that vaccination is not used for treatment but only as a preventive method. In addition, a significant number of doctors do not know that vaccination is effective to prevent serious complications of HZ. This lack of knowledge is observed statistically significantly more frequently among the older physicians (≥ 55 years old). We consider that medical specialists should be more interested in vaccination because it is an effective preventive method of this serious infection.

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Characteristics and intrahospital mortality of community-onset sepsis and septic shock patients in a tertiary healthcare facility in Latvia: a retrospective, single-centre, cohort study

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Background. Sepsis is a life-threatening condition characterized by inflammatory immune response due to infection, which may lead to organ failure and death. Community-onset sepsis (COS) is a major healthcare challenge and an economic burden. Analysing the characteristics of COS can improve timely diagnostics, thereby decreasing mortality.

Objective. The aim of the study was to assess the clinical presentation, microbiological data and outcomes of the COS patients admitted to Pauls Stradiņš Clinical University Hospital (PSCUH).

Methods. During a 12-month retrospective cohort study (September 2017 to September 2018) we identified 395 adult patients admitted to PSCUH with sepsis-related ICD-10 codes upon discharge. Using consensus definitions, we enrolled 289 COS cases for further analysis. We collected data on demographics, clinical presentation, risk factors, time-to-culture (TTC), blood culture (BC) turn-around-time (TAT) and intrahospital mortality.

Results. The median age in the cohort was 74 years (IQR 59.0–82.5), equal gender distribution with median Charlson Comorbidity Index of 6 points (IQR 4–8). Septic shock was present in 15.6 % of the cases. The overall intrahospital mortality was 47.2%, reaching 86.7 % in septic shock cohort. Infectious diseases as the reason of hospitalization were stated in 50.8 % of the cases, nevertheless, in 12.2 % of the patients with infection blood cultures (BC) were not performed, and in 36.2 % of COS cases antimicrobial therapy was initiated prior to the BC. Furthermore, patients lacking BC at the admission were significantly older ($p = 0.004$). The most common origin of COS was pneumonia (22.7 %), followed by urinary tract infection (16.3 %). From 173 BC performed, 59.0 % returned positive. The most commonly isolated pathogens were *Staphylococcus aureus* MS, *Escherichia coli* and *Streptococcus pneumoniae* in 47.1 %, 27.5 % and 14.7 % of the cases, respectively. The rate of positive BC was significantly higher in COS survivors ($p = 0.045$). Median TTC was 4.8 hours (IQR 2.8–16.4). Median TTC in COS patients initially admitted for non-infectious reasons was longer, reaching 5.4h (IQR 3.6–18.6). Median TAT was 93.7 h (IQR 78.3–115.0). TTC had no statistically significant correlation with the patients' age, comorbidities, previous exposure to long-term healthcare facilities, clinical presentation, source of infection or presence of septic shock.

Conclusions. We found intrahospital mortality remarkably higher than reported in similar European sepsis cohorts. However, the number of patients was limited and data collection will be continued to assess a larger population and improve data accuracy. Timely blood cultures could improve patient outcomes and should be emphasized, especially in the geriatric population.

Acknowledgements. The authors declare the absence of conflict of interest.

Prevalence of resistant *M. tuberculosis* strains at Riga East Clinical University Hospital's Centre of Tuberculosis and Lung Diseases according to phenotypic resistance testing results

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Background. The prevalence of multidrug-resistant tuberculosis remains relatively high despite the advances in diagnosis and treatment. The resistance to various anti-tuberculosis drugs varies across different regions, therefore, clarifying the current situation of susceptibility to various commonly used anti-tuberculosis drugs in Latvia is crucial.

Objective. The aim of the study was to determine the prevalence of resistance to the most commonly used anti-tuberculosis drugs in Latvia.

Methods. Data on the resistance of *M. tuberculosis* to first- and second-line anti-tuberculosis drugs tested by phenotypic drug-sensitivity tests was obtained from the mycobacterial laboratory of Riga East Clinical University Hospital's Centre of Tuberculosis and Lung Diseases. The resulting data was then analysed using Microsoft Office Excel.

Results. 3869 phenotypic resistance test results were included in the statistical analysis (2223 samples tested for resistance against first-line agents, 1646 against second-line agents). Resistance against at least one of the first- or second-line agents was detected in 841 (21.73 %) of the samples. Resistance against the first-line drugs were discovered in 543 samples (24.42 %, $n = 2223$), and 298 samples proved resistance towards the second line agents (18.10 %, $n = 1646$). Resistance was most commonly detected against the second line agent Kapreomycin (37.75 %, $n = 204$) and the first line agents Isoniazid (34.55 %, $n = 767$) and Pyrazinamide (34.55 %, $n = 191$).

Conclusions. Resistance was most commonly found against capreomycin and the first-line drugs: isoniazid and pyrazinamide. Additional studies should be conducted to determine the most common combined resistance.

Acknowledgements. The research did not receive any funding.

GASTROENTEROLOGY & NUTRITION

Low prevalence of Barrett's esophagus

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Background. Barrett's esophagus (BE) is an acquired esophageal condition, in which intestinal-type epithelium replaces the stratified squamous epithelium. BE is the only known precursor of esophageal adenocarcinoma. Gastroesophageal reflux is considered the predominant risk factor for BE; other risk factors are male gender, older age, obesity and smoking. The prevalence is difficult to ascertain, and it varies from 1.3 % to 1.6 % in European studies and 8.6 % in those carried out in the United States.

Objective. To determine the prevalence of BE among patients who have undergone upper gastrointestinal endoscopy.

Materials and methods. Patients who had an upper endoscopy at Digestive Diseases Centre "GASTRO" from May 2019 to July 2019 were included in the study. The presence of BE was assessed in two ways: endoscopic (the Prague C&M classification was not used) and histological. Endoscopic reports also included the presence of hiatus hernia, esophagitis and esophageal cancer. Symptoms were determined from questionnaire responses.

Results. The study included 1879 patients. The mean age of the patients with histologically confirmed BE was 56.8 (\pm 14.6) years, 50.0 % (n = 14) were male. The incidence of BE was 1.1 % (n = 20) – based on endoscopy, and 1.5 % (n = 28) – based on histology. Other findings included esophagitis – 15.2 % (n = 286) and esophageal cancer – 0.1 % (n = 1) of all the patients. Hiatus hernia was diagnosed in 10.2 % (n = 192) of all the patients and 46.4 % (n = 13) of BE patients. Of the 28 patients, 46.4 % (n = 13) had reflux symptoms (heartburn/regurgitation) and 50.0 % (n = 14) had dyspepsia.

Conclusions. The study confirms the low prevalence of BE. BE based on histology had a higher prevalence than shown by endoscopic reports. It could be caused by inadequate biopsies – taken from proximal gastric mucosa. More than a half of the patients did not report any symptoms.

Age-gender characteristics of pancreatic cancer incidence in Kazakhstan

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Background. According to the WHO about 460 thousand new cases of pancreatic cancer (PC) are registered in the world, moreover according to IARC forecasts, in 2040 more than 815 thousand people are expected to suffer from this illness. Numerous studies have identified the relationship of the incidence of PC with various exogenous and endogenous factors. The study of the epidemiology of PC has scientific and practical relevance, since it allows monitoring ongoing activities and assessing the impact of possible causal risk factors.

Objective. To study the incidence of PC in the country as a whole, taking into account age and sex.

Methods. The source used was data from oncological institutions on new cases of PC (form 7), as well as population data for 2009–2018. A retrospective study using descriptive and analytical methods of epidemiology was carried out. The age-specific incidence rates (ASIR) were calculated at 100 000.

Results. In the republic, 9 891 new cases of PC were recorded during this period: of these, 5 057 were men (51.1 %) and 4 834 (48.9 %) were women. The average annual incidence of PC was 6.1 ± 0.1 ‰_{0000} for men and 5.5 ± 0.1 ‰_{0000} for women, while the overall incidence was $1.1 \div 1.0$, and the largest difference in 50–59 (table).

Table. ASIR of PC in Kazakhstan, 2009–2018

Age	Both sexes (T, %)	Male (T, %)	Female (T, %)	M ÷ F
< 50	0.77 ± 0.02 (–2.6)	0.92 ± 0.03 (–2.2)	0.62 ± 0.04 (–3.3)	$1.5 \div 1.0$
50–59	13.2 ± 0.4 (–0.9)	17.5 ± 0.8 (–1.7)	9.6 ± 0.2 (+0.1)	$1.8 \div 1.0$
60–69	31.3 ± 0.6 (+0.5)	39.9 ± 0.9 (+0.7)	25.1 ± 0.7 (+0.3)	$1.6 \div 1.0$
70+	42.9 ± 1.1 (+0.4)	51.5 ± 2.3 (–0.6)	38.6 ± 1.1 (+1.1)	$1.3 \div 1.0$

The crude incidence of PC among the entire population tended to increase from 5.3 ± 0.2 ‰_{0000} (2009) to 6.0 ± 0.1 ‰_{0000} in 2018 ($t = 3.54$; $p = 0.000$, $R^2 = 0.3445$). Trends among men ($t = 1.65$, $p = 0.099$, $R^2 = 0.0985$) and among women ($t = 2.22$, $p = 0.027$, $R^2 = 0.333$) also grew.

ASIR of PC are characterized by unimodal growth with a peak in the older age group (70 and older) – 51.5 ‰_{0000} and 38.6 ‰_{0000} , respectively for men and women, while incidence trends had different patterns (see table).

Conclusions. The identified age- and sex-related epidemiological aspects of PC have to be used to conduct comprehensive and targeted interventions to strengthen prevention and reduce incidence.

Acknowledgments. The authors report the absence of conflicts of interest and express appreciation of the contribution from the Ministry of Healthcare of the Republic of Kazakhstan – the provided data and support of the public association “Central Asian Cancer Institute”.

Tumour regression after neoadjuvant chemotherapy in resectable gastric cancer

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Background. Gastric cancer is one of the most widespread cancers worldwide. It is the fifth most common and the third deadliest cancer. There is a significant global variation in incidence – the highest rates are seen in Eastern Asia, Eastern Europe and South America, while the lowest rates are in North America and Western Europe. Diagnostic and staging investigations should include physical examination, blood count, liver and renal function tests, endoscopy and CT scan of the thorax, abdomen and pelvis. For patients with stage IB-III gastric cancer radical gastrectomy is indicated and perioperative chemotherapy with a platinum/fluoropyrimidine combination is recommended. Pathologic evaluation of tumour response should be done after neoadjuvant chemotherapy (NAC) and surgery.

Objective. The aim of the study was to evaluate the effect of neoadjuvant chemotherapy on pathologic response.

Methods. Retrospective study included 43 patients with histologically diagnosed gastric cancer and prescribed NAC. The data were taken from Pauls Stradiņš Clinical University Hospital oncological council reports and included data from 2017 to 2019. Age, gender, chemotherapy regiment and pathologic response were documented. Collected data were statistically analysed in *IBM SPSS Statistics 22.0*.

Results. 17 (39.5 %) of enrolled patients completed NAC and underwent surgery. In a further study, we analysed only data of these patients. 13 (76.5 %) were men, 4 (23.5 %) – women. The average age of patients with gastric cancer was 63.6 ± 10.3 (min = 41, max = 76) years. Three chemotherapy regiments were used in these patients – FLOT (fluorouracil, leucovorin, oxaliplatin, docetaxel) in 14 (82.3 %) patients, FLO (fluorouracil, leucovorin, oxaliplatin) in 1 (5.9 %) patient, fluorouracil and cisplatin in 2 (11.8 %) patients. Pathomorphosis was assessed in 8 (47 %) patients and all of them achieved pathologic response. 6 (75 %) patients received FLOT chemotherapy regiment and had poor pathologic response. 2 (25 %) patients had pathologic complete response (pCR). One patient who achieved pCR was treated with FLOT chemotherapy regiment and the other patient – with fluorouracil and cisplatin. In total, FLOT was used in 7 (87.5 %) patients, while fluorouracil combined with cisplatin was used in 1 (12.5 %) patient.

Conclusions. In this study, neoadjuvant chemotherapy had an effect on pathologic response. The majority of these patients had poor pathologic response. FLOT chemotherapy regiment is used more often than fluorouracil combined with cisplatin.

Capsule endoscopy in LUHS Kaunas Clinics from 2013 to 2019

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Background. Gastrointestinal bleeding is the most common indication for capsule endoscopy. It is relatively new, painless and well tolerated gastrointestinal tract examination method, hence, there is a demand for analysis. Different hospitals and clinics have a variety of uses for this method, so in this study experience of Kaunas Clinics in Lithuania was evaluated.

Objective. To analyse capsule endoscopy indications and findings.

Methods. A retrospective study evaluating indications and findings of capsule endoscopy was carried out. 25 patients who were examined using capsule endoscopy in the hospital of LUHS Kaunas Clinics from 2013 to 2019 were included. All the information was obtained from medical records.

Results. There were 10 (40 %) women and 15 (50 %) men who had had capsule endoscopy, their average age – 60.04 years, $s = 13.25$. Generally, most patients had symptoms of gastrointestinal bleeding – active bleeding was present in 17 (68 %) of the patients (melena 10 (40 %), blood in the stool 6 (%), bloody vomit 4 (%)), 10 (40 %) were feeling weakness, 9 (36 %) were suffering pain. A half (52.4 %) of these patients had RBC transfusions. Therefore, the main indication for CE was unspecified GI bleeding, one patient had CE due to familial adenomatous polyposis.

Various tests besides capsule endoscopy were carried out. All of the patients had esophagogastroduodenoscopy and colonoscopy before CE, some of them – CT angiography 10 (19.2 %). The most common finding in capsule endoscopy was small intestine angiodysplasias 13 (52 %), others included colon angiodysplasias 1 (4 %), peptic ulcer 2 (8 %), colon polyps 2 (8 %), haemorrhage per diapedesem 2 (8 %), phlebectasis 1 (4 %), for 6 (24 %) patients CE was not informative or there were no changes in gastrointestinal tract. The possible bleeding site was found in 18 (72 %) of CE patients. After capsule endoscopy, 4 (16 %) of these patients had enteroscopy to either confirm the diagnosis or for treatment purposes, 4 (16 %) patients were further examined by SPECT scintigraphy, 1 (4%) due to unclear diagnosis had had both enteroscopy and SPECT scintigraphy. After the examination, in 3 out of 5 patients who had enteroscopy and in 4 out of 5 who had SPECT scintigraphy, the same results as in CE were confirmed, others had additional findings.

Conclusions. The main indication for capsule endoscopy was gastrointestinal bleeding. Capsule endoscopy is a highly effective and safe diagnostic method, which also assists in determining the need for interventional procedures.

Acknowledgements. The authors declare nothing to disclose: ID, PS, MU – no conflict of interest.

Decreased pepsinogen level in relation to presence of menopause in the GISTAR study population in Latvia

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Background. Studies suggest that female hormones reduce the risk of gastric atrophy and subsequently gastric cancer.

Objective. The aim of the current study was to analyse decreased Pepsinogen (Pg) level in relation to menopause.

Methods. Women aged 40–64 years from the GISTAR study in Latvia who completed a questionnaire, were tested for PgI, PgII by latex-agglutination test (Eiken Chemical, Japan) and *Helicobacter pylori* (*H. pylori*) IgG antibodies (Biohit, Finland). The presence and age at the onset of menopause (< 50 or ≥ 50 years), current/previous hormonal replacement therapy (HRT) was compared between women with and without decreased Pg (PgI/PgII ≤ 3 and PgI ≤ 70 ng/mL). A multivariate logistic regression was built for decreased Pg and menopause, adjusting for current/previous HRT, age (≤ 50 or > 50), level of education, income, smoking, *H. pylori*.

Results. A total of 911 women (the mean age 51.9, SD ± 6.8 years) were included in the study. Menopause was reported by 54.0 %; current HRT – by 4.3 %. Decreased Pg level was detected in 301 women and was observed more often in women with menopause compared to women without menopause (35.6 % vs 30.1 % respectively, $p = 0.08$). Women currently on HRT were less likely to have decreased Pg (17.9 % vs 33.6 % respectively, $p = 0.04$). In multivariate analysis, decreased Pg was no longer associated with menopause (OR = 1.1; 95 % CI 0.7–1.7; $p = 0.6$), inversely associated with current HRT (OR = 0.5; 95 % CI 0.2–1.1; $p = 0.09$), but had a strong association with *H. pylori* (OR = 2.8; 95 % CI 2.0–3.9; $p < 0.001$) and age > 50 (OR = 1.7; 95 % CI 1.3–2.3; $p = 0.001$).

Conclusions. Our findings suggest that menopause *per se* is not associated with decreased pepsinogen, however, protective effect of HRT against gastric atrophy should be studied in a greater detail among the women on HRT.

Acknowledgements. The study was supported by Latvian Council of Science, project No. lzp-2018/1-0135.

The role of the family doctor in invitation to do colorectal cancer screening

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Background. The aim of screening is to discover latent disease in the population in order to detect the disease in its early stages. The colorectal cancer screening method used in Latvia is the examination of occult blood in faeces. The target group is people who are 50–74 years old. There are two main ways of screening accepted in Latvia – family doctor referral to the laboratory or an envelope provided by the family doctor, which includes a test tube and instructions for the patient. In the latter case, the test must be returned to the family doctor

Objective. The objective of this study was to evaluate the role of the family doctor as a motivating factor for colorectal cancer screening.

Methods. The data was collected from November 2019 to January 2020. The study population were patients from a certain family doctor's practice, who have performed a colorectal screening test at least once. All participants gave official consent to being part of the research. A non-anonymous, self-administered questionnaire was used for data collection. The questionnaire consisted of 11 single-choice questions, 1 multiple-choice and 1 free-response question. The study was approved by the Ethics Committee.

Results. A total of 244 patients filled the questionnaire. Out of the 244 patients, 73 were male and 171 were female, the average age was 63 years. From those, 13 (5.3 %) visited their family doctor once a month, 74 (30.3 %) once every six months, 86 (35.2 %) once a year, 19 (7.8 %) once every two years, 52 (21.3 %) less than once every two years. Frequency of the colorectal cancer screening – 96 (39.3 %) people had it once, 123 (50.4 %) had it twice, 22 (9%) three times, and 3 (1.2%) people more than four times. The majority – 243 (99.6 %) people learned information about colorectal screening from the family doctor, only 1 (0.4%) learned about it from the media. Motivating factors to do colorectal screening included family doctor in 208 (36.9 %) cases, for 120 (21.3 %) people the fact that test is free of charge, in 82 (21.3 %) cases – medical assistant/nurse, in 3 (0.5 %) cases – other doctors, in 28 (5 %) cases – the fact that test is done at home, in 96 (17 %) cases – the simplicity of the test, in 24 (4.3 %) cases – recommendations from friends, in 3 (0.5 %) cases – other reasons.

Conclusions. The family doctor is the main motivating factor for patients to take part in colorectal cancer screening. Therefore, the family doctor represents the most important element of the screening programme.

The ability of gold nanoparticles sensors and metal oxide sensors to differentiate gastric cancer patients from healthy individuals

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Background. The detection of gastric cancer at an early stage is significant in the successful treatment of the disease. The analysis of volatile organic compound (VOC) from breath samples using sensors potentially is a new way to perform a rapid, non-invasive and inexpensive cancer screening method.

Objective. To compare the ability of gold nanoparticles sensors (GNP) and metal oxide sensors (MOX) to differentiate VOC profiles in gastric cancer patients from healthy individuals.

Methods. 25 healthy individuals (did not show any signs of cancer and were not examined) and 36 gastric cancer patients (had histologically confirmed gastric adenocarcinoma) exhaled in the four prototype devices – No. 1 – No. 4. Altogether 30 sensors: 8 GNP, 14 MOX digital, 8 MOX analogue sensors were included in each of the device. The ability of the sensors to differentiate gastric cancer patients from the healthy population was compared using ANOVA test for mean values of sensor readings. The level of statistical significance was set at $p < 0.05$.

Results. The device No. 4 demonstrated the best ability to differentiate between gastric cancer patients and healthy individuals: out of 30 sensors, 11 sensors (7 GNP sensors, 4 MOX digital) showed a positive result. Device No. 3: 8 sensors (2 GNP, 6 MOX digital) are capable of detecting gastric cancer patient. Sensors on both devices that show a statistically significant difference between both groups: GNP4, GNP8, ZMOD44103A, ZMOD44101B, ZMOD44102B, ZMOD44103B. Also, in device No. 2 GNP4 ($p = 0.0369$) (coincides with device No. 3, 4), GNP6 ($p = 0.0115$), TGS8100 ($p = 0.022$) showed a positive result. However, device No. 1 showed that only the GNP3 sensor has a positive result ($p = 0.0205$).

Conclusions. GNP and MOX sensors have shown potential to detect VOC profiles in gastric cancer patients. However, standardization of the device readings is required since not all the devices have provided equally good results.

Acknowledgements. The work was supported by FLPP (Fundamental and Applied Research Projects) Programme in Latvia, project No. lzp-2018/2-0228 "Volatile organic compounds for potential application in gastric cancer screening".

Characteristics and outcomes of peptic ulcer bleeding in different age and gender groups

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Background. Peptic ulcer bleeding (PUB) is one of the most common medical emergencies admitted to hospitals around the world, with a significant morbidity and mortality rate.

Objective. The aim of the study was to investigate the PUB according to age and gender differences and class of PUB.

Methods. Retrospective analysis of the medical records of patients over 18 years of age admitted to the Riga East Clinical University Hospital with acute PUB from August 2013 to September 2014. Bleeding severity on endoscopy was evaluated according to Forrest classification (classes Ia, Ib, IIa, IIb and IIc). We used Chi square test to assess differences between ages (grouped on 10 years) and gender. The level of significance was set at $p < 0.05$. Data was analysed using SPSS version 22.0.

Results. Out of 172 patients, 75 (43.6 %) were female and 97 (56.4 %) – male with the mean age 62.59 ± 17.80 years (Me = 62.5, IQR = 28.8; min 25, max 94). In the male group, the most common PUB was seen in the age group up to 50 years ($n = 35$; 36.1 %), in the female group – over 80 years ($n = 31$; 41.3 %). The most common PUB among males was duodenal PUB ($n = 53$; 52.5 % vs $n = 27$; 34.6 %), while among females – gastric PUB ($n = 48$; 61.5 % vs $n = 44$; 43.6 %). Significant differences were found between genders and ulcer localization ($p = 0.02$ for gastric and duodenal ulcer). No significant differences were found between genders in most common age groups and most common ulcer localization ($p = 0.38$ for women and $p = 0.22$ for male). The most common Forrest class among women was IIb ($n = 30$; 40 %), among men it was IIc ($n = 31$; 32 %). Forrest classes Ia and Ib were seen more often in men in all age groups ($n = 17$; 22.67 %). No relationships were found between genders and Forrest class ($p = 0.33$). The total number of deaths was 19 (11.0 %), ($n = 12$; 16.0 % female vs $n = 7$; 7.2 % male). The highest mortality was in the age group over 80 years ($n=7$; 58.3% female vs. $n = 4$; 57.1 % male). No significant differences were found between genders and mortality ($p = 0.07$).

Conclusions. The results of this study confirmed the important role of PUB in the mortality. The research findings are important for the growing number of elderly patients. Further studies are necessary for additional evaluation of ulcer ethology risks (e.g. smoking, medication use, family history of PUB) and successful PUB prevention.

***Helicobacter pylori* infection, cardiovascular disease and its risk factors in Latvia**

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Background. A higher prevalence of *Helicobacter pylori* (*H. pylori*) has been reported in individuals with cardiovascular disease (CVD).

Objective. Assess whether there is an association between *H. pylori*, CVD and its risk factors in Latvia.

Methods. 1855 participants aged 40–64 years completed a questionnaire and were tested for *H. pylori* IgG antibodies (Eiken Chemical, Japan) in the framework of the project “*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study” in Latvia. Gender, age, education, income and cardiovascular risk factors – decreased vegetable/fruit (≤ 400 g daily), increased salt intake (adding extra to food), < 150 min. moderate exercise weekly, smoking, ethanol (g/week), diabetes mellitus, blood pressure and BMI were compared for participants positive (HP+) and negative (HP-) for *H. pylori*, and with and without self-reported CVD. A multiple logistic regression model was built for CVD and HP+, including the factors above, additionally adjusting for history of peptic ulcer (associated with HP+ previously).

Results. HP+ was found in 1044 (56.3 %) participants. CVD was reported by 528 (28.5 %), of which myocardial infarction by 4.9 % and stroke 4.7 %. CVD was reported by 274 (26.2 %) of those HP+ and 254 (30.2 %) HP- ($p = 0.06$).

In multivariate analysis the association between self-reported CVD and *H. pylori* strengthened (OR 0.73; 95 % CI 0.57, 0.94; $p = 0.02$) in comparison to univariate analysis (OR 0.82; CI 0.67, 1.01; $p = 0.06$).

Conclusions. We found *H. pylori* to be inversely associated with self-reported CVD in contrast to most other studies showing either a positive or no association between *H. pylori* and CVD.

Acknowledgements. Study supported by Latvian Council of Science, project No. lzp-2018/1-0135 “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions.”

University students and nutritional habits

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Background. The immune system is affected by many endogenous and exogenous factors. Previous studies have showed that one of the main exogenous factors effecting the immune system is nutrition. Connection between immune system and nutrition is considered to be one of the main research topics starting from 20th century. Many researchers have demonstrated that some food components can modulate immune system response.

Objective. To evaluate students' nutritional habits in relation to the condition of their immune system.

Methods. The nutritional habits of the students from the Faculty of Medicine of the Lithuanian University of Health Sciences from 1st to 6th year of studies were analyzed using a questionnaire survey. Data analysis was performed using "SPSS 22.0 for Windows" and "Microsoft Excel" programs. χ^2 test was performed for qualitative analysis. Data was considered statistically significant when $p \leq 0,05$.

Results. The study involved a total of 319 students. Only about a half of the study participants consume food in accordance with the recommendations by WHO (frequency, consumption of water, no additional consumption of salt and sugar). Most students use the right amount of vegetables, choose poultry meat more often than beef and pork. The study also found a decreased consumption of fish products and over-use of sweets. 93.1 percent of students reported their health as good or very good. Only a small part of them often suffer from cold, allergies, while only isolated cases of oncological and autoimmune diseases were found.

Conclusions. Students' nutrition habits only partially correspond to WHO healthy dietary recommendations.

Acknowledgements. The authors declare no conflict of interests.

The impact of food consumption on sensor readings in a POC breath analysis device

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Background. Breath testing systems have proven to be valuable and accurate tools in laboratory settings, but a point-of-care breath analysis system can be used for various disease detection tests in an online mode (testing on-site and receiving the result immediately after). However, it is sensitive to everyday sources of VOCs like environmental factors, food and drink consumption before the test and hygiene routines of the tested person.

Objective. The aim of the current study was to test the impact of recent food consumption on breath testing system response (sensor response values).

Methods. A group of people (15 individuals) were recruited for an experimental study using a point-of-care modular breath analyser prototype, which included three modules with different type of sensors: 8 gold nanoparticle sensors (GNP) in development stage, 8 commercial analogue and 10 commercial digital metal oxide (MOX) sensors. The first test was carried out on breaths after 12 hours of fasting, then the participants were given a standardized meal and invited for a follow-up test 4 hours later to test for differences in the pattern of the breath analysis sensors. The readings of each sensor were analysed.

Results. When testing to see if all sensors ‘recognized’ breath (statistical tests between mean baseline (room) air readings and mean breath readings), 96.2 % of the sensors showed a significant difference ($p < 0.05$). When testing for difference in breath before and after food consumption, 12.5 % of GNP sensors, 87.5 % of analogue MOX sensors and 70.0 % of digital MOX sensors showed statistically significant differences.

Conclusions. The sensitivity to food consumption was dependent on the type of sensors. Most of the GNP sensors were not sensitive to food consumption. Most of the analogue MOX sensors discriminated well between breath before and after food consumption. Seven of the sensors in the digital MOX module showed statistically significant differences in readings of breath before and after food consumption. This leads to a conclusion that, although not all sensor readings seem to be affected by food consumption, it should be considered as a potential interference and taken into account when designing a proper sampling protocol.

Acknowledgements. This project has received funding from the European Union’s Horizon 2020 Research and Innovation Programme under grant agreement No. 824270, a grant from Latvia Research Council, project No. lzp-2018/2-0228 and funding from ERDF Postdoctoral Research Aid Project No. 1.1.1.2/16/I/001 research project No. 1.1.1.2/VIAA/2/18/270.

Detection of *Helicobacter pylori* by circulation in large cities of the Republic of Azerbaijan

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Background. *Helicobacter pylori* is the most studied factor leading to disability and mortality.

Objective. The aim of our study was to identify *H. pylori* in patients with various complaints related to the proximal gastrointestinal tract.

Methods. In the period from September 2017 to January 2020, 3 372 primary patients aged 18 to 70 years were examined at the clinics of Baku and Ganja; of which 2168 (64.2 %) were men and 1204 (35.7 %) women. Patients with oncological and functional pathologies ($n = 24$) were excluded from the study. The remaining 3348 patients underwent CLO-test, Endosfer-test for the detection of *H. pylori*.

Results. In patients with GERD, 63.5 % of the cases included in the study were positive (61 out of 96); in patients with Barrett's esophagus, positive results were found in 52.1% of the cases (24 out of 46 patients). In patients with superficial gastritis and bulbitis, 60.0 % were found positive (1192 out of 1986). In patients with erosive lesions of the gastroduodenal region, the tests were positive in 67.2 % of the cases (607 out of 903). With gastric ulcers, in 62.4 % (83 of 133 patients), with duodenal ulcers, in 80.4% (148 of 184 patients). No difference was found in the frequency of detection of *H. pylori* depending on the gender and age of the patients.

Conclusions. Thus, in the total group of patients, in 63.2 % of cases *H. pylori* was detected (2115 out of 3348 patients), which indicates an extensive prevalence of this infection in our population.

Acknowledgements. The authors declare the absence of conflict of interest.

BASIC MEDICAL SCIENCE

Antibiofilm activity of Ag nanoparticles against methicillin-resistant *S. aureus*

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Background. Currently methicillin-resistant *S. aureus* is one of the most important pathogens in medicine due to its antibiotic resistance and high aptitude to colonize different surfaces, forming biofilms. The microorganism causes development of severe infections and complications. Conventional antibiotics have been losing their role as the main antimicrobial remedy. This has led to seeking novel approaches to stop biofilm formation and its removal.

Objective. The aim of the current study was to determine the activity of AgNPs antibiofilm against methicillin-resistant *S. aureus* strain.

Methods. For the study, two different types of silver NPs were used. The first type was prepared by using polyol method, while the second type was created by utilizing the green synthesis approach. *S. aureus* was isolated from patients with pulmonary infections and stored at Sumy State University Microbiological Laboratory. Initially, minimal inhibitory concentration was determined by the broth microdilution method. The microbial biofilms were formed on polystyrene microtiter plates. The influence of AgNPs on biofilm formation was examined with gentian violet staining and resazurin assay.

Results. Both types of AgNPs displayed antimicrobial activity against methicillin-resistant *S. aureus*. However, AgNPs obtained with green synthesis possessed a higher effectiveness on early stage of biofilm formation than AgNPs prepared by polyol method. Ability of the silver nanoparticles to reduce the mass of biofilm formed by *S. aureus* was higher for AgNPs fabricated with green synthesis approach.

Conclusions. The proposed silver nanoparticles have antibacterial and antibiofilm activity upon the methicillin-resistant *S. aureus* and can be used for further development of antimicrobial agent.

Acknowledgements. The study was funded from the grant of the Ministry of Education and Science of Ukraine No. 0118U003577 “Antimicrobial effectiveness of nano-complexes (chitosan-nanometals) against the multi-resistant clinical strains”.

Behavioural phenotype of Sigma-1 receptor knock-out mice

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Background. Sigma-1 receptor (Sig-1R) is involved in the development of age-related diseases, such as Alzheimer's disease, depression, and neuropathic pain.

Objective. The aim of the present study was to perform a long-term (2 to 19 month of age) phenotyping of Sig-1R knock-out (KO) and age-matched Wild-type CD-1 (WT) male mice.

Methods. Thirty-nine CD1 and thirty-six CD1/Sig1R $-/-$ male mice were included in this study. Animals were housed under standard conditions (21–23 °C, 12 h dark/light cycle) with unlimited access to food and water. The behavioural tests were carried out to evaluate memory function (Barnes maze, passive avoidance, Y-maze), depression-like behaviour (tail suspension), anxiety (zero maze), locomotor (open-field) and voluntary physical activity (metabolic cages with and without running wheel), pain perception (hot-plate, Von-Frey and acetone tests) body weight and food intake in young-adult (2 to 4 months of age), adult (4 to 12 months of age) and aged mice (up to 19 months of age).

Results. In the Barnes maze test, aged Sig-1R KO mice spent more time in the target hole area as compared to the age-matched WT mice 1 and 7 days after learning. During the learning phase, latency to enter escape box was significantly increased in Sig-1R KO mice throughout the lifetime, while latency to reach the target hole was not different between adult and aged Sig-1R KO and WT mice. Passive avoidance test showed that young adult and aged Sig-1R KO mice had better contextual memory than WT mice. There were no differences among the groups in working memory assessed in Y-maze test. In tail suspension test, immobility time of the Sig-1R KO mice did not change throughout the lifetime, while WT mice with age showed an increase in immobility time. Until 4 months of age, Sig-1R KO mice demonstrated an increased voluntary wheel-running activity in metabolic cages. Food intake in Sig-1R KO mice was decreased throughout the study compared to WT mice. Young adult and adult Sig-1R KO mice had decreased body weight up to 4 months of age. Thermal and mechanical pain sensation were not altered in Sig-1R KO mice.

Conclusions. Phenotyping findings suggest that Sig-1R plays an important role in the control of depression-like behaviour, voluntary exercise abilities, cognition and food intake processes.

Acknowledgements. We thank Laboratorios Dr. Esteve, S.A. (Barcelona, Spain) for providing CD1-Sigma-1KO mice.

Changes of novel microRNA expression *in vitro* after silencing pivotal microRNA biogenesis elements

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Background. MicroRNAs (miRNA) are small (19–23 nucleotide long), highly conserved, non-coding endogenous posttranscriptional gene regulators, which function by binding to their target mRNAs and so regulate development, cell identity and disease (Mohr et al., 2015). To date, more than 2600 mature human miRNAs are known (miRbase v.22.1, 2018) and new ones are continuously discovered. To verify novel miRNAs, these molecules are usually defined by their biogenesis (Friedlander et al., 2014).

Objective. To evaluate changes of novel microRNA expression *in vitro* after silencing pivotal microRNA biogenesis elements.

Methods. Colorectal adenocarcinoma cell lines (Caco-2 and HT-29) were used in the study. Exogenous siRNA molecules were used to silence the expression of *DGCR8*, *DROSHA*, *DICER1* and *AGO2*. Total RNA was extracted by performing phenol/chloroform cell lysis and silica membrane based RNA purification. Complementary DNA was synthesised using both random and TaqMan specific primers. The expression of siRNA target genes, canonical miRNAs and novel miRNAs was determined by quantitative real-time polymerase chain reaction using TaqMan Assays. Expression analysis was performed using $2^{-\Delta\Delta C_t}$ method. Statistical analysis and data visualisation was performed using R studio software (R version 3.3.3). Data was considered significant when p was below 0.05.

Results. Results showed that siRNA transfection had no significant effect on *DGCR8* expression on mRNA level in both Caco-2 and HT-29 cell lines. Expression of *DROSHA* (Caco-2: 1.35 times ($p = 0.0013$); HT-29: 2.03 times ($p = 4.88 \times 10^{-4}$)); *DICER1* (Caco-2: 2.68 times ($p = 5.62 \times 10^{-6}$); HT-29: 2.34 times ($p = 1.10 \times 10^{-6}$)), *AGO2* (Caco-2: 1.45 ($p = 4.88 \times 10^{-4}$); HT-29: 1.49 times ($p = 7.79 \times 10^{-7}$)) decreased on mRNA level under experimental conditions. Silencing of pivotal miRNA biogenesis elements caused a significant expression decrease of canonical miRNA hsa-miR-324-5p in both Caco-2 (1.34 times ($p = 0.0013$)) and HT-29 (1.3 times ($p = 0.0049$)) cell lines. However, a significant decrease of hsa-miR-16-5p expression was determined only in Caco-2 cell line (1.32 times ($p = 0.0068$)). The analysis of novel miRNAs revealed that the expression of three candidates – miR-candidate-8-3p, miR-candidate-17-3p, miR-candidate-329-5p – had not changed significantly after silencing the main elements of miRNA biogenesis.

Conclusion. Despite the fact that computationally predicted structures of novel miRNAs (miR-candidate-8-3p, miR-candidate-17-3p and miR-candidate-329-5p) were miRNA-like, expression level of these candidates *in vitro* did not change after silencing pivotal elements of miRNA biogenesis. This suggests that novel miRNA candidates do not mature through canonical miRNA biogenesis pathway or belong to other class of small non-coding RNAs.

Acknowledgements. The authors declare the absence of conflict of interest. This study was funded by EU Structural funds, grant No. 09.3.3-LMT-K-712-10-0191.

Expression of GLUT-5 in chicken duodenal epithelium in norm and in T-2 mycotoxicosis

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Background. Glucose transporter-5 (GLUT5), a member of the facilitative glucose transporter family, allows for fructose to be transported from the intestinal lumen into the enterocyte by facilitated diffusion due to high concentration of fructose in the intestinal lumen. The small intestine regulates fructose absorption from dietary sources and expresses the greatest amount of GLUT5 in human, mice, rat, rabbit and chicken. Although there are notes about the diseases leading to adaptive changes in intestinal fructose transport, there are only few studies on GLUT5 expression and function under pathological conditions in the intestine. Animals and birds are exposed through food to T-2 mycotoxins, one of the most deadly toxins of the trichothecene group, which initial interaction is with the gut epithelium.

Objective. The aim of our investigation was to study the expression of GLUT-5 in the chicken duodenal epithelium comparatively in norm and in T-2 mycotoxicosis.

Methods. Material from 12 female broiler's (*Gallus gallus domesticus*) duodenum was collected from six 7 days old normal broilers (control group) and six 7 days old broilers with T-2 mycotoxicosis. Specimens were fixed with 10% formalin, embedded into paraffin, 7 µm thick slices were cut followed by immunohistochemical staining with polyclonal primary antibody Rabbit anti-GLUT-5 carried out according to the manufacturers' guidelines (IHC kit, Abcam, UK).

Results. In control group's chicken, strong staining of duodenal epithelium was noted in brush border membranes, a moderate expression of GLUT-5 was noted in the duodenal enterocytes, goblet cells were stained to a lesser extent. Weak staining for GLUT-5 was noted in duodenal epithelial cells in the group of T-2 mycotoxicosis.

Conclusion. Our results showed the decreased expression of GLUT5 in the duodenal epithelial cells in T-2 mycotoxicosis group, which indicates the reduced fructose transport in the diseased gut epithelium.

Acknowledgements. The authors would like to express their gratitude to Mrs. Mare Tamm for laboratory assistance.

Genetic variations in the *PSMC6* and *PSMA6* proteasome genes are associated with multiple sclerosis risk and response to interferon beta therapy in Latvians

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Background. The number of polymorphisms in genes related to the ubiquitin-proteasome system (UPS) exhibited an association with pathogenesis and prognosis of numerous human diseases. Recently, we reported data on the association between multiple sclerosis (MS) in Latvians and the rs2348071 polymorphism of the *PSMA3* gene.

Objective. The aim of the present study was to evaluate the *PSMA6* and *PSMC6* genetic variations in Latvians and their mutual interaction, as well as the interaction with the *PSMA3*-rs2348071 regarding the susceptibility to MS risk and response to therapy.

Methods. The *PSMA6*-rs2277460 and -rs1048990, as well as *PSMC6*-rs2295826 and -rs2295827 were genotyped in 280 MS patients. The data were consolidated in a single dataset with previously reported data on the loci genetic diversity in Latvians and *PSMA3*-rs2348071 genotyping of the Latvian MS case/controls study. Association with disease was analysed by alleles, single- and multi-locus genotypes and haplotypes. Prognosis of disease and response to therapy was evaluated in terms of “no evidence of disease activity (NEDA)”. Data produced were analysed in terms of genotype-phenotype correlation network.

Results. The *PSMA6*-rs2277460 and rs1048990 were identified as MS-neutral. The *PSMC6*-rs2295826-rs2295827 linkage block showed MS susceptibility ($p < 0.001$; OR = 1.949, 95 % CI [1.343–2.829]) and MS associated interaction with the rs2348071 ($p < 0.0001$; OR = 2.596, 95 % CI [1.598–4.222]) and rs2277460 ($p < 0.05$). The rs2295826-rs2295827-rs2348071 haplotype composed from rare alleles (G-T-A) showed a strong association with disease ($p < 0.0001$). The rs1048990 G allele was approximately twice as frequent in non-responders as in responders to interferon beta therapy (OR = 2.526 [0.901–7.081]). Using SNPexp dataset, a correlation has been revealed between the *PSMC6*-rs2295826-rs2295827 linkage block and *HLA-B* gene expression. The rs1048990 and rs2348071 genotypes exhibited a correlation with expression levels of genes encoding number of proteins involved in interferon signalling and other pathways implicated in MS pathogenesis.

Conclusions. Here for the first-time we report data on association between MS in Latvians and variations at the rs2295826- rs2295827 of the *PSMC6* gene being, in turn, involved in MS-susceptible interactions with the *PSMA3*-rs2348071 and *PSMA6*-rs2277460 loci. Our results suggest the potential for the rs1048990 of the *PSMA6* gene to be an independent marker for prognosis of INFB therapy response. Genotype-phenotype network presented in the study gives a new insight into the pathogenesis of the MS and other metabolic and autoimmune diseases and perspectives for future pharmaceutical interventions.

Acknowledgements. The current study was supported by ERDF project No. 1.1.1.1/16/A/016, and the University of Latvia research project “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”.

Immunohistochemical analysis of human breast capsular contracture

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Background. Capsular contracture (CC) is a frequent complication in breast augmentation, which compromises the aesthetic appearance of the breast. In addition, thickened or contracted periprosthetic capsule causes pain, shifting, distortion, and hardening of the post-operative breast.

Objective. The aim of the present study is to evaluate the peri-implant tissue inflammatory reactions and abnormal scarring in breast augmentation patients by silicone implants.

Methods. Tissue samples were obtained at the time of implant removal from the anterior side of capsules surrounding breast implants with CC from 8 female patients undergoing breast implant replacement. Breast capsule samples were stained with hematoxylin-eosin and with antibodies against CD3 (T cell lineage marker), CD20 (B cell lineage marker), CD 68 (macrophage marker), mast cell tryptase and alpha-smooth muscle actin (α – SMA).

Results. The inner layer of the fibrous capsule abutting the implant appears to be multi-layered containing silicone-laden macrophages, foreign body giant cells and fibroblasts. In three cases this layer undergoes synovial-type metaplasia. Sharply demarcated perivascular and periductal lymphoplasmocytic infiltrates (mostly CD20 positive) were commonly seen. The degree of foreign body reaction and local inflammatory response has a positive linear correlation with the severity of CC.

Conclusions. It seems reasonable that unstable tissue attachment to the implant leads to the development of exudate-filled periprosthetic space around the implant, thus enabling further increased micromotions. Obviously, such local micromotions will set up a wear mechanism, with particulate debris formation and filler leakage. This debris could induce an autoimmune reaction with capsular recruitment of lymphocytes and over-activation of macrophages. As a result, the excessive production of fibrogenic cytokines by these cells may cause the formation of the hardened scar tissue.

The interface between platelet membrane fatty acid composition and blood serum malondialdehyde in healthy and post-myocardial infarction men

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Background. Platelet membrane is extremely susceptible to peroxidation, providing a variety of lipid peroxides including malondialdehyde (MDA), which has been implicated in the etiology of cardiovascular diseases.

Objective. To assess the relation between changes in the composition of platelet phospholipid membrane fatty acids (FAs) and blood serum MDA concentration.

Methods. Fatty acid methyl esters of platelet membrane of 10 post-myocardial infarction patients (men aged 40–60 years) and 79 apparently healthy individuals (men aged 25–39 years) were identified by gas chromatography/mass spectrometry. MDA concentration in blood serum was measured by high-performance liquid chromatography. The composition of platelet membrane FAs was compared to blood serum MDA concentration and between the patients and apparently healthy men without any acute clinical condition at the time of the study (control group).

Results. Post-myocardial infarction patients had a statistically significantly lower level of total percentage of saturated FAs, but a higher level of polyunsaturated FAs, ω 3 FAs and ω 6 FAs in platelet phospholipid membrane compared to control group (median: 61.2 vs. 70.86, $p = 0.004$; 21.1 vs. 10.99, $p = 0.000$; 6.24 vs. 3.85, $p = 0.024$; 15.82 vs. 7.44, $p = 0.000$). There was no statistically significant difference of total percentage of monounsaturated FAs between the patients and control group (median: 17.82 vs. 15.18, $p = 0.143$). In blood serum, the MDA concentration was statistically significantly higher in post-myocardial infarction patients compared to the control group (median: 142.02 vs. 97.07, $p = 0.001$).

Conclusions. As a consequence of oxidative stress, MDA may stimulate platelets to increase synthesis and incorporation of polyunsaturated FAs in platelet phospholipid membrane and that may influence the future platelet activation.

Acknowledgements. The authors declare the absence of conflict of interest.

The value of the assessment of tumour infiltrating lymphocytes for the risk stratification and clinicopathological characteristics of melanoma

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Background. Melanoma is the most severe type of skin cancer and its incidence has increased in the last years. Prognosis for patients with melanoma depends on the stage of the disease at the time of diagnosis and it can be influenced by the immunologic response. Melanoma has been considered an immunogenic malignancy. It often contains great amount of tumour-infiltrating lymphocytes (TILs).

Objective. The objective of the current study was to compare the value of the assessment of TILs in different melanoma subtypes and its influence on tumour behaviour.

Methods. The patients who underwent melanoma surgical treatment at Riga East University Hospital in 2012–2015 were retrospectively enrolled in the study. The study was approved by the Central Ethical Committee. The histopathological characteristics were assessed according to the current WHO and AJCC 8th edition guidelines.

Results. 71 patients were enrolled in the study (of these, 24 males and 47 females). The mean age was 62.08 ± 14.15 years. The obtained results showed that the TILs were higher in nodular melanoma compared to superficial spreading melanoma ($p = 0.001$). In addition, a significant correlation between melanoma clinicopathological type and peritumoral lymphocyte infiltration was demonstrated ($Rho = +0.31$; $p = 0.009$). However, there were no differences between TILs and patient's age, patient's gender and melanoma cell type.

The negative correlation between Clark level and Breslow level and TILs was revealed (respectively, $Rho = -0.30$; $p = 0.012$ and $Rho = -0.36$; $p = 0.001$).

The correlation between peritumoral lymphocyte infiltration and invasion of lymph vessels has not been observed, however, the tendency of tumour vascular invasion was demonstrated.

Furthermore, the negative correlation between disease stage and TILs was found ($Rho = -0.36$; $p = 0.002$), and between mitotic activity and TILs ($Rho = -0.28$; $p = 0.002$).

Conclusions. The assessment of tumour-infiltrating lymphocytes in melanoma proved to have a prognostic significance value and it may help to identify potential biomarkers for a better risk stratification. In addition, TILs subtyping could open new vistas for new targets, personalized diagnostics and treatment.

Acknowledgements. The study was supported by the ERDF grant “Understanding the biology of the minimal residual disease after targeted therapy of BRAF mutant melanoma”.

Thoracic aortic aneurysm: expression of vascular smooth muscle cell phenotype regulators in human aortic wall tissue

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Background. Thoracic aortic aneurysm (TAA) is an asymptomatic disease which can lead to sporadic dissection and severe complications. Pathogenesis of TAA involves a phenotypic shift of vascular smooth muscle cells (VSMCs) from contractile to synthetic, but the underlying mechanism remains unknown. Epigenetic regulation of VSMC phenotype has mainly been studied *in vitro*, but validation on clinical samples is still scarce. MicroRNAs hsa-miR-143/145 and their target gene Krüppel-like factor 4 (KLF4) has been shown to play an important role in regulation of proliferation and differentiation of VSMCs and in development of TAA. Function of long non-coding RNA (lncRNA) CARMN, a host gene of hsa-miR-143/145 has not been studied in TAA yet, and could help to elucidate the pathway of a disease.

Objective. The aim of the current study is to test whether hsa-miR-143/145, their target gene KLF4, and their host gene lncRNA CARMN are differently expressed in clinical samples of TAA patients.

Methods. The study included aortic wall samples from TAA patients who underwent aortic reconstruction surgery (N = 24). Fragments of ascending aorta taken from patients during coronary bypass surgery (N = 36) or during heart transplantation from the heart donor aorta (n = 6) were used as controls. Relative expression of ncRNAs CARMN and hsa-miR143/145 in aortic tissue was determined using qPCR method. Evaluation of KLF4 positive cells was done using immunohistochemical staining of formalin fixed and paraffin-embedded tissues. Statistical analysis was implemented by using Mann Whitney U test and Pearson's correlation.

Results. lncRNA CARMN expression was significantly reduced in TAA tissue samples compared to controls ($p = 0.033$). However, we did not find any difference in levels of hsa-miR-143-3p ($p = 0.823$), hsa-miR-145-3p ($p = 0.336$), hsa-miR-143-5p ($p = 0.786$) and hsa-miR-145-5p ($p = 0.487$) between TAA and non-TAA groups. Interestingly, a significant correlation existed only between hsa-miR-143-3p and its host gene CARMN ($r = 0.275$, $p = 0.025$) in all aortic tissue samples. There was no significant correlation between hsa-miR-145-3p ($r = 0.239$, $p = 0.053$), hsa-miR-143-5p ($r = 0.081$, $p = 0.516$), hsa-miR-145-5p ($r = 0.073$, $p = 0.556$) and CARMN. TAA aortic tissue samples showed increased number ($p < 0.001$) of KLF4 positive VSMCs (median = 25.49 %) in aortic media compared to controls (median = 10.87 %).

Conclusions. Using clinical samples, we have shown that lncRNA CARMN might play an important role in TAA formation. Further studies are needed to assess the modulation of CARMN and hsa-miR-143/145 expression, as well as their role in KLF4 regulation.

Acknowledgements. This research was funded by the Research Council of Lithuania grant No. SEN-05/2016,

Ultrastructural changes of thymic macrophages under the influence of total dehydration

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Background. Macrophages are mononuclear phagocytes that provide a system of a non-specific immune response in various tissues and organs, including thymus. To date, morphological changes in cells of thymus under different pathological conditions represent a significant interest, primarily for clarifying specific pathogenetic mechanisms, as well as assessing the state of central organs of immunogenesis.

Objective. The aim of the current study was to determine the features of ultrastructural changes in thymic macrophages under experimental total dehydration of the organism.

Methods. 12 nonlinear mature male rats were involved in the experiment. The mild degree of total dehydration was simulated on 6 animals by keeping them on a completely anhydrous diet for 3 days. 6 rats represented the control group and were in the usual drinking regimen. The ultrastructure of animal thymus samples was investigated by electron microscopy. The macrophage differentiation cluster was determined by the immunohistochemical method with CD68.

Results. A greater number of thymic macrophages were revealed in experimental animals in comparison with the control ones. Phagocytized apoptotic bodies, phagolysosomes, and numerous predominantly elongated lysosomes of various sizes with homo- and heterogeneous contents were found in the cytoplasm of macrophages. The granular endoplasmic reticulum of macrophages was represented by channels with a large number of ribosomes on the inner membrane. The Golgi complex has an appearance of little cisterns with a small amount of separately located bubbles. The density of macrophages in thymus medulla is much lower than in the cortex due to the increased migration of macrophages into the cortical zone. It is confirmed by the immunohistochemical reaction with CD68. In our opinion, this reflects that in these zones the differences are in the intensity of apoptosis.

Conclusion. The dynamics of the amount and ultrastructural changes of macrophages in the thymus suggest that a mild degree of total dehydration of the organism is accompanied by the activation of a nonspecific immune response in the thymus, which, in turn, develops as a result of the intensification of apoptosis of the thymocytes.

Acknowledgments. The research was supported by the Center for Morphological Research of Sumy State University. The authors declare the absence of conflicts of interest.

Antimicrobial resistance in clinical isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

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Background. *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are the main causes of health-related infections (HAI). *P. aeruginosa* and *A. baumannii* induce various HAI, including bacteraemia, pneumonia, urinary tract infections. The resistance of these pathogens to antimicrobial agents has grown rapidly in recent years, and currently poses an acute problem.

Objective. To determine the resistance of gram-negative bacteria *P. aeruginosa* and *A. baumannii* to antimicrobial agents and to compare changes in antibacterial resistance over two years (2017 and 2019).

Methods. The samples were taken from sputum of clinical patients. The tasks included identification of isolates from respiratory tract by *BBL*TM *Crystal*TM system, performing of antibacterial susceptibility tests using the *Bauer-Kirby*TM disc diffusion test, determining the minimum inhibitory concentration using the ETM-test, as well as phenotyping of the isolates by antibiogram.

Results. In 2019, *P. aeruginosa* isolates most commonly were susceptible against meropenem – 93.34 % (n = 70), while resistant to ciprofloxacin 17.33 % (n = 13). In 2019, isolates of *A. baumannii* were 100% (n = 20) susceptible to colistin, while resistant to ceftazidime – 55 % (n = 11). *P. aeruginosa* isolates showed the highest increase in resistance over two years to ciprofloxacin – 6.56 % (n = 13). *A. baumannii* isolates showed the highest increase in resistance over two years to carbapenems – 12 % (n = 9). In both years, the most common phenotype of *P. aeruginosa* was phenotype I – 72.22% (n = 39) in 2017 and 68 % (n = 52) in 2019, which was susceptible to all antibacterial agents. A combined resistance was observed at 9.23 % in 2017 and 9.33 % in 2019. The most common phenotypes of *A. baumannii* were I (n = 5), III (n = 5) in 2017, and I (n = 6) and III (n = 6) in 2019. The phenotype I was susceptible to all antibacterial agents, but the phenotype III was resistant to almost all antimicrobial agents, however, not to colistin. Combined resistance was observed at 60 % (n = 9) in 2017 and 45 % (n = 9) in 2019.

Conclusions

Acinetobacter baumannii isolates showed the highest increase in resistance over two years to carbapenems – 12 % (n = 9).

Pseudomonas aeruginosa isolates showed the highest increase in resistance over two years to ciprofloxacin – 6.56 % (n = 13).

In both years, *Acinetobacter baumannii* phenotype III was resistant to almost all antimicrobial agents except colistin.

In both years, in *Pseudomonas aeruginosa*, the most common phenotype I was susceptible to all antibacterial agents.

Acknowledgements. The authors would like to express their gratitude to all the employees of the RAKUS TPSC Laboratory of Mycobacteriology for their support during this research.

Influence of creatine kinase on regulation of mitochondrial respiration supported by fatty acids

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Background. Mitochondria and intracellular ATPases in cardiomyocytes are in close proximity, and arranged into tightly coupled structural and functional complexes known as intracellular, energetic units. Strict interpositions of mitochondrion optimize the energy fluxes and interactions of mitochondria with surrounding organelles; however, at high workload the direct ATP transfer does not fulfil the energy requirements in heart cells.

Objective. We investigated the effect of fatty acid oxidation on the functional coupling between mitochondrial creatine kinase (mi-CK) and the ADP/ATP carrier in skinned cardiac fibres.

Methods. Respiration rates of skinned cardiac fibres were determined in the closed respiration chamber in physiological salt solution at 37 °C or 25 °C by the means of the Clark-type oxygen electrode. The coupling of mitochondrial creatine kinase (mi-CK) and ADP/ATP carrier was estimated using two approaches. (1) The apparent K_m^{ADP} and V_{max} values were estimated from ΔV vs. ADP concentration relationships in the presence or in the absence of 20 mM creatine; the results were compared with corresponding kinetic parameters without creatine; (2) 60 μ M ADP was added into the respiration chamber followed by the addition of 20 mM of creatine. The stimulation of respiration by creatine, i.e., the creatine effect, was expressed as the ratio of the respiration rates with creatine and with 60 μ M of ADP without creatine.

Results. The exogenous creatine stimulated the respiration of cardiac fibres oxidizing pyruvate + malate or palmitoyl-L-carnitine in presence of low 60 μ M ADP concentration, accordingly by 1.37 ± 0.05 times and 1.42 ± 0.04 times (data of six unpaired experiments, 20 °C). When palmitoyl-L-carnitine-supported respiration of skinned cardiac fibres was stimulated by exogenous ATP, endogenous ADP was produced from exogenous ATP by ATPases in myofibrils and the sarcoplasmic reticulum, and it was delivered directly to the mitochondria. In this case, the stimulating effect of creatine on mitochondrial respiration appeared to be very close to that observed in the experiments with the exogenous ADP; i.e., 1.38 ± 0.06 and 1.47 ± 0.05 times, respectively, with 23 and 37 μ M of ATP (20 °C). The maximal effect of creatine on mitochondrial respiration with octanoyl-DL-carnitine, similarly to palmitoyl-L-carnitine, was observed at 60 μ M concentration of exogenous ADP ($n = 3-5$).

Conclusions. The creatine-induced decrease in the apparent K_m^{ADP} reflects the maintenance of functional coupling in the intermembrane space between ADP/ATP carrier and mi-CK in the mitochondria respiring on fatty acids.

The effect of age-related Wnt signalling on breast cancer cell viability and mitochondrial membrane potential

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Background. Cancer is one of the diseases showing the largest correlation with age. We believe that there is a more specific connection between cancer and cellular senescence. This connection is explained by the Wnt signalling pathway, which can lead to senescence and apoptosis in healthy cells but also favours the survival of carcinogenic cells. C1q is a component of complement system, which is a part of innate immune system and its expression is elevated in cancer. C1q expression and its concentration in blood increases with aging, which causes impaired regeneration capacity of various tissues by activating canonical Wnt signalling pathway. It has been reported that Wnt signalling results in the increased expression of the transcription factor PPAR- δ , which may be involved in development of cancer, but there is no consensus, whether it promotes or prevents cancer formation.

Objective. The aim of this study is to find out whether age-related Wnt signalling can help breast cancer cells to avoid ECM (extracellular matrix) apoptosis induced by loss of attachment (LOA) conditions and evaluate the effect of C1q on mitochondrial membrane potential ($\Delta\psi_m$) in normal and in LOA conditions, as well as its effect on PPAR δ expression.

Methods. Cell viability and mitochondrial membrane potential was measured by flow cytometry assay using 7AAD and JC-1 dyes. Protein expression was evaluated by Western blot analysis and immunocytochemistry. LOA conditions were created by coating cell culture flasks and plates with poly (2-hydroxyethyl methacrylate).

Results. Protein C1q increases Wnt signalling pathway activity and PPAR δ expression in breast cancer cells. During growing cells in LOA conditions, cell viability decreased in comparison with the adherent cell. C1q (5 $\mu\text{g/ml}$) did not show any significant effect on cell viability after 72 h of treatment, but decreased the growth of MCF-7 cells. Adherent BCC and MCF-7 cells after treatment with C1q did not show any significant changes to mitochondrial membrane polarization ($\Delta\psi_m$), but in LOA conditions $\Delta\psi_m$ decreased in all the analysed cell lines. C1q caused mitochondrial depolarization after 48 h in BCC, MCF-7 and BT-474 cells, and in MCF10A cell after 24 h in LOA conditions.

Conclusions. Protein C1q increased Wnt signalling pathway activity and PPAR δ expression, but did not protect cells from ECM apoptosis as expected. C1q decreased mitochondrial membrane polarization in LOA conditions.

Acknowledgements. This study was partly funded by the Research Council of Lithuania grant “Effects of aging on lipid metabolism and cancer cell survival” (2016–2018).

The importance of DNA dynamics in neurogenerative diseases

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Background. DNA molecule has a dynamic nature and DNA conformational dynamism plays a significant role in biological functions. The critical role of the non-B-forms of DNA was reported many times in relation to pathophysiology of neurogenerative diseases like Huntington's chorea, Alzheimer's disease, amyotrophic lateral sclerosis and others. Conformational transitions in DNA (B to Z or X form) or propensity to fold into stable structures such as G-quadruplexes, parallel and antiparallel duplexes may affect the expression of pathologically important genes. Accordingly, the consideration and understanding of the conformational roles of DNA in the context to neurodegeneration could provide essential knowledge of molecular mechanism of disease. Polymorphic d(GT)_n microsatellite sequences considerably affect the regulation of gene expression and sometimes induce non-B-DNA structure formation.

Objective. To test the ability of PSMA6 microsatellites related to multiple sclerosis (MS) with different number of GT repeats (13, 18, 25) to modify the DNA structure *in vitro*.

Methods. The dynamism of PSMA6 microsatellites *in vitro* was studied using very sensitive circular dichroism (CD) method. 1) Detection of transition between B, A, Z and X forms: Complementary oligonucleotides were annealed using classical protocol and diluted in 0.6 mM phosphate and 0.03 mM EDTA buffer. B-A transitions were investigated in the presence of high percentage ethanol (70 %) and Cs ions, B-Z in a high ionic strength (3.5 M), B-X in the presence of methanol (57 %) and Mg²⁺ ions or in a presence of HGM1 protein 2) Detection of quadruplexes and duplexes: single-stranded oligos were incubated with a high concentrations of Na, K and Zn ions after annealing.

Results. Applying all experimental variations, a slight transition was detected only in the B-A.

Conclusions. PSMA6 microsatellites with different number of GT repeats did not show any dynamic changes, excluding a slight B-A transition. The formations of second structures were not detected, as well. However, it should be mentioned that the investigation of conformational dynamics of DNA involves great amounts of experimental variations: temperature, different metal ions and their concentrations, protein binding, dehydration levels, etc. Thus, the study of the impact of PSMA6 microsatellites on DNA dynamism needs a more comprehensive investigation.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment", the Faculty of Medicine, University of Latvia.

Assessment of selected preservation solution flow in graft's vessels based on analysis of its rheological parameters

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Background. An organ taken from a donor should be transferred to the recipient's transplant centre as soon as possible. To maintain normal vital functions, the graft is washed of the blood and then stored in an appropriate preservation solution (hypothermia / 4 °C), providing effective protection against ischemia-reperfusion damage. The solution should have optimal composition and physicochemical properties.

Objective. The aim of the study was to assess the flow a model, cold preservation solution UW (developed at the University of Wisconsin) in graft's vessels based on an analysis of its rheological parameters.

Methods. UW as a model cold storage solution was analysed. For rheological tests, the rotational rheometry method was applied using the Lamy RM 200 Touch laboratory rheometer equipped with MS-R1 (paddle measuring system). The measurement temperature was 4 °C. Flow and viscosity curves were plotted in controlled shear rate mode in the range 2.0–50.0 s⁻¹ within 120 sec. The analysis of the obtained results was performed using Rheometric-P Software.

Results. The flow curve is typical for non-Newtonian shear thinning fluids. The solution shows a high dynamic viscosity at low shear rates (η_a (2 s⁻¹) = 63.8 Pa·s), which decreases by ~ 73 % at shear rate 50.0 s⁻¹ (η_a = 17.2 Pa·s). The analysed solution shows features of a pseudoplastic fluid without a yield stress $\tau = 0$.

Conclusions. The results indicate no flow resistance when flushing the organs with the model UW cold storage solution. This suggests good properties of organ perfusion.

Acknowledgements. The authors declare that they have no conflicts of interest.

PHARMACY

Evaluation of essential oil composition of different parts of *Heracleum sosnowskyi* Manden using GC-MS

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Background. *Heracleum sosnowskyi* Manden (*Apiaceae*) produces a great amount of chemical compounds. It is one of the most dangerous plants for human health because contact with the sap leads to intense skin burning. The main function of the sap is to protect the plant from vertebrates, invertebrates, fungi, bacteria and viruses, being both repellent and toxic to them. It has already been shown that the extracts obtained from above-ground parts of different types of hogweeds exhibit a wide range of physiological activities.

Objectives. The aim of the current study was to evaluate qualitative and quantitative composition of essential oil in different parts (leaves, flowers, stems and roots) of *Heracleum sosnowskyi* M., using GC-MS.

Methods.

Plant material. The plants were collected during flowering phase. Raw material was dried at 25 °C for chemical analysis.

Distillation. 40 g of dried material were weighed into a 1 L round-bottomed flask, 1000 mL of distilled water was added and the mixture was stirred. The thermostatic bath with glycerol was used for extraction, maintaining a constant temperature of 120 °C. The prepared test samples were kept in a thermostatic bath for 3 hours until the essential oil layer was separated. 1 mL of hexane was added to the collected distillate.

Gas chromatography-mass spectrometry. Analysis of essential oils was performed by GC-QP2010 (Shimadzu, Japan) with a mass spectrometer (RTX-5 MS column, 30 m × 0.25 mm × 0.25 µm; Perkin Elmer, USA). Analytical conditions: injector temperature 240 °C, column temperature 60 °C, injectable sample volume – 1 µL. The temperature in the gas chromatograph was programmed step by step from 60 °C (0 min.) to 150 °C 2 °C /min. speed and from 150 °C to 285 °C raise 10 °C /min. speed.

Results. Qualitative and quantitative composition of essential oil in different parts of *Heracleum sosnowskyi* M. was evaluated. 30 essential oil components were identified in leaves, 22 – in flowers and stems, and 26 – in roots. Six components (4(10)-Thujene, beta-Myrcene, p-Cymene, beta-Ocimene, gamma-Terpinene, alpha-Terpinolene) of essential oil in different amounts were identified in all parts of the plant. The main component of essential oil in different amounts in leaves and flowers was Germacrene D (36.46 % and 36.65 % respectively), in stems – 2(3H)-Furanone (50.19 %) and in roots – p-Cymene (80.40 %).

Conclusions. According to the results, the qualitative and quantitative composition of essential oil in leaves, flowers, stems and roots of *Heracleum sosnowskyi* M. differ significantly.

Encapsulation of *Elsholtzia ciliata* extract by spray-drying: effect of coating materials on the moisture content and solubility of the spray-dried powders

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Background. Spray-drying is the most popular encapsulation method used for stabilization and protection of biologically active compounds from various environmental conditions, such as oxidation, moisture, pH, and temperature. As core material for microencapsulation was used *Elsholtzia ciliata* ethanolic extract and essential oil, as wall materials skim milk (SKIM), sodium caseinate (SCAS), gum Arabic (GUM), maltodextrin (MD), beta-maltodextrin (BCYC), and resistant maltodextrin (RMD).

Objective. The aim of this work was to study the effects of different wall materials and concentrations on spray-dried powders moisture content (MC) and solubility.

Methods. Powdered material of dried *E. ciliata* was extracted with 70 % (v/v) ethanol in a flask by ultrasound-assisted extraction performed in an ultrasound bath at 25 °C for 30 min. Ethanolic extract and wall material solutions (10–30%) were mixed together. The prepared liquid feeds were spray-dried in a Buchi B-291 Mini Spray-Dryer. Spray-drying conditions: temperature was 160 °C, outlet temperature – 80–90 °C, spray flow feed rate – 30 mL/min, air pressure – 6 bar, aspirator – 100%.

Results. The MC of spray-dried powders ranged from 2.99 to 7.6 %, and was the highest when wall material contained GUM (10 %) and the lowest for MD (30%). The MC decreases with increasing the amount of wall material in liquid feed solution for spray-drying: MD 10 – 3.78 ± 0.18 %, 20 – 3.28 ± 0.11 %, 30 – 2.99 ± 0.07 %; GUM 10 – 7.6 ± 0.14 %, 20 – 6.7 ± 0.14 %, 30 – 6.55 ± 0.11 %; and RMD 10 – 3.85 ± 0.05 %, 20 – 3.54 ± 0.1 %, 30 – 3.43 ± 0.09 %.

Spray-dried powder solubility ranged from 42.5 to 99.9 % and was the highest when wall material contained RMD (20 %) and the lowest for BCYC (30 %). Higher concentrations (10 % > 20 % > 30 %) of wall material influenced higher solubility of spray-dried powders (SCAS 80.05 % > 80.9 % > 81.25 %, SKIM 95 % > 95 % > 99.9 %, respectively), however, using BCYC in the same concentration range solubility decreases (55 %, 45 %, and 42.5 %, respectively).

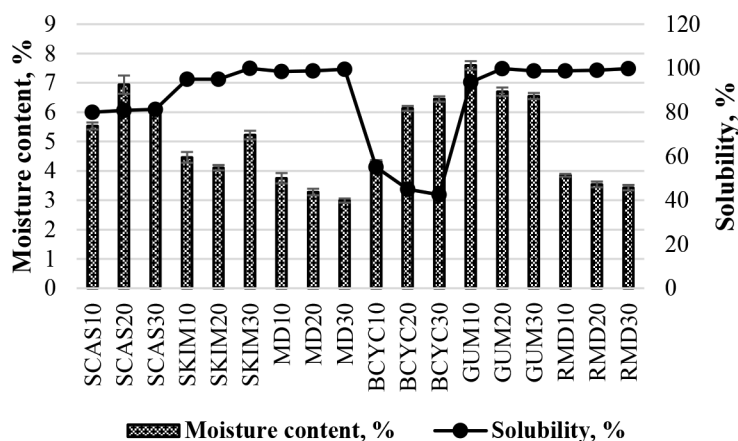


Fig. Moisture content (%) and solubility (%) of spray-dried powders using different wall materials and their concentrations

Conclusions. According to data the different coating materials and their concentrations affected moisture content and the solubility of the spray-dried powders prepared by spray-drying technique.

Acknowledgements. The authors are thankful for financial support provided by Science Foundation of Lithuanian University of Health Sciences.

Evaluation of the qualitative and quantitative composition of phenolic compounds in the European plum (*Prunus domestica* L.) fruit grown under Lithuanian climatic conditions

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Background. Various groups of biologically active compounds, such as phenolic compounds, vitamins, and organic acids, found in the fruit of the European plum are essential for human health. They improve cognitive functions, reduce the risk of cardiovascular diseases and have a laxative and antimicrobial effect.

Objective. The aim of this research was to evaluate the variation in the composition of phenolic compounds in the fruit of the European plum (*Prunus domestica* L.) grown in Lithuania.

Methods. The samples taken from 17 different cultivars of the European plum were analysed. The plum trees were grown in the garden of the Institute of Horticulture, Lithuanian Research Centre for Agriculture and Forestry. The slices of pitted plums were lyophilised. The samples were extracted with 83.64 % (v/v) ethanol in an ultrasonic bath for 40 minutes at room temperature. The analysis of the phenolic compounds was performed on the basis of ultra-high-performance liquid chromatography mass spectrometry (UPLC–ESI–MS/MS) methods. All the results of the experiments were calculated for the absolute dry raw material.

Results. The UPLC–ESI–MS/MS analysis revealed phenolic compounds of different groups: flavonols – avicularin, isorhamnetin-3-O-rutinoside, isoquercitrin, hyperoside, rutin, quercetin, flavan-3-ols – procyanidin A2, procyanidin C1, (+)-catechin, chlorogenic acid, which is categorised as a phenolic acid, and quinic acid, which is not a phenolic compound. The highest total quantity of phenolic compounds (5019.26 ± 202.07 µg/g) was determined in the samples of ‘Zarechnaya Rannyaya’ cultivar. Chlorogenic acid prevailed among all determined phenolic compounds. The highest content of chlorogenic acid (3.13 ± 0.16 mg/g, $p < 0.05$) was determined in the samples of plum fruit of ‘Zarechnaya Rannyaya’ cultivar. Rutin dominated among compounds of the flavonol group. The highest content of rutin (537.81 ± 26.89 µg/g and 565.85 ± 28.29 µg/g, $p < 0.05$, respectively) was found in the samples of plum fruit of ‘Herman’ and ‘Rausvė’ cultivars. The highest total quantity of compounds of the flavan-3-ol group (2210.04 ± 110.50 µg/g, $p < 0.05$) was found in the samples of ‘Kometa’ cultivar. The highest content of quinic acid (8.88 ± 0.44 mg/g, $p < 0.05$) was determined in the samples of plum fruit of ‘Jubileum’ cultivar.

Conclusions. The information obtained during this research is valuable both from a theoretical and practical viewpoint – the extracts of the European plum fruit of certain cultivars were found to contain the highest quantity of phenolic compounds, which could be promising for further studies, the production of functional food and nutritional supplements, the isolation of individual compounds and their use for purposes of practical medicine.

Locomotor activity in mice assessed by the home cage phenotyping system four months after the stroke surgery

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Background. Stroke is among the leading causes of serious disability in population. An interruption of the blood supply to the different brain areas causes a most typical symptom of stroke, which is a muscular weakness. PhenoMaster is an automated home cage phenotyping system that allows collecting the locomotor activity data in rodents continuously for several days in their home cage environment. There are no data available on the long-term effects of stroke on the *locomotor* function in mice.

Objective. The aim of this study was to assess the *locomotor activity* 120 days after the stroke surgery in mice by using individual home cage phenotyping system.

Methods. C57BL/6HNSd male mice divided into a stroke group (n = 9) and a sham group (n = 9) were used for this study. Stroke was induced by middle cerebral artery occlusion using endovascular filament (fMCAO). Animal behaviour in a home cage environment was examined by the PhenoMaster software-hardware complex (TSE Systems PhenoMaster), which allows simultaneous recording of a motor activity such as total distance moved, vertical activity, voluntary distance walked and time spent in the running wheel in individually-kept mice. The parameters mentioned above were recorded for 4 days. The first two days were counted as adaptation period for the mice to the new environment, respectively, home cage phenotyping system. Only the data of daily dynamics of locomotor activity of the third day was used for quantitative analysis. Graph Pad Prism software was used statistical analysis of the data.

Results. Activity indicators (vertical activity, total distance moved, distance voluntary moved and total time spent in the running wheel) were not significantly different between the two experimental groups. However, a significant change was observed between both groups in the total time voluntary spent in the running wheel in the light time of the day.

Conclusions. The obtained results demonstrate that general activity indicators are not altered four months after stroke, however, there are still some changes in activity comparing the light and dark time of the day.

Acknowledgements. This study was supported by ERA-NET project “Multi-scale investigation of synaptic dysfunction after stroke (MISST)”, project No. ES RTD/2018/29, and the Fundamental Research Grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, the Faculty of Medicine, University of Latvia.

Long-lasting effects of stroke on mitochondrial function demonstrated in mouse model of middle cerebral artery occlusion

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Background. Stroke is a leading cause of death and disability worldwide. Cerebral ischemia is a common form of stroke. It is caused by insufficient blood supply to the brain. Mitochondria have a key role in the regulation of cell cycle and energy. Disrupted functionality of mitochondria is recognized as a hallmark of ischemic neuronal death. The functional impairment of the brain mitochondrial respiratory plays an important role in stroke pathology.

Objective. The aim of this study was to investigate the mitochondrial respiration of both hemisphere 3 months after stroke procedure in mice.

Methods. Male C57BL/6NHsd mice (10 weeks old; n = 11 per group) were used for this study. The intraluminal monofilament model of middle cerebral artery occlusion (fMCAo) and following reperfusion after 60 min. of surgery was performed. A laser-Doppler (LD) probe was used for the continuous monitoring of regional cerebral blood flow during operation. We applied high-resolution fluoro respirometry (HRFR) to analyse the integrated Complex I, II and III linked respiration and the combined CI&II-linked oxidative phosphorylation (OXPHOS) and electron-transfer system (ETS) capacity in both cerebral cortex (both hemispheres) and hippocampus. Mitochondrial respiration was analysed in the tissue homogenates (thom-MiRO₅) by using an adapted substrate-uncoupler-inhibitor titration (modified SUI-001/008) protocol.

Results. The oxygen consumption data revealed that the complex I, II and III linked respiration rate, OXPHOS state and ETS capacity was significantly lower in fMCAo mice ipsilateral hemisphere (the left side of cerebral cortex) compared to ipsilateral hemisphere of sham mice. In addition, there was significant difference observed between both hemispheres in fMCAo mice (contralateral vs. ipsilateral side). There was no significant difference observed in hippocampus oxygen consumption between groups.

Conclusions. Our study demonstrates that brain's mitochondrial functionality reveals a significant impairment 3 months after the event of stroke.

Acknowledgements. This study was supported by: ERA-NET project "Multi-scale investigation of synaptic dysfunction after stroke (MISST)", No. ES RTD/2018/29, and the Fundamental Research Grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment", the Faculty of Medicine, University of Latvia.

Qualitative and quantitative composition variability of phenolic compounds in old cultivars of the apple grown in Lithuanian climatic conditions

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Background. The problem is important because the old cultivars of the apple, whose chemical composition has not been studied are being replaced by the cultivars of the commercial apple grown in the industrial gardens. Therefore, it is useful to determine variability of the most widely detected phenolic compounds composition characteristic to the old cultivars of the apple, which have long cultivation traditions in Lithuania

Objective. The aim of the current study was to determine the qualitative and quantitative composition variability of phenolic compounds in the apple samples of old cultivars, which have long cultivation traditions in Lithuania.

Methods. The objects of study were the old cultivars of apple: 'Avenarijus', 'Baltasis alyvinis', 'Beržininkų ananasinis', 'Birutės pepinas', 'Danų karalienė Luiza', 'Geltonasis arkadas', 'Montvilinis'. The apple trees were grown in the garden of the Institute of Horticulture, Lithuanian Research Centre for Agriculture and Forestry, Babtai, Lithuania. The apple was assigned a collection of genetic resources. The slices of whole apples were lyophilized. The samples of whole apples extracted with 70 % (v/v) ethanol in the ultrasonic bath for 20 minutes at room temperature. Phenolic compounds analysis was performed by high performance liquid chromatography method. The results of the experiments were calculated in the absolutely dry lyophilized raw material.

Results. Analysis of the composition of phenolic compounds of old cultivar of the apple samples resulted in determining the following phenolic compounds: avicularin, (+)-catechin, chlorogenic acid, (-)-epicatechin, phloridzin, hyperoside, isoquercitrin, procyanidin B1, procyanidin B2, procyanidin C1, reynoutrin, rutin, quercitrin. The highest total amount (0.56 ± 0.06 mg/g) of identified phenolic compounds was detected in the apple sample of old cultivars 'Geltonasis arkadas'. In old cultivars of the apple sample of all identified and quantified of phenolic compounds (-)-epicatechin predominated. The highest amount of (-)-epicatechin (0.22 ± 0.11 mg/g) was detected in the apple sample of old cultivars 'Geltonasis arkadas'. The highest amount of avicularin (0.07 ± 0.02 mg/g), chlorogenic acid (0.02 ± 0.004 mg/g), isoquercitrin (0.03 ± 0.02 mg/g), procyanidin B1 (0.09 ± 0.05 mg/g), reynoutrin (0.03 ± 0.01 mg/g) were determined in the apple sample of old cultivars 'Baltasis alyvinis'.

Conclusions. The old cultivars of the apple are an important environmental factor, which affected the composition variability of phenolic compounds in the apple sample. The highest total amount (0.56 ± 0.06 mg/g) of the identified phenolic compounds out of the tested old cultivars of the apple samples was detected in apple sample of cultivars 'Geltonasis arkadas', the lowest (0.13 ± 0.01 mg/g) – in the apple sample of old cultivars 'Birutės pepinas'.

Acknowledgements. The study was supported by LAT-LIT programme project No. LLI-181 "Heritage Gardens".

Antioxidant activity of the essential oil from *Myristica fragrans* seeds with magnesium aluminometasilicate as excipient

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Background. The antioxidant activity is important in many areas. The binding of free radicals can prolong the shelf life of products (pharmaceutical industry: capsules, creams, lotions, and other, food industry, etc.) [1, 2] exceeding the expected values indicating possible interactive synergism. This effect prompted us to investigate the potential of NM, CP and NM-CP extracts in imparting oxidative stability to meat balls during frozen storage. NM-CP was evaluated at two concentrations 0.5% (NMCP). The nutmeg seeds have many properties and one of them is antioxidant activity. In our previous studies [3], we have noticed that magnesium aluminometasilicate increases the yield of essential oil. Thus, we decided to check whether this substance could affect the antioxidant activity of nutmeg essential oil.

Objective. The aim of this study was to determine the antioxidant activity of pure nutmeg essential oil and essential oil made with excipient, and to compare results.

Methods. The nutmeg essential oil was prepared by using hydrodistillation. Two samples were prepared: pure nutmeg essential oil (EO) and essential oil (EO M) with magnesium aluminometasilicate as excipient. 15 g of nutmeg powder, 300 mL of water and 3 g of excipient were used. Hydrodistillation was carried out for 4 h. Antioxidant activity of nutmeg essential oil was evaluated by using DPPH. A total of 1 mL of DPPH solution was placed in spectrophotometer cuvette and 100 µL of ethanolic essential oil solution at concentrations ranging from 5 % to 20 % was added. All samples were incubated for 20 min. in the dark and absorbance was taken at 515 nm (UV Spectrophotometer UV-1800, Japan). The activity was calculated by using the following formula:

$$\text{DPPH scavenging effect \%} = (A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}} \times 100$$

Results. The antioxidant activity of pure essential oil was statistically significantly higher than of essential oil with excipient (EO: 5 % - 44.53 ± 1.4 %, 20 % - 84.01 ± 1.27 %, EO M: 5 % - 34.92 ± 1.24 %, and 20 % - 72.71 ± 1.18 %). Comparing 10% concentration of essential oils, the EO M was more active but insignificant (62.11 ± 1.43 %, EO - 61.01 ± 1.39 %). When the essential oils were mixed (1:1) and the antioxidant activity was determined, the MIX oil (5 % and 10 %) had a higher antioxidant activity than the essential oils individually (55.06 ± 2.39 % and 74.79 ± 1.17 %).

Conclusions. The study showed that nutmeg essential oil has a higher than 60 % antioxidant activity (essential oil's concentration 10 % and higher). The magnesium aluminometasilicate can increase antioxidant activity significantly (5 % and 20 %). However, the MIX essential oil (5 % and 10 %) has a significantly higher antioxidant activity than EO and EO M separately. Consequently, a lower concentration of MIX essential oil has a higher antioxidant activity.

Acknowledgements. The authors declare absence of conflict of interest.

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The pharmacovigilance of non-narcotic analgesics

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Background. Self-medication is currently widespread and the most frequent reason for this is the easy access to various over-the-counter medicines. Non-narcotic analgesics (NNA) are one of the most widely consumed self-medication drugs. Increased attention should be paid to pharmacovigilance, considering the frequency of side effects.

Objective. The aim of the current study was to clarify the pharmacovigilance and the using habits of non-narcotic analgesics in Latvia.

Methods. A questionnaire intended for anyone with previous background in the usage of NNA was made. Altogether, 128 respondents of both sexes from 21 to 60 years of age were enrolled in this study. The questionnaire consisted of 16 closed and open-ended questions about the habits of NNA usage, public knowledge about NNA and its pharmacovigilance. In addition, side effect occurrence in most frequently used over-the-counter NNA (ibuprofen, naproxen, diclofenac, paracetamol, dextetoprofen) was researched based on Medicinal Product Register of Latvia.

Results. The most commonly used NNA among the respondents is ibuprofen (73 %). According to 88 % of respondents, no side effects from NNA were observed. However, considering those who had experienced side effects, in 53 % of respondents they were caused by ibuprofen, in 27 % by diclofenac and in 20 % by paracetamol. The most common side effects after taking ibuprofen were vomiting and nausea, after diclofenac – dizziness and after paracetamol – sweating. According to State Agency of Medicines (Republic of Latvia), paracetamol is the only NNA that does not cause common side effects. Knowledge of the side effects caused by NNA is not sufficient in 40 % of respondents, furthermore, 63 % of respondents do not know where to report the side effects. Self-medication is chosen by 70 % of respondents, 22 % took advice from acquaintances and 8 % from doctor. Simultaneous usage of several NNA is indicated by 35 % of respondents.

Conclusions. It can be concluded that the knowledge of using NNA and the side effects they cause is insufficient, therefore NNA should be distributed in pharmacies. Also, paracetamol induced less side effects than other NNA and according to side effect occurrence, all side effects of paracetamol are rare, therefore it should be the first-choice medicament for pain management.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, the Faculty of Medicine, University of Latvia.

Long-term effects on post-stroke locomotor activity in mice

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Background. Post-stroke neurological deficits, including impairments in sensorimotor function, behavioural changes in anxiety, depression, etc., are common in humans and can be demonstrated in rodents. The middle cerebral artery occlusion (MCAo) model is most closely related to human ischemic stroke. The open field test is widely used to evaluate motor function and spontaneous exploratory locomotion in rodents. Open field test can be used as a robust measure of recovery after stroke. There is a lack of scientific data about post-stroke recovery for a long-term period, e.g. several months after stroke.

Objective. The aim of the current study was to evaluate motor activity and spontaneous exploratory locomotion in mice for a period of 4 months after stroke.

Methods. Spontaneous locomotor activity (total distance walked in cm, velocity) and time spent in the central part of arena as well as turning preference were evaluated in C57Bl/6 male mice by open field test. Mice were divided in two groups: sham-operated and stroke-operated and activity was recorded by overhead camera for 10 min. using video tracking software EthoVision XT (Noldus) and performed on post-stroke (MCAo stroke model) day 7, 14, 30, 60, 90, 120. The experimental data were analysed with GraphPad Prism software.

Results. In the open field test stroke and sham, mice did not show a significant effect on total distance walked and velocity on tested post-stroke days. Sham-operated mice spent less time in the center zone on day 60 vs. day 7. On post-stroke day 7, stroke mice showed a marked preference in turning towards the non-impaired side (counter-clockwise) in comparison with the sham group. On post-stroke day 30 and 60, stroke mice showed a lower preference in turning towards the non-impaired side as compared to day 7.

Conclusions. Stroke had no significant effect on overall locomotor activity. On post-stroke day 7, stroke mice displayed an apparent preference in turning towards the non-impaired side (counter-clockwise) that equalized with time. Stroke-operated mice starting from day 90 after stroke have a tendency to alter activity patterns.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” by the Faculty of Medicine, University of Latvia, and ERA-NET project “Multi-scale investigation of synaptic dysfunction after stroke (MISST)” No. ES RTD/2018/29.

Cell-SELEX-enriched aptamer selectivity screening with flow cell cytometry

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Background. Cancer is a major public health issue worldwide and early diagnosis and precise treatment of cancer may greatly improve the quality of life for patients (Siegel, et al., 2020). Aptamers are short single-stranded oligonucleotides, which can bind to many different targets with high affinity and selectivity. They are selected with SELEX method (systematic evolution of ligands by exponential enrichment) in vitro from synthesized combinatorial nucleic acid libraries (Tuerk and Gold, 1990). Recently, aptamers have gained attention as promising cancer detection and therapy molecules. Compared to antibody molecules, aptamers have advantage in affinity, specificity, low cost, ease of synthesis and modification, low molecular weight, low immunogenicity and high stability (Zhou and Rossi, 2017).

Objective. In the current study we evaluated cell-SELEX derived aptamer selectivity on different human renal and breast cancer-derived cell lines using flow cytometry method.

Methods. Aptamers were selected with cell-SELEX method against clear cell renal carcinoma cells (RCC-MF). Renal epithelial cells (RC-124) were used as a control. Aptamers were sequenced using Illumina MiSeq high throughput sequencer and after data analysis it was found that several sequences bind to both cell types, but the affinity is stronger for RCC-MF cells. Sequence 36 (seq36) showed strongest binding to both cell types and it was used for further selectivity screening. Seq36 was ordered from Metabion with FAM label on 5' end for flow cytometry tests. Cells were cultivated in monolayer, separated with non-enzymatic dissociation solution and incubated with seq36 on ice. After incubation, cells were analysed on Amnis ImageStreamxMarkII imaging flow cytometer. Data were analysed with IDEAS 6.2 software.

Results. Seq36 selectivity was tested on five different cell lines: RC-124 (renal epithelial cells), RCC-MF (renal clear cell carcinoma), MDA-MB-231 (metastatic breast adenocarcinoma cells), and MCF-7 (primary breast adenocarcinoma cells). Flow cytometry results showed that seq36 highest affinity was for MDA-MB-231 cells but the lowest for MCF-7 cells.

Conclusions. We have tested selected aptamer sequence seq36 on four different cell lines. Results show that aptamer seq36 has highest affinity against MDA-MB-231 cell line. Further investigation on seq36 selective binding is needed to understand its target and why it binds to different cancer cell lines with different affinity.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment" by the Faculty of Medicine, University of Latvia.

Analysis of necessity of pharmacists' consultation for patients with constipation disorder

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Background. The constipation is a quite common disorder in patients, however, it does not always receive a sufficient attention. The studies indicate that only a limited number of patients ask for medical advice.

Objective. The aim of the study was to analyse the study participants' attitude to constipation and evaluate the pharmacists' involvement in providing professional advice.

Methods. 250 patients and 54 pharmacists from community pharmacies answered the questions of the questionnaire. Patients' responses were analysed by gender and age (18–45 years of age; 46–65 years of age; above 65 years of age). Descriptive and comparative statistics have been used – the results are presented in frequencies and percentages. Chi-square test was executed to measure responses association with gender and age. The study was approved by the Lithuanian Bioethics Committee.

Results. The 12.8 % ($n = 32$) constant constipation and 42.8 % ($n = 107$) occasional constipation rate was identified in the study group with no differences according to gender, although more males reported no constipation events (50.5 % vs 39.9 %). Constipation frequency was associated with the patients' age ($p = 0.000$) – a higher number of constipation events was identified in the group above 65 years of age.

The majority of the study participants knew the most possible risk factors for constipation, however, 43.1 % ($n = 60$) of the respondents with constant and occasional constipation did not identify the main cause for their constipation (no differences by gender or age), and 30.9 % ($n = 43$) of them did not undertake any measures to relief this disorder. 41.0 % ($n = 57$) of the respondents with constipation events reported an inappropriate lifestyle as possible factor for their constipation (77.2 % of females ($n = 44$, $p < 0.05$) and 56.1 % respondents from the age group 18–45 ($n = 32$, $p < 0.05$)).

A quarter (24.0 %, $n = 60$) of the study participants were concerned about the constipation, 15 % ($n = 9$) of them reported the consultation with health care specialists (including pharmacists). The pharmacists' advice might be helpful to the patients, as 96.3 % ($n = 52$) of the pharmacists clarify whether constipation is a constant disorder, and 23.1 % of them refer patients to physician's consultation, 28.8 % – recommend nutrition changes and doctor's advice. Furthermore, 79.6 % ($n = 43$) of the specialists clarify the patient's concomitant diseases and taken medications before administration of a laxative.

Conclusions. The study identified that the surveyed respondents did not relate the constipation with their health. The pharmacists should increase their proactive participation in helping to identify the possible causes of constipation and providing professional advice to patients.

Acknowledgements. The authors declare the absence of conflicts of interest.

***In vitro* Antimicrobial study on starchy aqueous extract of *Tinospora cordifolia* (Wild.) Miers compared with Ciprofloxacin and Nystatin**

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Background. Since Vedic period, the plant *Tinospora cordifolia* (Wild.) Miers has been used as a potential medicinal plant for various ailments including *kustha* (skin disorders), *krimi* (infection/worm) and useful in many diseases for preventive as well as curative purposes. Its safety and nontoxic nature have been reported in experimental and clinical studies on various systems of the body. The claims found in traditions and folklore along with scientific studies of various extracts of the plant encourage to work on the sediment starchy aqueous extract of the plant, known as *Guduchi Satva* (GS) in Ayurveda.

Objective. The aim of this study was to evaluate and compare the antimicrobial activity of the plant (extract) that climbs over *Azadirachta indica* (*Neem*) tree used as GS-I with the plant that climbs over the plants other than *Neem* trees as GS-II on two gram positive (*Staphylococcus aureus*, *Streptococcus pyogenes*); two gram negative (*Escherichia coli*, *Pseudomonas aeruginosa*) and two fungi (*Candida albicans*, *Aspergillus niger*) in comparison with the standards Ciprofloxacin and Nystatin.

Methods. Two test samples of GS-I and GS-II were prepared as per standard Ayurvedic guidelines (conventional exothermic method). Chloroform extract of the test samples converted to solution (100 mg/ml as 100 % solution) and used at the concentration of 25 %, 50 %, 75 % and 100 % for the study against microbial strains – *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus niger*. Ciprofloxacin and Nystatin were used as standards against bacteria and fungi, respectively. Antimicrobial study was implemented, using Disc Diffusion Method (IP). It was determined through Minimum Inhibitory Concentration (MIC) by Broth dilution method (Andrews JM, 2001).

Results. Both the test samples exhibited remarkable anti-microbial activity, which was more pronounced in higher concentrations. Zone of inhibition (ZOI) of GS-I / GS-II / standard exhibited 14/13/17 mm in case of *P. aeruginosa*; 13/12/15 mm in case of *S. pyogenes* and 16/15/19 mm against *C. albicans*, respectively. GS-I showed a better result than GS-II. The statistical study was not implemented, as the current study is a preliminary screening for antimicrobial activity.

Conclusions. The present preliminary experiment established the traditional claim that both the test samples (GS-I and GS-II) have an effective anti-microbial activity, which is more pronounced in higher concentration with better efficacy in GS-I. Further evaluation on various microorganisms is necessary before clinical trials.

Acknowledgements. The authors would like to acknowledge the support of the Bio-Lab laboratory, Bhubaneswar, Odisha, which assisted and provides the necessary facilities for this research work. The resources for the study were supplied by the research scholar in the framework of research for PhD thesis. Authors confirm the absence of any conflict of interest.