

Issued since 1920

2019

VOLUME 55 SUPPLEMENT 1

MEDICINA

- ABSTRACTS

International Scientific Conference
on Medicine

77th International Scientific Conference
of the University of Latvia

February 22, 2019
Riga, Latvia

ISSN 1648-9233

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BASIC MEDICAL SCIENCE & PHARMACY

Medicina (Kaunas) 2019;55(Supplement 1):1

Assessment of hematopoietic stem cells in normal and pathology in cell culture *in vitro* and *in vivo*

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Background. Chronic myeloid leukemia (CML), originated from leukemia stem cell, was the first oncological disease whose cause was clearly associated with the target molecule, tyrosine kinase BCR-ABL. This led to the discovery of targeted drugs – tyrosine kinase inhibitors (TKIs), which provide selective action only on cells of the leukemic clone. Identification of the effectiveness of targeted therapy drugs criteria for leukemic clone cells in chronic myeloid leukemia is a current issue of modern hematology, cell biology and medicine. It was established that cells of leukemic clone are capable of differentiating into hematopoietic cells, including erythroid lineage. However, there is a large number of controversial data regarding the role of the erythroid progenitor cells in the pathogenesis of CML.

Aim. The aim of the current study was to determine the role of erythroid lineage of differentiation side by side with granulocyte-macrophage progenitor cell in the mechanism of resistance for TKIs therapy.

Methods. Hematopoietic progenitor cells obtained from bone marrow of 32 patients with CML were studied in semisolid agar culture *in vitro* and *in vivo* (in diffusion chambers). Cultured cells were analyzed regarding their phenotypes and functions using flow cytometry, colony-forming unit (CFU) assay and long-term culture-initiating cells (LTC-IC) assay.

Results. With the application of the original model for determination of hematopoietic progenitor cells in gel diffusion chambers *in vivo*, the influence of soluble microenvironment factors on the erythroid progenitor cells in CML was detected. Correlative relationship was found between the number of erythroid colonies and the number of leukemic cells in the patient's bone marrow. It was established that the acquisition of resistance by leukemic clone cells to TKI is characterized by increased proliferative activity and insensitivity to the presence or absence of soluble microenvironmental factors, granulocyte-macrophage colony stimulating factor and erythropoietin in the culture medium.

Conclusion. The role of erythroid lineage of hematopoiesis in the mechanism of leukaemia process was shown. It was proved that prognostic value of patient's bone marrow cells functional activity is comparable with a recognized prognostic factor – Sokal index.

Acknowledgements. We would like to acknowledge prof., dr. Dyagil I. S. from National Scientific Center of Radiation medicine, Kyiv, Ukraine for support with primary material and clinical data. No conflict of interest is declared.

Features of damage and recovery of rats hematopoietic system following the exposure to sublethal doses of ionizing radiation

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Background. The fate of irradiated organism, as it is known, is determined by the state of hematopoietic tissue, which is one of the critical systems upon radiation exposure. In this regard, it seems appropriate to clarify the role of hematopoietic stem and progenitor cells in the mechanisms of damage and recovery of hematopoietic function after irradiation in sublethal doses.

Aim. The aim of the current study was to determine colony-forming activity of granulocytic-macrophage and erythroid progenitor cells in non-irradiated animals and after irradiation in sublethal doses and to investigate the process of hematopoietic recovery using cell culture *in vivo*.

Methods. For the study, two groups of Wistar rats were used. The first group consisted of non-irradiated animals, the second group included rats irradiated in the dose of 6 Gy. Peripheral blood from the tail vein was obtained on day 0, 9 and 21. Along with that, bone marrow was excised from femoral bone and after preparing smears was inserted in original diffusion chambers (1×10^5 cells per chamber). Hematopoietic cells were cultivated for 7 days and examined under an inverted microscope; numbers of clusters and colonies were determined.

Results. After irradiation, deep cytopenia was detected in the peripheral blood and bone marrow smears. The study has shown that compared to non-irradiated animals whose colony-forming activity was 48.5 ± 3.2 per 1×10^5 , for the irradiated animals this index equaled to 56.1 ± 1.2 colonies per diffusion chamber. It indicates that after the radiation exposure hematopoietic progenitor cells remained viable and their proliferative activity increased.

Conclusion. Thus, radiation injury of the organism is revealed in significant leucopenia in peripheral blood and bone marrow after irradiation and is followed by a significant increase in the relative proportion of proliferating bone-marrow cells, which was shown during cell cultivation. Higher proliferation of bone marrow progenitor cells will further provide the recovery of hematopoiesis, which is confirmed by peripheral blood and bone marrow indices on the 9th and 21st day of investigation.

Acknowledgements. We would like to acknowledge Prof. V. Nikolaev from Kavetsky Institute of experimental oncology, pathology and radiobiology for the idea of these investigations. The authors declare that there is no conflict of interests regarding the publication of this abstract.

Identification of proteasome related genetic markers for multiple sclerosis

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Background. Multiple sclerosis (MS) is a lifelong demyelinating disease, an autoimmune disorder triggered in genetically predisposed subjects by environmental factors. Ubiquitin proteasome system is important in immunity; its deregulation can influence MS development and progression. Proteasomes have been identified as major autoantigens in MS patients.

Modulation of UPS efficiency could be influenced by polymorphisms in the genes encoding UPS related proteins. Genetic variations in the 14q11-24 proteasomal genes were implicated previously in susceptibility to autoimmunity, type 2 diabetes mellitus, cardio-vascular disorders, and population adaptation to environment (Sjakste et al., 2014a,b; 2016; Kalnina, 2014; Paramonova 2014, for references). It appears that there is large potential for some of these mutations to be also associated with multiple sclerosis.

Aim. The aim of the current study was to investigate an association between *PSMA6* proteasome gene polymorphisms with MS and with treatment efficiency in MS patient's groups.

Methods. The *PSMA6* proteasomal gene (rs2277460 un rs1048990) single nucleotide polymorphisms (SNPs) were genotyped on MS subtype-, sex-specific and treatment efficiency association in 280 cases /305 controls study.

Results. Locus rs1048990 were identified as disease neutral. The rs2277460 rare alleles and heterozygotes was found in nominal association ($P < 0.05$) with the disease phenotype in females with prevalence in the SPMS female group ($P = 1.90 \times 10^{-3}$; OR=2,68, 95% CI [1,39-5,11] and $P = 1,10 \times 10^{-3}$; OR=3,02, 95% CI [1,51-6,05], respectively).

Minor alleles of the *PSMA6* rs1048990 SNP were found to have a borderline significant difference in distribution between responders and non-responders to interferon-beta therapy.

Conclusion. We provide evidence that proteasomal *PSMA6* gene genetic variations may contribute to the risk of MS and influence the treatment process in the population of Latvia.

Acknowledgements. The study was funded from the UL research project ERAF SAM Nr. 1.1.1.1/16/A/016 project "Determination of proteasome-related genetic, epigenetic and clinical markers for multiple sclerosis".

Prevalence of BRAF somatic mutations in solid tumours—the pilot study

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Background. BRAF is protein kinase gene, included in RAF family protein kinases. These kinases downregulate RAS signaling cascade, that induces cell proliferation and survival. Mutations of BRAF system leads to activation of MEK-ERK signaling. Although BRAF mutation was described in 7-15 % of solid tumors, it is mostly characteristic for melanoma. Other tumors with known BRAF mutations are hairy cell leukemia, histiocytotic sarcoma, thyroid papillary carcinoma, serous ovarian carcinoma, colon adenocarcinoma, non-small cell lung cancer and multiple myeloma.

The aim of this study was to compare BRAF mutation in different types of solid tumours.

Materials and methods. 83 patients with different types of solid tumours (melanoma, colorectal adenocarcinoma, lung non-small cell carcinoma, ovarian cancer, breast cancer and gastric adenocarcinoma) that underwent surgical treatment in the Riga East University Hospital during 2015 till 2017 were enrolled in the study. The study was approved by a Central ethical committee. The histopathological characteristics of the cancer was assessed according to current WHO and AJCC 8. edition guidelines.

The targeted next-generation sequencing (NGS, *Foundation One*) for 315 somatic mutations was performed on all cancer types formalin-fixed paraffin embedded tissue (FFPE).

Results. BRAF mutation was identified in melanoma, colorectal carcinoma and non-small cell lung cancer, however, there was no BRAF mutation detected in other cancer types. BRAF mutation was observed in all melanoma patients (that includes primary and metastatic melanoma), however only 60% of patients had mutation in V600E region. Furthermore, all melanoma patients additionally had N-RAS mutation. There was no statistical significant difference between size of the tumor and existence of specific mutation in BRAF ($p > 0.05$).

Only 1 patient with colorectal carcinoma had specific BRAF mutation in D594N region.

There was no specific BRAF mutations among patients with non-small cell lung carcinoma.

Conclusion. BRAF V600 E mutations were characteristics for the melanoma, however other type of BRAF gene mutations were frequently observed in colorectal carcinoma. The personalized treatment strategy with BRAF inhibitors was different in melanoma and colorectal carcinoma.

Acknowledgement. The study was supported by ERDF project within the framework of the Pharma and Chemistry Competence Centre of Latvia “Elaboration and standardization of novel tumour diagnostic technologies providing high quality tumour biomarker research, diagnostics and personalized treatment”.

X chromosome doubling correlates with triploidy in malignant transformation of male tumours

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Background. Numerical chromosome aberrations (aneuploidy) are consistently observed in cancer cell karyotypes. A frequent manifestation of this phenomenon is para-triploidy (62-76 chromosomes), as it is associated in some solid cancers with progression, chemotherapy resistance and poor prognosis. However, the origin of para-triploidy in cancer, and subsequently the mechanism through which it impacts the severity of the disease, remains unclear, necessitating research. A possible mechanism implicated in the origin of cancer aneuploidy is whole-genome karyotypical rearrangements, or 'meio-mitosis'.

Aim. The aim of this study was to investigate the possible involvement of whole genome rearrangements in the origin of aneuploidy (para-triploidy in particular) and in malignant transformation from preneoplastic states, in male tumours using the advantage of the presence of two different sex chromosomes, X and Y.

Methods. Bioinformatic meta-analysis was performed (using Python scripts) on malignant and premalignant male tumour karyotypes stored in the Mitelman Database of Chromosome Aberrations and Fusions in Cancer (12 types of solid malignant and 3 types of premalignant lesions, a total of 2772 karyotypes). In order to detect the signs of whole-genome alterations, chromosome numbers (ploidy) and the most frequently encountered combinations of sex chromosomes were determined and correlatively compared.

Results. Karyotype heterogeneity was observed in all malignant tumours, with modal chromosome numbers varying between 2n and 4n. In most cases, a distinct para-triploid fraction was also present (especially pronounced in germ cell tumours). The para-triploidy for all tumour types strongly correlated with X chromosome doubling (an XXY or XX,-Y karyotype, $R \approx 0.8$). The premalignant lesions (colon adenoma, astrocytoma, kidney adenoma and oncocytoma) were mostly diploid or hyperdiploid and also exhibited karyotype heterogeneity, but to a lesser degree. The para-triploid component was also present, however in smaller proportion than in malignant counterparts. XXY and XX,-Y karyotypes were quite rare and more pronounced in colon adenoma. However, even this small fraction of karyotypes with extra-X was also mostly para-triploid. Hyper-diploidy negatively correlated with X chromosome gain in both malignant tumours and premalignant counterparts.

Conclusion. The correlation between the doubling of the X chromosome and para-triploidy in male tumours points towards whole-genome rearrangement and its germline origin. The para-triploid XXY or XX,-Y karyotypes in premalignant lesions may be causative for malignant transformation and as such be tested as a future prognostic marker.

Acknowledgements. N. M. V. - Alfreds Raisters scholarship.

No conflict of interest was disclosed.

Analysis of polyamine levels in blood serum of patients with breast cancer using optical SPR-based immune biosensor

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Background. Oncological diseases are very common throughout the population of many countries of the world, especially among middle-aged and elder people. The main threat of cancer diseases underlies in the difficulty of diagnosing them in the early stages. That is why it is extremely important to search, create and work out the latest diagnostic methods for oncological diseases that would allow to determine them more precisely and in shorter terms

Aim. The aim of the study was to develop a method for qualitative and quantitative analysis of polyamines as potential tumour markers in blood serum of patients diseased with breast cancer with use of newly created immune biosensor based on effect of surface plasmon resonance.

Methods. In the process of the study there were used basics of immune analysis, methods of biosensor analysis with preliminary modification of analytical surface of biosensor with certain reagents such as protein A and BSA for better orientation of sensitive layer made from antibodies. Also there were use methods of statistical analysis for comparison of results obtained from study of blood samples obtained from patient with different age, tumour size, and other parameters.

Results. During the study there were analysed 30 samples of blood serum, 20 of which were samples obtained from patients diseased with breast cancer and 10 samples were normal, taken from healthy people and used as controls. Analysis of blood serum samples were made, using previously created calibration curve, made on basis of polyamine solution in concentration from 10 ng/ml to 1.5 µg/ml. This allowed to determine as the presence of polyamines in blood samples and approximate concentration of polyamines comparing resonant angle shifts in calibration curve and blood samples. According to the results obtained there were studied that concentration of polyamines exceeds physiological levels of polyamines and were in range from 20 to 100 ng/ml. Elevation of levels of polyamines correlated with enlargement of tumour size of the patients and slightly with the age of the patients.

Conclusion. Proposed approach allows to determine presence and approximate concentrations of polyamines in range from 10ng/ml to 1.5µg/ml in samples of blood serum of patients with breast cancer which correlates with tumour size and age of the patients.

Acknowledgements. Study were made with help of biosensor device "Plasmonest" given by Institute of Cybernetics of V. M. Glushkov, Kyiv, Ukraine. The samples of blood serum were given by diagnostic laboratory "Alpha-lab service", Kharkiv, Ukraine.

Auronofin reduces brain amyloid- β (A β) load in Alzheimer disease *APP^{NL-G-F/NL-G-F}* mice model

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Background. Neuroinflammation, deposition of the A β and Tau protein are main factors that plays significant role for development of Alzheimer disease (AD). Current available drugs are capable shortly reduce some of the symptoms in AD, and therefore is a need for a drug therapies that could slow down the progression of AD pathogenesis. Auronofin (AR) is anti-inflammatory drug that pharmacologically has been used to reduce the neuronal loss caused by neuroinflammation (Madeira J. *et al* 2012). Moreover, no published studies have examined the effects of AR to prevent neuroinflammation and cognitive deficits in AD mice models.

Aim. The aim of the current study was to evaluate the effects of small doses of AR on the cognition and immunohistochemical (IHC) markers in *APP^{NL-G-F/NL-G-F}* mice.

Methods. For this study, we used 14 months-old male *APP^{NL-G-F/NL-G-F}* mice. Mice received once a day intraperitoneal injections for 30 days of either control (saline 1 ml/kg) or AR (1 mg/kg and 5 mg/kg). 19 days after the start of treatment, the animals were tested in behavioural tasks, i.e., object location task (OLT) and open field, zero maze and water maze tests. For – IHC, we assessed macroglial marker glial fibrillary acidic protein (GFAP), IBA-1 and mouse anti-human A β_{4-10} (W0-2 antibody) in cortical and hippocampal structures. Behaviour tests and quantitative IHC data were analyzed using one-way ANOVA followed by Bonferroni's multiple comparison test.

Results. IHC data shows that both injected doses of AR markedly reduce A β load in the hippocampus (1 mg/kg $p = 0.0004$ and 5 mg/kg $p = 0.02$) but not in cortex. Staining for the GFAP and IBA-1 did not show any significant differences among groups in average density, measured in both brain structures. From behaviour studies, only the water maze test showed a tendency for learning faster at lower dose 1 mg/kg AR. There were no significant differences between treatment groups and control treated mice in the open field, zero-maze and OLT tests.

Conclusion. In summary, the present data demonstrated that at small doses AR can reduce A β deposition which plays a significant role in the pathophysiology of AD and thereby may decrease the neurodegenerative process. Overall, there is a need for further studies to determine more possible effects of AR in neurodegenerative disease-models.

Acknowledgements. Study was supported by No. lzp-2018/1-0275 and NIH P30 NS 47466.

Discovery of new sortase A inhibitors from *Staphylococcus epidermidis* by fluorescence resonance energy transfer (FRET) screening system

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Background. The antimicrobial resistance is considered as a significant medical issue due to the lack of novel antimicrobial therapy ideas. In case of nosocomial infections methicillin resistance of *Staphylococcus epidermidis* is particularly widespread. The ability of *S. epidermidis* to form biofilms is considered as a severe virulence factor. Surface proteins that bind plasma and extracellular matrix proteins are one of the probable cause of biofilm formation. Surface proteins not only promote interaction between the bacteria and patient's tissues, but also provide new strategies to escape from the host's immune system. Being a thiol transpeptidase sortase A has been known to catalyse sorting reactions on the cell wall, cleaving surface proteins between threonine (T) and glycine (G) of the LPXTG motif. Inhibition of surface protein formation by sortase A can be a potentially new way of antimicrobial therapy in case of multi-resistant pathogens.

Aim. The aim of this study was to find novel drug-like compounds for inhibition of sortase A from *Staphylococcus epidermidis* in order to prevent formation of multiresistance.

Methods. For this purpose, the DNA construct encoding the catalytic domain of *S. epidermidis* sortase A has been created by inserting sortase A gene into pET22b and pET28a (*Novagen*) vectors. Proteins have been expressed by IPTG induction in *Escherichia coli* system (BL21). Sortase A in the pET22b vector has been purified by anion exchange and size exclusion chromatography. Sortase A in the pET28a vector has been purified by immobilized metal affinity chromatography. *AmiconUltra* (3kD) has been used to concentrate proteins after each purification procedure. The activity of the enzyme and the potency of its inhibitors have been determined using FRET analysis (*Tecan Infinite 200 PRO*) measuring fluorescence of Abz-LPETG-K-(DPN) and Dabcyl-LPETG-Edans (*GL Biochem*) peptide cleavage products.

Results. The sortase A gene has been successfully inserted into pET28a and pET22b vectors to express His6-tagged and untagged sortase A, respectively. In total, 324 drug-like compounds have been screened using FRET analysis. Preliminary results showed that at least one compound (1-(3,4-dichlorophenyl)-3-dimethylamino-1-propanone) showed high (98%) inhibitory activity. Two compounds ('3-{1-[2-(trifluoromethyl)pyridin-4-yl]pyrrolidin-2-yl}oxan-4-ol and '2-[[[(2S,4S)-4-fluoro-2-(hydroxymethyl)pyrrolidin-1-yl]sulfonyl]benzotrile) demonstrated moderate (60% and 63%, respectively) inhibitory activity.

Conclusion. Results show that compounds having rather different structural moieties can inhibit sortase A from *S. epidermidis*.

Acknowledgements. This study was supported by the ERDF project No. 1.1.1.1/16/A/107

Extracellular vesicles reverse dysfunctions in 6-OHDA-induced Parkinson's disease model-rats

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Background. Parkinson's disease (PD) is the second most common neurodegenerative disorder that is characterized by the loss of dopaminergic cells in nigro-striatal pathway resulting in dramatic impairment in motor functions. PD is affecting more than 1% of the population aged over 65 years and nearly 5% of those aged over 80 years [Shulman et al, 2011]. At present, there is no effective cure for PD. Currently available treatments are symptomatic and do not prevent neurodegeneration [Cheng et al, 2010]. Stem cell research has the potential to significantly impact the development of disease-modifying treatments for PD. Extracellular vesicles (EVs) which are secreted by almost every type of cells and carry multiple proteins, coding and non-coding RNAs, lipids and metabolites can be considered as promising neuroprotective agents against PD. Previously *in vitro* study showed that exosomes derived from human exfoliated deciduous teeth stem cells (SHEDs) suppressed 6-OHDA-induced apoptosis in dopaminergic neurons (Jarmalaviciute et al., 2015).

Aim. The purpose of this study was to assess whether intranasally (i.n.) administered exosomes can reverse gait impairments and normalize tyrosine hydroxylase (TH) expression in nigro-striatal pathway in 6-OHDA-induced PD model rats.

Materials and methods. EVs were prepared and purified in State Research Institute Centre for Innovative Medicine, Vilnius, Lithuania. Male Wistar rats (280±20 g) were randomly divided into 6 groups (n=8) and PD model was obtained by injecting neurotoxin 6-OHDA (20 µg/3 mL) or aCSF (control) into the medial forebrain bundle. Animals were treated by i.n. administered exosomes (7.7 * 10⁷/10 mL) starting on day 7 post-lesion for 15 consecutive days. Gait test (*CatWalk*TM XT apparatus, Noldus, NL) was performed 7 days prior to 6-OHDA injection, on post-lesion days 7 and 20. Immunohistochemical detection of dopamine synthesizing enzyme TH in the *striatum* and *substantia nigra* (SN) was performed *ex vivo*.

Results. Administration of 6-OHDA-induced gait impairments (e.g. stand, stride length, step cycle and duty cycle) and significantly decreased striatal and SN expression of TH. EVs effectively protected against 6-OHDA-induced deficits by improving gait and normalizing TH expression in both brain structures.

Conclusions. For the first time we demonstrated anti-parkinsonian therapeutic efficacy of i.n. administrated SHEDs-derived extracellular vesicles in a rat model of PD. Our findings could potentially be exploited in the development of new treatment strategies to combat PD.

Acknowledgements/Funding. This study was supported by the National Research Programme "Healthy ageing" (Grant No. SEN-15090) from Research Council of Lithuania, and the University of Latvia patron LLC „Mikrotik”.

Vaccinium genus berry pomace extracts inhibit secretion of pro-inflammatory cytokines in LPS induced THP-1 monocytes

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Background. Anthocyanidins are plant phytochemicals found at high concentrations in berries, vegetables and flowers. Anthocyanidins have been extensively investigated due to their antioxidant and anti-inflammatory properties (Blando et al., 2018). Circulating monocytes are key players in the host defence against pathogens therefore the modulation of their function is a suitable approach for anti-inflammatory treatment (Chanput W. et al. 2010). Lipopolysaccharide (LPS) is the major component of Gram-negative bacteria cell walls and it is a potent activator of monocytes. LPS induces the production of cytokines, such as TNF α , IL1 β , IL6, IL8, IL10, and TGF β in monocytes (Tucureanu et al., 2017).

Aim. The aim of the study was to develop an *in vitro* assay to study the anti-inflammatory properties of *Vaccinium* genus berry pomace extracts, using LPS stimulated human monocytic THP-1 cell line.

Methods. Five *Vaccinium* berry species – bilberries (extract 1), highbush blueberries (extract 2), American cranberries (extract 3), bog cranberries (extract 4) and lingonberries (extract 5) were harvested, berry residues were extracted and purified (Muceniece et al. 2019). THP-1 cells were pre-incubated with berry extracts at concentrations 1, 0.2 and 0.04 mg/ml for 30 min following bacterial lipopolysaccharides (LPS, Sigma-Aldrich) stimulation for 1 h. NF- κ B induction was assessed by flow cytometry using mouse anti-NF- κ B PE antibody (BD Biosciences). Cell culture supernatants were harvested and TNF- α , MMP-9, IL-23, IL-10, IL-1 β , CCL22 and IL-8 secretion was analysed by Luminex assay (R&D Systems) and human IL-8/CXCL8 DuoSet Elisa kit (R&D Systems).

Results. Incubation with LPS at 1 μ g/ml for 1h resulted in NF- κ B nuclear translocation in 75% of in THP-1 cells. Extracts 1-4 at 1 mg/ml inhibited LPS-induced NF- κ B nuclear translocation to the level of unstimulated cells (10%). Extracts 1-5 at 0.2 and 1 mg/ml significantly down-regulated LPS-induced cytokine IL-8, TNF- α , IL-1 β and IL-23 secretion. Extracts 1-4 at 0.2 mg/ml induced secretion of MMP-9.

Conclusions. An assay was developed to study the effects of *Vaccinium* genus berry pomace extracts on LPS stimulated human monocytic THP-1 cell line. LPS induced activation of transcription factor NF- κ B and secretion of downstream pro-inflammatory cytokines in monocytic THP-1 cell line. Extracts 1-4 significantly inhibited LPS induced NF- κ B activation in THP-1 cells. Extracts 1-5 inhibited the secretion of LPS induced pro-inflammatory cytokines IL-8, TNF- α , IL-1 β and IL-23. Thus, *Vaccinium* genus berry pomace extracts could serve as a valuable source of anti-inflammatory agents.

Acknowledgements. This work has been supported by the European Regional Development Fund within the project No. 1.1.1.1/16/A/047 “Genus *Vaccinium* berry processing using “green” technologies and innovative, pharmacologically characterized biopharmaceutical products”. Authors declare no conflict of interest.

Prognostic calculations for grown-up congenital heart disease patients in Latvia

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Background. The remarkable improvement in survival of patients with congenital heart disease (CHD) has led to a continuously growing number of grown-up congenital heart disease (GUCH) patients, in particular those with more complex disease. Importantly, a significant reduction in mortality is associated with referral to a GUCH center with professional care and is most pronounced in patients with severe forms of CHD. There is growing number of patients with complex CHD in children population in Latvia what will increase the GUCH population in near future. Data on GUCH population in Latvia are still lacking. It is very important to realize the amount of expected GUCH population to adequately plan and organize medical care for those patients.

Aim. We aim to calculate approximate number of GUCH population in Latvia in 8 years according to Latvian Children Congenital Heart Disease Registry.

Methods. This is single-center retrospective data analysis of Children Congenital Heart Disease Registry from Children's Clinical University Hospital in Riga, Latvia. Patients with CHD were included in registry from January 2006 until December 2016 consecutively. Parents of all patients did consent for inclusion in registry. Data about date of birth, gender and diagnosis were collected. Patients with moderate to severe CHD complexity according to ACC/AHA 2008 guidelines were defined as complex CHD and analyzed for 10 years after inclusion of first patient. Prognostic estimates of age and disease complexity for 2, 5 and 10 year prognosis were calculated starting from December 2016. Statistical analysis was performed with IBM SPSS Statistics 23.

Results. From January 2006 until December 2016 2726 children were included in the Registry with mean age by inclusion 3 years (Median 134 days, Mode 0 days) and 50,4 % were male patients. By December 2016 there were 389 (14,3 %) adult patients from whom 49 (12,6 %) patients had complex CHD. In 5 years there will be around 726 GUCH patients with 98 (13,4%) of them with complex CHD. In 10 years there will be around 1589 GUCH patients with 249 (15,6 %) of them with complex CHD.

Conclusion. After 5 and 8 years there will be considerable number of complex GUCH patients with need for organized and professional medical care in specialized GUCH center.

Acknowledgements. No conflicts of interest. No funding.

Does the extent of surgical repair in acute Stanford type A aortic dissection affects early outcome? Single-centre experience in acute aortic dissection surgical repair

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Background. The optimal surgical strategy for repair of acute Stanford type A aortic dissection remains controversial. Due to heterogeneous patient population and diverse clinical presentation, there is no consensus in previously made studies regarding the best approach. Some studies had shown comparable outcomes between limited and extensive approaches (Shi et al., 2014, Di Eusanio et al, 2015, Castrovinci et al., 2016), however others suggest that more extensive repair is associated with higher mortality and morbidity (Rylski et al., 2014, Lio et al., 2016).

The aim of the study was to determine the impact of the extent of surgical repair to intrahospital and intraoperative mortality of patients who underwent surgical repair of acute Stanford type A aortic dissection.

Materials and methods. The study consisted of 82 consecutive patients with acute Stanford type A aortic dissection who underwent surgical repair in our institution from year 2006 to year 2018. Patients were divided in four groups: I – isolated supracoronary ascending aorta replacement, II – hemiarch, III – total arch replacement, IV – aortic root replacement.

Results. Mean age of study population was 56.6 years (SD±13.7) and majority of patients were males (73.2%). History of primary arterial hypertension was seen in 82.9% of all patients. Dissection extending to iliac arteries in preoperative computed tomography angiography was seen 43.0% and cardiac tamponade in 34.1% of all cases. Significant aortic valve insufficiency (Grade III-IV) in screening echocardiography was evident in 25.6% of all cases. Majority of all patients (58.5%) underwent supracoronary ascending aorta replacement, 12.2% hemiarch, 11.0% total arch replacement and 18.3% had aortic root replacement. Overall intrahospital mortality of study population was 24.4%. In group I intrahospital mortality was 18.8%, group II – 30.0%, group III – 33.3% and in group IV – 33.3% (p=0.477). Intraoperative mortality of study population was 2.1% in group I, 0.0% in group II, 0.0% in group III and 26.7% in group IV (p=0.019).

Conclusion. In our study extent of surgical repair into aortic arch had no statistically significant impact to overall intrahospital mortality and we emphasize that it is due to a relatively small patient population. However, aortic root replacement was associated with significantly higher intraoperative mortality.

Acknowledgements. Nothing to disclose.

Increase in direct oral anticoagulant use 6 months after electrical cardioversion over 4 years

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Background. Atrial fibrillation (AFib) is the most common encountered sustained cardiac arrhythmia. Electrical cardioversion (ECV) can be considered as an urgent or optional method for restoring normal sinus rhythm in patients with AFib. ECV is associated with higher thromboembolic risk after conversion to sinus rhythm, therefore anticoagulation is necessary to prevent thromboembolic events.

Aim. The objective of this study was to determine change in use of anticoagulation therapy in comparison with data from a similar study.

Methods. A prospective study includes patients with electrocardiographically confirmed atrial fibrillation. The study was conducted at the Latvian Centre of Cardiology, Pauls Stradins Clinical University Hospital. Between January 2017 and December 2017, 168 patients were interviewed. Data from medical records were collected. All participants provided written informed consent. 6-month follow-ups were conducted by a telephone interview. Our collected data were compared with data from a similar study, performed in Latvia in year 2014.

Results. Mean age of patients was 63.9±10.7 years, 52% were men. After 6-months 34 (20.4%) of patients used rivaroxaban, 16 (9.5%) used dabigatran and 47 (28%) used warfarin. Overall 36 (21.4%) patients were taking aspirin of whom 77% had CHA₂DS₂-VASC >2. Comparing our results with a similar study (Pupkevica et. al., 2014) 6 months after ECV, the overall use of anticoagulants increased by 11.6%, the use of direct oral anticoagulants increased by 18.7% and the use of warfarin decreased by 7.1%.

Conclusion. Over 4 years, the use of anticoagulants increased by 11.6% and the use of direct oral anticoagulants increased by 18.7%. The rate of use of warfarin and DOAC is consistent with global data. Despite indications a group of patients were found to take aspirin, which does not lower thromboembolic risk, instead of anticoagulants.

Real-life and estimated attainment of low-density lipoprotein cholesterol goals in patients with familial hypercholesterolemia on maximal statin and ezetimibe therapy.

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Background. Familial hypercholesterolemia (FH) is the most common inherited lipoprotein disorder causing premature atherosclerotic cardiovascular disease (ASCVD), due to extremely elevated low-density lipoprotein cholesterol (LDL-C). Attainment of LDL-C goal is critical for this group, but not possible in many cases even with maximal statin doses in combination with ezetimibe. Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) are potent drugs that additionally lower LDL-C by 60%, but are not reimbursed in Latvia.

Aim. To estimate the proportion of patients in the Latvian Registry of FH (LRFH), who have not or are predicted to not achieve LDL-C goals and would therefore benefit from PCSK9i.

Methods. Patients with clinical FH with known lipid-lowering therapy (LLT) status were selected from the LRFH. For patients not on maximal dose of atorvastatin or rosuvastatin plus ezetimibe, the effect of theoretically applied maximal LLT was calculated according to widely accepted formula of LDL-C reduction by 6% when doubling a statin dose, 20% when adding ezetimibe, and by 70% reduction for LLT-naive patients. Indications for PCSK9i were evaluated according to 2017 ESC/EAS Task Force Practical clinical guidance for PCSK9i therapy.

Results. By December 2018, 191 of 241 clinical FH cases were valid for analysis: 155 (64.3%) patients on any LLT, 19 (12.3%) on maximal LLT and 86 (35.7%) on no LLT. Remaining patients were excluded from analysis due to non-standard or unclear doses. Altogether, 13 patients (8.4% of those on any LLT) had achieved their LDL-C goals: one in maximal LLT and 12 in non-maximal LLT group. After calculating theoretical expected results of switching all patients to maximal LLT, predicted attainment of LDL-C goals increased to 76 (39.8%). Number of patients who would benefit the most from PCSK9i therapy are summarized in Table.

	Clinical ASCVD and LDL-C > 2.6 mmol/L	No clinical ASCVD		Total
		Additional indices of risk and LDL-C > 3.6 mmol/L	No additional indices of risk and LDL-C > 4.5 mmol/L	
Patients meeting strong indication criteria for PCSK9i, n (%)	23 (12.0)	13 (6.8)	2 (1.1)	38 (19.9)

Conclusions. Only 39.8% of FH patients would reach LDL-C goal with maximal statin and ezetimibe therapy, and almost 20% of FH patients would meet criteria for indications of PCSK9i therapy according to 2017 ESC/EAS Task Force recommendations.

Characteristics of lipid profile in pediatric population of Children's Clinical University Hospital in Latvia

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Background. Dyslipidemia is known as a major risk factor for development of cardiovascular disease (CVD). Studies have demonstrated that the process begins in the second decade of life and dyslipidemia, obesity and other risk factors in childhood predict adult CVD. Identification and treatment of youth dyslipidemia is important in the reduction of future CVD.

Aim. To evaluate lipid profile in pediatric patients and analyse it in association with other cardiovascular risk factors.

Methods. A retrospective study was done in Children's Clinical University Hospital (Riga, Latvia), analysing the data of a 2-year period (2016–2017). Data of patients in cardiology and endocrinology departments were collected. Inclusion criteria were age ≥ 2 years and a measured total cholesterol (TC) level. Percentiles for the respective age and gender were used for assessment.

Results. Data from 556 patients were analysed (52.5% males). The median patient age was 12 (IQR 9 to 15) years. Out of all patients 218 (39.2%) had diabetes mellitus (DM). Body-mass index was normal in 50.3% of patients (n=170) and $>95^{\text{th}}$ percentile in 20.1% (n=68). Complete lipid profile (TC, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG)) was done in 257 (46.2%) cases. Lipid levels are summarized in the Table. TC level was abnormal ($^{395^{\text{th}}$ percentile) in 60 patients (10.8%), borderline (75^{th} to 95^{th} percentile) in 111 (20.0%). Out of all cases the levels of LDL-C, non-HDL-C and TG were measured in 59.0%, 49.3% and 72.7%, respectively. The levels of LDL-C, Non-HDL-C and TG were abnormal in 11.3% (n=63), 5.9% (n=33), 18.5% (n=103) and borderline in 9.5% (n=53), 7.2% (n=40) and 22.3% (n=124), respectively. Maximal registered levels of TC, LDL-C, TG and non-HDL-C were 7.96, 6.02, 8.36, 6.43, respectively. In 6 patients (1.1%) LDL-C was 35 mmol/L.

Table. Lipid levels in total sample, DM and non-DM groups.

	Total (n=556)	DM (n=218)	Non-DM (n=338)	p-value
TC, mmol/L (mean \pm SD)	4.08 \pm 0.91	4.30 \pm 1.0	3.94 \pm 0.82	<0.001
LDL-C, mmol/L (mean \pm SD)	2.62 \pm 0.87	2.80 \pm 0.94	2.50 \pm 0.80	0.001
TG, mmol/L (median, IQR)	1.03 (0.72 to 1.35)	1.12 (0.82 to 1.53)	0.95 (0.7 to 1.3)	0.015
Non-HDL-C mmol/L (mean \pm SD)	2.79 \pm 0.92	3.02 \pm 0.99	2.67 \pm 0.85	0.002

Conclusions. In significant number of pediatric patients lipid levels are above the 95^{th} percentile. Patients with diabetes have higher levels of TC, LDL-C, TG and non-HDL-C compared to non-DM group.

Incidence of congenital heart defects in Kazakhstan

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Background. Congenital heart defects (CHD) are called congenital functional or structural disorders of the heart, which may be discovered much later and depending on the severity they affect the quality and duration of life. CHD are today an important topic for study, because this pathology is one of the main factors leading to disability and mortality. Earlier studies have identified risk factors that could affect the incidence of CHD. The majority of risk factors affecting the formation of the CHD in the fetus are manageable, as evidenced by the numerous studies.

Aim. To study the incidence of CHD in Kazakhstan.

Material and Methods. The research is based on accounting-reporting forms of the MOH of the Republic of Kazakhstan relative to the CDH. A retrospective research was conducted in the period from 2011 to 2015. According to the generally accepted methods of sanitary statistics computed extensive and intensive incidence of CHD.

Results. During the studied period was registered for the first time 40,401 new cases of CHD. While a high proportion was set among patients up to 15 years (81.9%) and the lowest figures in the age of 15-17 years (4.6%).

Table. CHD in Kazakhstan, 2011-2015

Age	<15	15-17	≥18	Total
Number (%)	33,096 (81.9)	1,852 (4.6)	5,453 (13.5)	40,401 (100)
Incidence, $\frac{0}{0000}$ P±m (95% CI)	151.3±28.5 (95.5-207.1)	50.6±3.4 (43.8-57.3)	9.2±0.5 (8.2-10.1)	47.5±8.0 (31.9-63.1)
T, %	+20.8	+9.8	+1.2	+19.5

Intensive average annual incidence of CHD was $47.5\frac{0}{0000}$ (95% CI=31.9-63.1), the dynamics of the indicators are growing from $36.8\frac{0}{0000}$ (2011) to $75.1\frac{0}{0000}$ in 2015, the average annual growth rate of aligned index T=+19.5%.

It was also revealed that in patients up to 15 years, the incidence rate was more than 16.5 times relative to patients aged 18 years and older. Trends in the incidence of CHD in all age groups have a tendency to increase (T_{<15}=+20.8%; T₁₅₋₁₇=+9.8%; T_{≥18}=+1.2%).

Conclusions. The incidence of CHD in recent years in Kazakhstan are growing. Age indicators of CHD was highest in the age of 15. The results of the study determined that the CHD are characteristic not only for children but for teenagers and adults (over 18 years). Based on this analysis you can see that this problem remains important and results necessary for planning targeted activities.

Exploring variations of acute myocardial infarction coding, management and 30-day mortality in Latvia: the nationwide linked administrative data study

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Background. According to statistics of Organisation for Economic Cooperation and Development (OECD) Latvia has one of the highest 30-day mortality for acute myocardial infarction (AMI). To explain the causes of it, the output data used in the calculation of this indicator was analysed at a hospital level to explore the variations in AMI coding and management.

Aim. The aim of the current study was to investigate which factors can explain high mortality rates in AMI cases.

Methods. Data from Health services reimbursement system linked to the data at Causes of death registry from 2014 – 2017 were analysed. Defined exclusion criteria were applied and 11675 emergency AMI admissions to 20 hospitals were indexed. Evaluating the inter-hospital differences in non-ST elevation myocardial infarction (NSTEMI) revealed significant inconsistency in coding of NSTEMI events. Therefore the 30-day mortality and the factors influencing it, was exclusively analysed for 9168 ST elevation myocardial infarction (STEMI) cases. The outcomes of different reperfusion scenarios were analysed for five groups of hospitals of size, location, the availability of percutaneous coronary interventions and cardiac surgery. The multivariable logistic regression was employed to adjust the results for potential explanatory variables as patient age, gender, comorbidities, the distance between their residence and hospitals.

Results. 30-day mortality for all indexed AMI admissions (17,4%) was in line with the value of the indicator in OECD reports. However only 21,5% of all cases have been coded as NSTEMI (12,2% mortality). The mortality of the patients with STEMI have reached 18,8% composed by mortality in range from 13,7% for patients directly admitted to tertiary university hospitals to 23,7% for patients initially admitted to local hospitals. Significant variations in mortality between reperfusion scenarios as well as the variations in the frequency of application reperfusion methods between hospital groups were observed. Some variation in mortality between hospital groups persisted also after adjustment to the reperfusion therapy scenario and other potential confounders.

Conclusion. The improvement of coding practice is needed to measure the actual AMI mortality in Latvia. Among patients with STEMI, there are wide inter-hospital variations in care and mortality. There is a substantial room for improvements in all types of hospitals to increase reperfusion rates and to reduce delays in initiation of it.

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

In-hospital Complications Following PCI for True Bifurcation Lesions

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Background. Treatment of coronary artery bifurcation lesions remains one of the biggest challenges for interventional cardiologists despite the rapid development of technologies in this field over the past decade. Percutaneous coronary intervention (PCI) for bifurcation lesions, in comparison with the technically simpler treatment for non-bifurcation lesions, is accompanied by a higher risk of intraprocedural complications. This can require immediate change of a stenting strategy and affect the outcome of the entire procedure. Thus, further studies are required to find an optimal tactic for the treatment of this type of lesion.

Aim. The study compares intraprocedural complications and evaluates clinical and angiographic in-hospital outcomes of PCI with one-stent versus two-stent techniques for the treatment of true coronary bifurcation lesions.

Material and methods. A 2-year retrospective study of the Latvian Centre of Cardiology Coronary Bifurcation Treatment Registry. A total of 231 patients with true coronary bifurcation lesions were included. The patients were divided into 2 groups. For 199 of these patients, the provisional one-stent technique was applied, whereas for the other 32 patients, the systematic two-stent technique was used. All PCI were performed between 11th January 2017 and 12th December 2018. Patients with ST segment elevation myocardial infarction (STEMI) in the last 24 hours were excluded. Perforation, dissection, main branch and side branch occlusions, cardiogenic shock, death, stroke, transistor ischemic attack, periprocedural myocardial infarction (MI), stent thrombosis were analysed. For 32% of patients, creatine kinase MB (CK-MB) measurements were performed after the procedure.

Results. Procedural complications were vessel perforation (one-stent 0% (n=0) vs two-stent 3.1% (n=1), p=0.012), side branch occlusion (one-stent 2% (n=4) vs two-stent 0% (n=0), p=0.418). In-hospital complications were stent thrombosis (one-stent 0.5% (n=1) vs two-stent 0% (n=0), p=0.688) and periprocedural myocardial infarction (one-stent 4% (n=8) vs two-stent 3.1% (n=1), p=0.808). One of the 9 cases of myocardial infarction was Q MI, the rest were non-Q MI. There were no cases of main branch occlusion, cardiogenic shock, in-hospital death, stroke and transistor ischemic attack detected in both groups.

Conclusions. Analysis of the results of this study has demonstrated that both bifurcation stenting techniques were associated with similar rates of intraprocedural complications and in-hospital outcomes.

The two-year retrospective analysis of pulmonic embolism diagnostics and treatment quality

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Background. According to the actual guidelines for pulmonic embolism (PE) diagnostics and treatment, thrombolytic reperfusion therapy is indicated for patients with proved high-risk acute PE with unstable hemodynamic 15 minutes or longer. Studies show that thrombolytic therapy results in lower PE mortality. However, there is almost no data about the length of prehospital instability and vital functions.

Aim. The aim of this research was to analyse the quality of diagnostics of high-risk PE, and to evaluate the adequacy of treatment choice basing on the PE severity.

Methods. The retrospective study was performed in Riga Eastern Clinical university hospital. The materials of 2013 and 2016 years were analysed. Prehospital/intrahospital vital parameters, primary laboratory and imaging data, as well as general health status (age, comorbidities, used medications) were evaluated. We included all the patients with diagnosed PE by computed tomography angiography or by autopsy. We used *PESI* (Pulmonary Embolism Severity Index) for PE severity evaluation. *IBM SPSS 25.0* was used for data processing.

Results. Altogether, 256 patients with diagnosed PE were included – 102 in year 2013 and 154 in year 2016. Thrombolysis was performed in 4 cases of severe PE. In 2013, strong indications for thrombolysis were in 17 cases (performed in 3 cases or 17.7%), and in 2016 – 40 cases (performed in only 1 case or 2.5%). In all cases of high-risk PE with thrombolysis mortality rate was 0%. However, it was 7.1% and 28.2% among high-risk patients with only anticoagulation therapy in 2013 and 2016 respectively ($p < 0.005$). Strong association between mortality and hemodynamic instability also was proved ($p < 0.001$), also the outcome was associated with presence of PE signs on primary ECG ($p < 0.05$).

Conclusions. The severity of PE is not evaluated adequately, and the appropriate attention to prehospital/intrahospital instability is not paid. Timely evaluation of disease severity and choice of acceptable therapy methods may significantly decrease the mortality and improve the outcome.

Acknowledgements. None.

Differences in stress, anxiety and depression by diagnosis of cardiovascular patients in Latvia

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Background. The prevalence of stress, anxiety and depression in patients with cardiovascular disease (CVD) is three times higher than prevalence in the general population. The American Heart Association recommends that depression should be recognized as a major risk factor for coronary heart disease, similar to hyperlipidemia, hypertension and smoking.

Aim. To investigate the level of stress, anxiety and depression in hospitalized patients and differences between CVD diagnoses.

Materials and methods. Cross-section study was performed in Pauls Stradins Clinical University Hospital (PSCUH) and Riga East University hospital (REUH) between March 2017 – July 2018. Study questionnaire contained 90 items further grouped in categories of stress, anxiety, depression levels. Patients with cardiovascular diagnoses, 18-80 years old from PSCUH, REUH were enrolled in the study. Chi square test was performed to analyze differences in levels of stress, anxiety and depression between six types of diagnoses.

Results. 948 patients were enrolled in the study, of them 418 from PSCUH and 530 from REUH. 547 (57,7%) of them were males with mean age 65.9 (SD=10.2). Medium and high level of stress were in 54,7% of patients, subclinical and significant level of anxiety were in 18,3%, medium severe and severe level of depression – in 4,2%. of patients. There were no statistically significant differences between diagnoses concerning level of stress, depression and anxiety. Patients with atrial fibrillation/flutter showed the highest level of stress 47,1% (p=0.12), anxiety 38.4% (p=0.41) and depression 33.3% (p=0.18). Patients who attended planned coronarography and percutaneous coronary intervention displayed as high depression – 33.3% (p=0.18).

Conclusions. There were not differences in levels of stress, anxiety and depression between CVD. There were many patients with medium and high levels of these psychological symptoms; it displays the necessity of special attention for CVD patients.

Comparing quality of life in healthy children and in pediatric obesity in Latvia

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Background. Dimensions of health related quality of life (HRQoL) determinates significant aspects of health that often are not considered as significant ones and cannot be revealed by traditional physiological or clinical measurements. It is known that emotional and physical well-being is very important to keep health in good condition, but overweight and obesity can be a vital reason for children's low indicators of quality of life.

Aim. To analyze if quality of life in its different categories vary between healthy children with optimal weight and children with overweight and obesity.

Methods. This study included 200 children and their parents. All of them were divided in to two main groups – first group included 100 children aged 8 to 17 years with overweight and obesity according to age related BMI percentile charts, and their parents. The second group included 100 healthy children aged 8 to 17 years with optimal weight according to age related BMI percentile charts, and their parents. Afterwards the child and his parents were asked to participate in research to analyze their quality of life according the *KIDSCREEN-52* survey (Ravens-Sieberer U. et al., 2005, The KIDSCREEN Group Europe, 2006). The IBM SPSS Statistics 22.0 software and Pearson's chi-squared test was used to make statistical analysis of data.

Results. The main age of 200 children who participated in the study was 12.6 years. After analyzing data with Pearson's chi-squared test, significant association ($p < 0,05$) was found between children with optimal weight and children with overweight and obesity in such HRQoL survey categories like physical well-being, self-perception, moods and emotions, and autonomy. The most relevant association between healthy children and pediatric obesity was found in *KIDSCREEN-52* survey about physical well-being ($p = 0,075$) and health evaluation in general ($p = 0,085$), respectively children with overweight and obesity estimated their life quality much lower than health children.

Conclusions. Obesity and overweight has a moderate to strong negative influence on overall HRQoL in pediatric populations. It was observed that many aspects of health related quality of life contain the outcome of a health condition on the child's everyday activities, physical symptoms, social interactions and emotional well-being.

Characteristics of faecal microbiome enterotypes of preschool children

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Background. At present a lot of data show the importance of composition of gut microflora in the development of different diseases. Three different enterotypes have been identified: type 1 – characterized by high levels of *Bacteroides*, type 2 – by *Prevotella*; type 3 – by *Ruminococcus*. Since gut microbiota changes in early infancy and continues to develop later in life, it could be influenced by a variety of factors.

Aim. To detect the composition of intestinal microbiota, to identify main enterotypes in healthy preschool children and to analyze association between age and delivery type with microbial diversity.

Methods. The study was performed at the Children's Clinical University hospital, primary health care centers and kindergartens in Latvia, including healthy infants and children below seven years of age. Parents of children were asked to answer a questionnaire (life anamnesis, feeding, diseases) and bring a faecal sample of their child. Further, DNA was extracted from feces and sequencing of the bacterial 16S rRNA gene followed by bioinformatics and biostatistical analyses of sequence data was performed. Shannon species diversity and number of species identified was analyzed. Statistical analysis: *Chi-Square*, *Fisher* test.

Results. Patient sample included 63 children (30 boys); mean age – 7,9 months (range 1,5 – 80 months), median of age – six months (25–75 percentile: 3 – 17 months). Out of them – 40 predominantly breast-fed infants, 23 – toddlers and preschool children. The majority of children (51) were born vaginally; twelve – by C-section. In infants predominance of *Bifidobacterium*, *Escherichia*, *Clostridium*, *Veillonella*, *Bacterioides*, *Streptococcus* was observed, while the dominating microflora in toddlers and preschool children was *Bifidobacterium*, *Clostridium*, *Blautia*, *Bacteroides*, *Faecalibacterium*, *Ruminococcus*. Development of several types of microbiota could be identified among children: 66.7% (42/63) had type-1 enterotype, 27% (17/63) – type-3. Only 6.3% (4/63) resembled type-2 enterotype, although a large number of *Bacteroides* was also identified in microbiota. Type-3 enterotype was observed more often in children born by C-section compared to children born vaginally 66.7% (8/12) vs 17,6% (9/51), $p=0.001$ and among toddlers compared to infants 63% (12/19) vs 12.5% (5/35), $p=0.001$.

Conclusions. Although the majority of children had predominance of *Bacteroides*, microbiome with high levels of *Ruminococcus* was also identified, while type 2 enterotype was observed rarely. Enterotype could be influenced by type of delivery and age. Since some data suggest that *Ruminococcus* prevalence and dysbiosis might be associated with development of allergic, gastrointestinal, respiratory diseases, possible outcomes of early life composition of intestinal microbiota should be studied further.

Electronic media device usage and impact to children's (6–36 months old) sleep duration and quality

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Background. Sleep is vital to children's mental and physical development. Electronic media devices have become a big part of children's lives and may impact children's sleep duration and quality.

Aim. The aim of the study was to analyse and compare how electronic device usage can impact children's sleep and whether parents are worried about children's sleeping habits.

Methods. Survey of children's (6–36 months) living in Latvia, conducted in 2018–2019 about their usage habits of electronic devices. Data were collected via online test and was given to kindergartens. For sleep function we used BISQ (brief infant sleep questionnaire). Statistical analysis: ChiSquare, ANOVA.

Results. The final sample consisted of 1975 respondents (49,5% female) – 6 to 36 months old children (mean 21.8(SD ±9,6) (p<0,0001); median 22.0). 63,1% of them use their media devices versus 36,9% who do not. Children's who do not use media devices wake up more often versus who do: 1,70 (SD ±1,49) VS 1,11 (SD ±1,12) (P<0,0001). 6–12 months old children's wakes up more often in night than 24–36 months old: 2,22(SD±1,51) (P<0,0001) VS 0,70(SD±0,83) (P<0,0001). Awake time is much higher for those who fall asleep during feeding than kinds who fall asleep in their own: 2,67 (SD±1,52) (P<0,0001) VS 0,92(SD±1,03) (P<0,0001). More girls fall asleep in their own bed but boys in their parents bed: 43,26%(n=305) VS 41,35%(n=292). 4,43% (n=62) of parents are very worried about children's sleeping habits, 25,53%(n=358) are a little worried and 70,04%(n=982) are not at all.

Conclusion. Not surprisingly, more often wakes up children's who are younger and who fall asleep during feeding. More girls fall asleep in their own beds but boys in their parents. The main reasons why parents are worried about children's sleep are frequent awakening (6 months old), cannot fall asleep in their own bed (13 months old) and it takes too long to put child to sleep (25 months old).

Association between improvement of psychomotor function and a type of underwent therapy in children with autisms spectrum disorders in Latvia

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Background. Autism spectrum disorders (ASD) is a social communication deficits and repetitive sensory-motor behaviours, characterized by difficulties in socio-emotional reciprocity, verbal communicative behaviours and in developing and maintaining relationships. Recently, a growing evidence on positive effect of therapies on children with ASD was described, however, their effect is not fully proven.

Aim. The purpose of this study was to to investigate the association between a type of a therapy that was attended by child and the improvement of his psychomotor functions.

Methods. Children that attended the Children Clinical University Hospital and the Social Paediatrics Centre of the University of Latvia at 2013-2015 were enrolled into the study and were diagnosed for presence of ASD according to DSM-5 definition. We assessed next psychomotor categories: hearing, visual perception, language development disorders, small motor disabilities, and gross motor development using the Denver functional test. After the initial assessment, children participated in sessions with a special teacher, Montessori therapy, sand therapy, water treatment, dance movement, or animal assistant-therapy according to recommendations of child's physician. Six to eight months later, changes in psychomotor functions were assessed using the same Denver test.

We performed descriptive statistic for all study variables. We built multiple logistic regression models adjusted for age, compliance of development to age norms, and initial diagnosis to investigate the association between the improvement of psychomotor functions with a type of a therapy, comparing with children that did not attend any therapy. The level of significance was considered as 0.05.

Results. Study sample consisted of 100 children (median age of 4, range 2 - 5). Twenty-three percent of children had a development according to their age norms. There were no relationships between the age of a child and his compliance to the age norms of development ($t = -1.40$; $p = 0.16$). Thirty-eight children do not receive any kind of therapy. In fully adjusted multiple logistic regression models, each kind of the therapy was significantly associated with improvement of some or all psychomotor functions. For example, Montessori therapy mostly increased the progress in hearing (odds ratio, OR=19.3 [95% confidence interval, CI 1.7; 221.1]) and fine motor skills (OR=3.8 [2.81; 757.0]).

Conclusions. To attend a therapy is essential for children with ASD, but specific type of a therapy should be matched to the needs of each child individually.

Dentofacial and myofunctional disorders of preschool children in Latvia

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Background. It is asserted that sucking and chewing habits, mouth breathing, atypical (infantile) swallowing, bad oral habits (thumb and finger sucking, pacifier sucking), as well as morphology of prolonged respiratory diseases are closely related to oral dysfunction. Muscles can affect tooth alignment, speech production, chewing and swallowing. Abnormal use of muscles of tongue and lips is called orofacial myofunctional disorders (OMD). Very few studies have been performed worldwide to investigate the interrelation between malocclusion and OMD, whereas such studies have not been performed in Latvia and little attention has been devoted to this subject matter.

Aim. We aimed to investigate the association between malocclusion and OMD.

Methods. Cross-sectional study was performed in a kindergarten in Latvia. Children's myofunctional situation, occlusion, and speech defects were assessed during an examination. Children's mothers were interviewed on their socio-demographic situation, feeding and habits of the child, history of diseases, and the number of sources used to obtain information on children's oral health. Multiple logistic regression models were built to investigate associations between the types of occlusion and OMD/health characteristics.

Results. The study sample comprised 141 children-mothers' pairs. Types of occlusion associated with OMD/health characteristics were: normal occlusion with prolonged respiratory diseases (odds ratio, OR=0.345 [95% confidence interval, CI 0.16; 0.75]); combined type with tongue thrust habits (OR=3.11 [0.99; 9.90]), lip closing strength (OR=0.99 [0.98; 0.99]); cross-bite with speech (OR=3.55 [1.07; 11.78]).

Conclusion. Myofunctional disorders, deleterious effects habits, long-term colds, inflammation of the middle ear have negative effect on overall quality of well-being of children and a potentially negative effect of quality of life in future. To prevent time and cost consuming treatment procedures early interdisciplinary examinations should be performed. Close cooperation between oral health specialists, general practitioners and pediatricians is highly recommended. While creating preventive programs of oral health, the topology for explaining the causes of malocclusion should be provided.

Screen time exposure among toddlers aged 2-3 years and its impact on cognitive and motor function development

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Background. On the last decade digital device usage among parents and toddlers for diverse reasons have become a daily habit. But it seems with parents and medical specialists there is a significant worry whether these activities affect normal development of child.

Aim. The aim of this study was to analyze digital device usage habits between sex and compare digital device usage time with cognitive, fine and gross motor skill development.

Methods. Survey was carried out in paper and digital version among numerous of kindergartens and online groups. Parents of toddlers assessed their digital device usage habits. Development data was collected using Denver developmental scale and Munich functional developmental diagnostic test. Statistical analysis: ANOVA, Chi - squared test.

Results. Final data concluded 894 respondents aged 19-36 months – 49.9% (n= 446) of them were girls. As for digital media usage - 50.7% (n= 389) girls use digital devices on their daily routine, where boys do only 49.3% (n=379). Most of toddlers use screen 15-30 minutes per day (37.6%) from whom 32.4% (n=145) were boys. (P=0.004) Only 25% (n=130) of children spent their time using developmental programs. Fine motor skills were successful in 91.4% (n= 470) of users and 89.6% (n=95) of non-users. Gross motor skills are developed in 74.9% (n=386) of media consumers and 70.6% (n=75) of non-consumers. Finally, cognitive skills were fortunate in 97.5% (n= 500) of children who use media and 95.3% (n=101) of those who do not. (P=0.023)

Conclusion. As expected, most of the toddlers use digital devices on daily basis for various of reasons, but only few uses them for educational purpose. In usage incidence, there is only a slight difference between boys and girls. Surprisingly, digital media does not affect fine or gross motor skill development, as well as cognitive functions. Furthermore, results did not differ whether toddlers used electronic devices or not.

Assisted reproductive technology and the risk of preterm birth

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Background. The World Health Organisation (WHO) defines preterm birth (PTB) as any birth before 37 completed weeks of gestation. It is the principal cause of infant mortality and a significant contributor to childhood morbidities. Previous research has shown that singletons conceived by assisted reproductive technology (ART) have an increased risk of PTB compared with those conceived spontaneously.

Aim. To investigate the risk of PTB among singletons to primiparas who conceived with ART; to investigate perinatal and obstetric parameters are associated with clinical outcomes.

Methods. Retrospective study in Infertility treatment clinic IVF Riga. Inclusion criteria were: 25–35 years old nulliparous women with singleton pregnancies, without pre-existing maternal diseases. I group – ART pregnancy, II group – spontaneous pregnancy. The data were analyzed by statistical program SPSS ver.23 and $p < 0,005$ was taken as the level of significance.

Results. In total, 153 women were included in the study, 87 (56.9%) conceived after ART and 66 (43.1%) conceived spontaneously. Measurements of cervical length in II trimester were similar in both groups – 36,60 (SD=6,31) in the study and 37,02 (SD=7,67) mm in the control group ($p=0,716$). Mean delivery time in the ART group 39,05 (SD=2,8), but in the spontaneous group 39,47 (SD=3,52), PTB, respectively were 10 (11,5%) and 3 (4,5%), but significant association between ART and spontaneously conceived pregnancies was not manifested ($p=0,127$). The mean weight of the new-borns in the study group was 3501 g (SD=515), but in the control group 3489 g (SD=564), $p=0,887$.

Conclusion. The risk of PTB in singleton pregnancies resulting from ART is not greater than that in spontaneously conceived singletons. There are no statistical difference between neonatal outcomes in both of groups.

Acknowledgements. None

Association between work tension and professional burnout in nurses population in Latvia

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Background. The quality of care provided by nurses is influenced by many factors. One of them is the development of technologies that increases the range of professional duties of nurses, but not always reduces work tension. This can provide the increase in occupational burnout, leading to premature leave of work. Investigations of relationships between the work tension and professional burnout of nurses are scarce.

Aim. The aim of the study was to find out the relationship between work tension and the professional burnout of the nurses in Riga, Latvia.

Methods. For this cross-sectional study we used the translated version of the questionnaire from the international study “Age-related working conditions in hospitals” (AwAKE) that takes place in Germany, Israel, and Latvia to assess work- and health-related factors of nurses in Riga, Latvia. Questionnaire was previously validated in Latvian population and contained 160 questions. We assessed the work tension with 10-items of effort-reward imbalance scale and built a work tension index (WTI) as a weighted ratio between efforts and rewards where higher index showed higher tension. Professional burnout was assessed using eight questions on irritation, two questions on depressiveness and four questions on professional weariness. We included all nurses from three major hospitals in Riga that agreed to participate in the study. Descriptive statistics and univariate analysis were performed for all study variables according to their classification. Multiple linear regression models adjusted for age of nurse (dichotomized by median), wage, position, and years of experience were built to investigate the association between WTI of nurses and their burnout.

Results. Study sample included 221 nurses, 95.5% women, with median age 45 years (range 20–74). 83.3% of participants worked the full wage and were in median 19 years in profession. Most of nurses were certificated (43.0%) or registered (26.2%). Median burnout was 25 (range 0–59), and median WTI was 0.2 (range 0.0–1.5). Significant differences in burnout were found between nurses-head of department and nurses-helpers ($p < 0.01$). In fully adjusted linear regression models higher WTI as well as a higher work position increased a possibility of burnout (effect estimates $\beta = 11.2$ [95% confidence interval 1.0; 21.3] and $\beta = 2.0$ [0.1; 3.9], respectively).

Conclusions. Although direct relationships between the higher working position of nurses and their work tension were not found, both factors together can increase professional burnout, thus leading to premature retirement of highly qualified specialists.

Association between professional burnout and self-reported health of nurses from different hospitals in Riga, Latvia

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Background. In aging societies there is increased interest in keeping older people in the workforce. This is especially true in the health care system where at the same time due to increasing age of the population more people need medical help and nursing, while the staff becomes older too and tends to leave the work force prematurely, thus leading to a shortage of health care workers. Association between professional burnout of medical personal and their physical health is still underestimated and not fully explained.

Aim. The objective of the current study was to investigate the association between professional burnout of nurses and their self-estimated health-related quality of life.

Methods. For this cross-sectional study we used the translated version of the questionnaire from the international study “Age-related working conditions in hospitals” (AwAKE) that takes place in Germany, Israel, and Latvia to assess work- and health-related factors of nurses in Riga, Latvia. Questionnaire was previously validated in Latvian population and contained 160 questions. Twelve questions (scale 0 – 100) assessed self-reported health, and we calculated the mean value for sum of all twelve answers. Professional burnout was assessed using eight questions on irritation, two questions on depressiveness and four questions on professional weariness. We included all nurses from three major hospitals in Riga that agreed to participate in the study. Descriptive statistics and univariate analysis were performed for all study variables according to their classification. Multiple logistic regression models adjusted for age of a nurse (dichotomized by median), wage, position, and years of experience were built to investigate the association between professional burnout of nurses and their self-reported health.

Results. Study sample included 221 nurses, 95.5% women, with median age 45 years (range 20–74). 83.3% of participants worked the full wage and were in median 19 years in profession. Most of nurses were certificated (43.0%) or registered (26.2%). Median burnout was 25 (range 0–59), and median self-reported health was 76.7 (range 10.8–98.3). In fully adjusted logistic regression model burnout and age higher than median decreased self-reported health (odds ratio, OR = 0.92 [95% confidence interval 0.90; 0.95] and OR = 0.46 [0.23; 0.92], respectively).

Conclusions. Nurses of higher ages should be particularly treated to decrease their burnout as both factors decrease their health and can lead to premature leave of the work.

Association between stress and workability among medical personal from three major hospitals in Riga, Latvia

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Background. In aging societies there is increased interest in keeping older people in the workforce. This is especially true in the health care system where at the same time due to increasing age of the population more people need medical help, while the staff becomes older too, and tends to leave the work force prematurely, thus leading to a shortage of health care workers. The development of technologies increases the professional duties of the medical staff and nurses but doesn't reduce work stress. This can provide the increase in occupational burnout, which can lead to a decrease in workability further leading to premature leave of work. Several studies investigate a range of parameters related to working condition of nurses, for example, widely known Nurses' Health Study established in 1976 which in its third stage examines nurses' lifestyle conditions. Nevertheless, association between work stress of medical personal nurses and their workability is still underestimated.

Aim. In this study we aimed to investigate the association between work stress and workability of medical personal from three major hospitals in Riga, Latvia.

Material and Methods. We assessed cross-sectionally work- and health-related factors of medical personal from three major hospitals in Riga, Latvia, using structured questionnaires. Workability was assessed by self-reported 1 to 10 scale. Work stress was assessed using eight questions on anxiety, two questions on depressive symptoms, and three question on burnout. Multiple linear regression models adjusted for presence of children, years of experience, wage and position were built to investigate the association between work stress and workability.

Results. Study sample included 232 participants, of them 54.5% nurses and 17.7% physicians (mean age 44.3, SD 14.2 years). Participants had median 19 years of experience, mostly worked full wage. In fully adjusted multiple regression models, workability was associated with work stress (effect estimate, $\beta=-0.03$ [95% confidence interval -0.04; -0.01] and with position ($\beta=-0.23$ [-0.42; -0.05]). Nurses displayed higher workability than other medical workers (physicians, medical students and medical helpers).

Conclusions. Although nurses have higher workability than other medical personal, they should be particularly treated to reduce their level of stress to prevent a shortage of health care workers.

The withdrawal of Marketing Authorization Applications from European Medicines Agency: reasons and financial health of companies

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Background. Investments in biopharmaceutical companies remain challenging due to inherent uncertainties in risk assessment. The major risks that these companies face may be classified to idiosyncratic (pertaining to their drug pipelines) and systematic (pertaining to general economic environment) risks (Thakor et al., 2017). The stocks of biopharmaceutical companies are well known to be volatile, however since the 2000s, companies in this branch are becoming increasingly more profitable (Thakor et al., 2017). It was shown, that Phase III clinical trials and regulatory decisions by the US Food and Drug Administration (FDA) have impact on the market value of the pharmaceutical companies (Rothenstein et al., 2011) and that median decline in cumulative abnormal returns due to negative events was larger in magnitude than gains due to positive events (Hwang, 2013). It has also been shown that Regulatory decisions converge to a high degree among Swissmedic, US Food and Drug Administration (FDA) and European drug regulatory authorities (EU) (Dalla Torre Di Sanguinetto S et al.2018).

Aim. The aim of the current study was to analyse the marketing authorization application withdrawals (MAPWS) from European Medicines Agency (EMA) and analyse the financial health of the submitting companies.

Methods. All companies that had withdrawn the application of marketing authorization from EMA were included in the data set; in the period lasting from 2017 01 01 till 2018 12 31. Financial health of companies was assessed with the Altman Z-score and Z-score Private Firm Model, variations of multiple discriminant analysis used, from the external analytical standpoint. Companies with high Z-scores (4.0) were regarded as having strong balance sheets (e.g., Z-score below 2.0)(Altman, Altman, & I., 2018). Financial data was obtained from <http://financials.morningstar.com>.

Results. 34 MAPWs were identified with 45 issues. 3 most common issues were insufficient evidence to assess the risk benefit ratio (n=21), manufacturing issues (n=9) and pharmaceutical quality concerns (n=2). The most common answer from the company to explain the MAPW was the preliminary view of the Committee for Medicinal Products for Human Use (n=13) and that the company needs more time to generate the additional data (n=10). We recovered the financial data of 14 companies with MAPWs. Altman Z-score model 1968 Mean(M)=1.44, Standard Error (SE) 1.86, Median(Md)=2.70, Z-score Private Firm Model 1993 M=0.81, SE=1.95, Md= 1.14.

Conclusion. There are various reasons for MAPWs and even financially healthy companies decide to take such action.

Acknowledgements. No conflicts of interest to declare.

Exploring latvian teachers' readiness to learn online for adapted e-learning course design

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Background. Lifelong learning participation rates of adults (age 25-64) are lower in Latvia than in European Union (for 2017, 7.5% and 10.9%, respectively). National Centre for Education implements European Social Fund project "Competency based curriculum"; it includes a self-learning e-course for teachers'. For sustainability of the project results it is important that all teachers take part in the e-course.

Aim. The objective of the study was to investigate teachers' level of readiness for online learning according to education levels and subject areas they teach.

Material and Methods. A self-evaluation survey has been developed based on the TOOLS questionnaire - a stable and simple structured validated tool with high reliability. Latvian teachers working in 100 pilot schools were invited to participate in the survey in November 2018. Responses from teachers from all education levels and all subject areas (languages, mathematics, social sciences, culture and arts, natural sciences, technology, health and physical activities) from the entire country were obtained. We summarized TOOLS answers to obtain five major skills that are necessary for successful e-learning: "Independent learning", "Dependent learning", "Need for distance studies", "Academic skills" and "Digital skills". Descriptive statistics was performed for all study variables. We analysed univariately differences between genders, teachers' subject areas, and place of living. Significance level was considered as $\alpha=0.05$.

Results. Study sample consisted of 1092 participants, mostly 50 to 59 years old, of them 95% were women lived in small cities and worked in Vidzeme. We observed statistically significant difference between genders in Digital skills (Mann-Whitney test, $p<0.01$) showing higher scores in men than in women, but not for other skills. We observed significant differences in Digital skills between teachers' subject areas ($p<0.01$) for all subject areas, and in other skills according to teachers' main subject. For example, for teachers from the social subject differences were found in Independent learning ($t=-2.10$ $p=0.04$). Differences in place of living were found in Need of distance learning ($F=6.48$ $p<0.01$). Differences were significant comparing Riga and big cities (mean difference -1.68 , $p<0.01$), Riga and small cities (mean difference -1.33 , $p<0.01$), as well as Riga and Rural areas (mean difference -1.58 , $p<0.01$). Significant differences were found between age groups in Dependent learning (ANOVA $F=2.88$, $p=0.01$), Academic skills (ANOVA $F=3.68$ $p<0.01$), and Digital skills (Chi square test, $p<0.01$).

Conclusions. E-learning course design must be adapted to the learners' readiness level and skills to achieve as high completion rate as possible.

Insufficiencies in Realization of Patients' Right to Complain to the Health Inspectorate of Latvia

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Background. The right to complain is a basic right of all patients. In the event of a breach of rights, rights must be enforceable. The right to complain allows patients to report these breaches and to be heard. It is especially important to patients, or their next of kin, in cases when treatment had severe negative consequences, like injury, death, involuntary treatment, or refusal of same. The Health Inspectorate of Latvia is an administrative institution mandated by the Law on the Rights of Patients to protect and safeguard their rights, as well as to investigate patients' complaints.

Aim. The aim of the current study is to investigate how efficiently the Health Inspectorate of Latvia safeguards patients' right to complain, as well as to reveal insufficiencies of the process.

Methods. The legal regulations regarding functioning of the Health Inspectorate, particularly in protecting the patients' rights, have been analysed. Relevant case law has been studied. Data concerning the organizational framework and capacity of the institution have been collected un analysed. The scientific literature regarding the role of the relevant state institutions, protecting patients' rights to complain, has been studied.

Results. The data collected within this study revealed, that exercise of the right to complain in practice often turns out to be a quite complicated issue. The quality of the investigation process of the Health Inspectorate is unpredictable. The number of cases poorly or partially investigated is high. Serious insufficiencies in the complaint procedure have been disclosed by courts as well. The Supreme Court concluded, that the expertise report, prepared by the Health Inspectorate, was not legally binding. The Ombudsman stated, that the practices of the Inspectorate are contrary to the principles of good governance.

Conclusion. The complaints handling processes of the Health Inspectorate are not appropriately safeguarding the patients' right to complain. There is an urgent need to improve the practices and proficiency within the Health Inspectorate.

Assessment of preparedness of Latvian Healthcare Facilities for Disaster Management

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Background. In the last decades, the world assisted to a remarkable increase in the number of disasters of all kinds as well as people affected by it. Due to this, hospitals and physicians are more likely to face this scenario.

Aim. To assess the preparedness of disaster management of Latvian healthcare facilities and medicals doctors.

Methods. The material was collected between October 2016 and February 2017. Was given to the hospital administrators or emergency managers of 21 Latvian hospitals and adapted survey of The Hospital Emergency Response Checklist (World Health Organization Regional Office for Europe, 2011), comprising four key components of the checklist: Command and Control; Triage; Continuity of Services and Human Resources. To 305 physicians of the same hospitals, was given an adapted survey of Djalali *et al.* (2004).

Results. Only a minority (19.05%) of Latvian healthcare facilities apply basic principles and strategies in respect of incident action plan, as well as training their staff to be Incident Command System (23.81%), coordinate between neighboring hospitals and health authorities (23.81%) and ensure availability of essential life lines (23.81%). Just a minority of Latvian physicians (13.77%) are not aware of the current emergency management plan of their hospital, do not receive formal training in Incident Command System (11.80%) or disaster medicine (11.80%) but are willing to attend disaster medicine training (71.15%).

Conclusion. Latvian hospitals and physicians are not well prepared to face a disaster situation. A collective and standardized strategy planning and preparedness approach, together with the implementation of a disaster medicine course to medical student must be a priority.

Acknowledgements. No conflict of interest to declare.

Musculoskeletal overuse injury prevalence and comfort perception of military boots

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Background. Load carriage, physical training and sports activities causes 90% of musculoskeletal injuries among military populations, 80% of these injuries are lower leg biomechanical overuse musculoskeletal injuries (OMSKI). Biomechanical OMSKI is multifactorial cumulative micro-trauma caused by altered load distribution.

Aim. The purpose of this study was to assess the OMSKI prevalence and comfort perception of military boots in Latvian infantry soldiers.

Methods. Cross-sectional study among infantry soldiers during annual medical check-up. Injuries were classified according to body regions and injury types (acute or overuse). Military boot comfort was assessed for 6 dimensions: overall comfort, forefoot, arch and heel cushioning, arch and heel support using 10-point Likert scale.

Results. 160 soldiers at average age 30.4 ± 7.3 years participated in this research, with mean service time 7.8 ± 4.1 years. 95% of all participants were males ($n=152$), 5% females. Prevalence of lower extremity OMSKI was 14.4%. Most common sites for OMSKI are lower leg and ankle (39%) and knee (23%). Military boots rate for forefoot cushioning, heel cushioning and for arch support was 6.1 (SD=2.0), arch cushioning rate 6.0 (SD=2.0), heel support rate 6.3 (SD=2.0) and overall comfort rate was 6.4 (SD=1.9). Presence of lower leg overuse injuries are associated with overall military boots comfort [$\chi^2(9) = 120.3$; $p < 0.001$].

Conclusion. Lower leg overuse injuries are common for infantry soldiers and it is suggested to provide proper fitted military boots according to foot types and lower leg alignments to prevent OMSKI.

Acknowledgements. The author would like to thank soldiers who participated in the study and State Military Medicine Centre for the support.

Component analysis of thyroid cancer incidence dynamics in Kazakhstan

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Background. According to International Agency for Research on Cancer there are about 567,000 new cases of thyroid cancer (TC) registered in the world in 2018, and age-standardized incidence rate is 6.7 per 100,000.

Aim: to study the dynamics of thyroid cancer incidence in Kazakhstan by component analysis.

Methods. Primary data were for registered patients with thyroid cancer (ICD 10 – C73) in the whole country during the period of 2007–2016. Evaluation of changes in TC incidence in the population of Kazakhstan was performed using component analysis according to the methodological recommendations of VV Dvoirin and EM Axel.

Results. In 2016, the number of patients with thyroid cancer increased for 42.8% compared with 2007 (430 patients) and amounted to 752 patients. It can be concluded from the researches that in general the dynamics of the number of patients with thyroid cancer for the entire population of Kazakhstan can be caused by the following factors:

1. Growth population number $\Delta_p = +63$ case (+19.7%).
2. Changes in the age structure of the population $\Delta_A = +11$ case (+3.6%).
3. Combined effect of changes in population number and its age structure $\Delta_{pA} = +2$ case (+0.5%).
4. Change of illness risk $\Delta_r = +221$ case (+68.6%).
5. Combined effect of changes in the disease risk and population number $\Delta_{pr} = +33$ case (+10.1%).
6. Combined effect of changes in the disease risk and age structure of the population $\Delta_{AR} = -7$ case (-2.2%).
7. Combined effect of the changes in the disease risk of the population and its age structure $\Delta_{pAR} = -1$ case (-0.3%).

Thus, the number of patients with thyroid cancer in Kazakhstan is steadily increasing. Carrying out this component analysis, we confirmed the growth of patients' number due to changes of illness risk and population growth, and also to combined effect of changes in the disease risk and population number.

Conclusion. This investigation was the first epidemiological study of dynamics of thyroid cancer by component analysis in population of Kazakhstan. Implementation of the results of the study is recommended in management of anticancer activities for TC.

Acknowledgements. The study supported by public association "Central Asian Cancer Institute".

Vaccination coverage rates and the incidence of vaccine preventable diseases among children in Sumy region of Ukraine

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Background. Routine childhood vaccination remains the most cost-effective public health strategies to reduce morbidity and mortality associated with vaccine preventable diseases. The World Health Organization established the expanded program on immunization with the goal of ensuring full accessibility of routine vaccinations to all children. However, during last quarter-century Ukraine and other European countries are facing outbreaks of well-known and emergency infections. Particularly alarming is the increase in the incidence of vaccine preventable diseases, which may be the result of a sharp decline in routine childhood vaccination that leads to the accumulation of susceptible individuals in the population.

Aim. Assess routine immunization uptake and its effect on the incidence of vaccine preventable diseases (VPDs) among children in Sumy region of Ukraine.

Methods. State Statistical Reporting Form No. 2 “Report on Certain Infections and Parasitic Diseases”, and No. 6 “Report concerning Persons of Selected Age Groups Immunized to Infectious Diseases” were used as main data sources.

Results: An analysis of data in Sumy Region of Ukraine in general has consistently indicated reducing the level of vaccination coverage for children. The vaccination coverage rate began to decrease starting from 2013. It is significantly reflected at the level of morbidity for vaccinated infectious pathologies, which at the moment are recorded mainly in the form of outbreaks. This is because an immune layer of inadequate durability is formed among the population, and if the level of vaccination coverage is kept to a low level, this can lead not only to outbreaks, but also to epidemics. This assumption is also confirmed by calculations of the correlation coefficients between the number of vaccinated children and the number of children who were infected with vaccine-derived infections. The correlation coefficients between them are in the range of 0.9-1, which indicates the presence of cause-and-effect relationships between these indicators. During some years, only 50-60 % of Sumy region children had received all recommended vaccines, which is far below World Health Organization target of 95 %.

Conclusions: Routine immunization uptake in Ukraine is still below World Health Organization target. The main reason for the ongoing vaccine preventable diseases was low vaccination coverage for routine immunization antigens because of which collective immunity decreased to a critical level. Strict monitoring of the implementation of the immunization schedule by medical institutions at all levels are recommended to improve vaccination status of Ukrainian children.

Impact of free-living interval walking training managed through smart mobile devices on cardiovascular risk factors 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 cardio-metabolic factors in type 2 diabetes (T2D). The aim of this study was to investigate the effects of interval walking training delivered through smart mobile devices in patients with T2D in a real-life setting.

Methods. 56 patients with T2D aged 35–75 and were randomized control (26) and interval training group (30). Training group was prescribed 3 sessions per week (60 min/session). Each session consisted of consecutive 3-min intervals of walking with the intensity of 40% and 70% of the maximal oxygen consumption, which was delivered by a mobile phone application. Variables measured before and after the 4 month intervention were fasting glucose, HbA1c, lipid profile, HOMA-IR, body mass index (BMI), waist circumference, blood pressure, eGFR, albuminuria. For statistical analysis repeated measures robust ANOVA and repeated measures ANCOVA were used.

Results. The adherence to training in the interval training group was low. Only 15 patients performed trained 2–3 times a week, other participants trained less frequently. Without adjusting for covariates, we observed significant effect of the training programme on albuminuria, but no difference in other clinical variables. After adjustment for covariates, we observed a statistically significant interaction ($p=0.04$) for total cholesterol and a trend for significant difference ($p=0.07$) for HbA1c between groups.

Conclusions. Uncontrolled 4-months long free-living interval walking training managed through smart mobile devices is has minor effects on cardio-metabolic factors in T2D patients, which can be explained by low compliance, short duration of intervention and variability of response to physical activity.

Acknowledgements. Project of the University of Latvia “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment” and MIKROTIK donation administered by Foundation of University of Latvia.

Mortality causes in type 2 diabetes *mellitus* patients from Genome Database of the Latvian Population

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Background. Over the past 30 years the number of patients with type 2 diabetes *mellitus* (T2DM) has quadrupled (Bin Zhou, 2016) and it is seventh leading cause of death in the world based on CDC data. The most common complications causing T2DM patients' death was cardiovascular disease and chronic kidney disease with incidence of 50% and 10-20%, respectively (OECD, 2009). Since its start in 2006, The Genome Database of the Latvian Population (LGDB) has collected biosamples and associated phenotypic and clinical information from over 35 500 participants from Latvia and provide valuable data source for analysis of risk factors for T2DM

Aim. To determine the most common causes of death and to calculate the demographic, socio-economic, and biological predictors of all-cause mortality in patients with T2DM.

Methods. Quantitative statistical analysis and Cox Proportional-Hazards model were used to interpret the data from n=1758 healthy non-diabetic volunteers and participants with T2DM matched by age and sex. Statistical analyses were performed by using MS 2010 and IBM SPSS 18.0, R program.

Results. In total 848 (25,9%) of 3277 T2DM patients from LDGB died within 10 years after the recruitment. The most common diagnosis in patients' death certificates were cardiovascular diseases (71,58%). The next most common co-morbidity were oncological diseases (32,19%). Third cause of death by occurrence were infectious diseases (10,14%) closely followed by renal pathologies (8,37%).

In the model with data from participants with T2DM only the mortality was positively associated with age (HR 1,06 [95% CI 1,04 – 1,08]; p<0,001), smoking (HR 1,92 [95% CI 1,3 – 2,83]; p<0,001), and baseline level of glycated haemoglobin >8% (HR 1,48 [95% CI 1,07 – 2,04]; p<0,018). Active lifestyle (HR 0,24 [95% CI 0,09 – 0,7]; p<0,001) or even low activity level (HR 0,59 [95% CI, 0,41 – 0,85]; p<0,001) decreased risk of mortality. Baseline level of high-density lipoprotein, low-density lipoprotein, triglycerides, duration of diabetes, use of insulin and consumption of alcohol were not significantly associated with mortality.

Conclusion. The major cause of death in T2DM patients in LGDB was cardiovascular diseases and number of deaths was higher in comparison to the previous data obtained from Latvian population. Among people with diabetes, older age, smoking, higher baseline level of HbA1c and physically inactive lifestyle were important predictors of mortality.

Acknowledgements. The authors have no conflict of interest to disclose. No funding was received for the study.

Non-small cell lung cancer computer tomography evaluation with RECIST criteria for patients who received palliative chemotherapy

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Background. In RECIST (Response evaluation criteria in solid tumors), imaging is recognized as indispensable for objective response evaluation of chemotherapy for solid tumors. The most important advantage of RECIST is standardization of treatment results by using a “common language” for comparison of results from different trials. Evaluation of target lesions is divided in 4 stages: *Complete response (CR)*: Disappearance of all target lesions, *Partial response (PR)*: At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD, *Stable disease (SD)*: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started, *Progressive disease (PD)*: At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions. If the treatment response after RECIST evaluation is stable disease, then currently used chemotherapy regimen can be proceeded if there are no other indications to change it.

Aim. The aim of the current study was to compare how many patients with stable disease (evaluated using RECIST criteria) had chemotherapy regimen changed.

Methods. Altogether 79 patients were enrolled in the retrospective and descriptive study. Patients' data were taken from oncological council reports of patients with stage IV non-small cell lung cancer who received only palliative chemotherapy. Computer tomography (CT) imaging data were collected from Pauls Stradiņš Clinical University hospital computer programs TELEMIS and AIRIS. Data were conducted from January 2016 to March 2018. Descriptive data were collected and analyzed using IBM SPSS Statistics program.

Results. The average age of the patients were 67.2 years \pm 7.74 (max=82, min=38) years. 18 (22.8%) were women, 61 (77.2%) were men. The most common histological variant of non-small cell lung cancer was adenocarcinoma (41 patients (51.9%)). After analyzing CT imaging data with RECIST criteria, 38 (48.1%) patients had progression, 24 (30.4%) had stable disease, 16 (20.3%) had partial remission, 1 (1.3%) had complete remission. 7 (29.1%) from 24 patients with stable disease had chemotherapy regimen changed.

Conclusions. Almost one third (29.1%) of the patients with stable disease had chemotherapy changed to second line treatment. Benefit of using RECIST criteria in everyday basis would make the decision of following treatment for medical oncologist easier.

Plasma non-esterified fatty acids and long-chain acylcarnitines are markers for tissuespecific insulin resistance

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Background. The main diagnostic markers of insulin resistance and type 2 diabetes are related to measurements of glucose metabolism. It is known that insulin plays important role in the regulation of carbohydrate and lipid metabolism, but the link between lipidrelated metabolites and tissuespecific insulin resistance is not well defined.

Aim. The aim of this study was to assess whether the changes in plasma non-esterified fatty acids (NEFA) and acylcarnitine (AC) levels during the glucose tolerance test reflect muscle and adipose tissue insulin resistance.

Methods. Concentrations of circulating AC, NEFA and other biochemical parameters were measured in the fasted state and after glucose administration in high fat diet (HFD)fed, *db/db* and respective control mice. Additionally, tissue uptake of [³H]deoxyDglucose was measured to evaluate tissuespecific insulin sensitivity.

Results. Glucose administration decreased both NEFA and longchain AC levels in plasma in healthy control animals by 30% (120 min). The glucose tolerance test and [³H]deoxyDglucose uptake in tissues revealed that HFDinduced lipid overload evoked insulin resistance in adipose tissue, and plasma levels of NEFA did not decrease after glucose administration. *Db/db* mice developed type 2 diabetes with impaired insulin sensitivity and up to 70% lower glucose uptake in both adipose and muscle (skeletal muscle and heart) tissues and concentrations of NEFA and longchain AC levels did not decrease in response to glucose administration.

Conclusion. These results clearly link impaired adipose tissue insulin sensitivity with continuous NEFA release in the transition from a fasted to postprandial state, while a blunted decrease in longchain AC levels is associated with cardiac and skeletal muscle insulin resistance.

Acknowledgements. This work was supported by the ERDF Postdoctoral Research Aid program project No.1.1.1.2/VIAA/1/16/245.

Impact of different factors on outcome of radioiodine therapy of differentiated thyroid cancer

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Background. Radioiodine (I-131) therapy (RIT) for differentiated thyroid cancer (DTC) (papillary and follicular thyroid cancer) is used to ablate remnants of normal thyroid tissue after thyroidectomy and to treat residual or recurrent tumor. RIT effectiveness depends on sufficient elevation of TSH that can be reached by endogenous or exogenous TSH stimulation. Before the treatment radioiodine activity should be determined. Post-therapy whole-body scintigraphy (rx-WBS) is performed a few days after RIT. Thyroglobulin (Tg), anti-Tg antibodies (TgAb) levels are measured and neck ultrasound (US) is performed after 6-12 months to control RIT success so to make a decision about necessity of repeated therapy.

Aim. To evaluate success of RIT depending on different factors.

Materials and methods. Retrospectively 309 patients who had received RIT for a period 2016–2017 were analyzed. 95 patients were excluded because Tg level or results of neck US were not available. 214 patients were included in the study. 203 patients had been undergone total thyroidectomy and 11 patients – subtotal thyroidectomy: female 82.7% (n=177) versus male 17. % (n=37). Mean patient age was 58.22 years (18–85 years). The indication of the second RIT course or repeated surgery was: a detectable Tg in the absence of TgAb with or without the presence of a specific lymph node or local recurrence on neck US. The ablation or treatment were considered unsuccessful if rxWBS after the second RIT showed tissue remnants or metastases or repeated cytological/histological examination revealed the disease.

Results. Papillary thyroid carcinoma was treated in 94.4% of cases, follicular carcinoma in 4.2% of cases, and mixed carcinomas in 1.4 % of cases. Stage I-III was seen in 90.7% (n=194) of patients and stage IV in 9.3 % (n=20) of patients. Endogenous TSH stimulation was used in 174 cases and exogenous TSH stimulation in 40 cases. Mean radioiodine activity administrated was 2991.59 MBq, minimal administrated 608 MBq, maximal – 7400 MBq. RIT was unsuccessful in 21 patients (9.8%). There is statistically significant difference in the outcome of RIT between male and female ($p < 0.001$) but difference is not significant between the histological types of DTC ($p = 0.381$) and between endogenous and exogenous TSH stimulation ($p = 0.240$). The results also revealed weak correlation between radioiodine activity and outcome of RIT (Spearman's $\rho = 0.203$; $p = 0.003$).

Conclusions. Success of RIT depends on radioiodine activity however histological types of DTC and endogenous versus exogenous TSH stimulation do not have impact on outcome of the therapy.

Randomized, double-blind, placebo-controlled, crossover design study of two herbal dietary supplement products in patients with moderate persistent, uncontrolled bronchial asthma

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Background. Asthma is one of the most common chronic internal diseases. Although effective pharmacotherapy treatment is available, more than half of the asthma patients remain uncontrolled.

Aim. This study was performed to investigate the effectiveness of two food supplement herbal formulations, in comparison to placebo, as an add-on treatment to traditional medication, on asthma control, cough, lung function, nitric oxide (FeNO) in exhaled breath and blood eosinophils in patients with moderate persistent uncontrolled asthma.

Methods. It was a prospective, randomized, double-blind, placebo-controlled, crossover design study. Patients were randomly assigned to all treatment options, either Formulation 1 (extracts of *Boswellia serrata* resins 130 mg, *Passiflora edulis* fruits 110 mg, *Euphrasia officinalis* herbs 83 mg, *Pinus sylvestris* bark 20 mg, *Hedera helix* leaves 17 mg, *pterostilbene* 20 mg, *quercetin* 20 mg, *lycopene* 10 mg, *Haematococcus pluvialis* algae 10 mg), Formulation 2 (extracts of *Boswellia serrata* resins 130 mg, *Passiflora edulis* fruits 110 mg, *Euphrasia officinalis* herbs 83 mg, *Pinus sylvestris* bark 20 mg, *Pimpinella anisum* fruits 50 mg, *pterostilbene* 20 mg, *quercetin* 20 mg, *lycopene* 10 mg, *Haematococcus pluvialis* algae 10 mg), or placebo for four weeks, by crossover study design. 2-weeks wash-out period was performed between each treatment period. Patients remained on the unchanged pharmacological treatment regime throughout all clinical study. Asthma control questionnaire (ACQ) data, cough visual analogue scale (VAS) data, FEV1, FEV1/FVC%, MMEF%, FeNO, and blood relative and absolute eosinophil count measurements were obtained before and after each treatment period. Permission to do study was obtained in Ethics Committee of Institute of Cardiology and Regenerative Medicine.

Results. 30 patients were recruited in our study. We found significantly more patients with controlled asthma (ACQ7 \leq 1.0) after active compared to placebo treatment periods ($p=0.039$). Formulation 1 and Formulation 2 treatment demonstrated numerically higher mean reduction in VAS score, but this difference did not reach statistical significance. Analysis of the change of FEV1/FVC% and MMEF% showed significant improvement versus placebo in Formulation 1 treatment period ($p<0.05$) The Formulation 2 therapy period demonstrated a statistically significant reduction in the eosinophil percentage by 0.46% compared to the placebo period when it increased by 0.82% ($p = 0.032$).

Conclusion. Our clinical study showed that both formulations might improve disease control in patients with moderate persistent uncontrolled asthma. Formulation 1 mostly improved lung function characteristics, while Formulation 2 reduced blood eosinophil count.

Acknowledgements. Study performance was sponsored by Silvanols LLC.

Steroid metabolomics in the diagnosis of adrenal diseases

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Background. Steroid metabolomics is highly sensitive and specific new tool for research of steroidogenesis in endocrinology. Recently a few studies showed the significance of urinary steroid profiling for differentiation of malignant and benign adrenal tumores.

Aim. The aim was investigation of urine steroid profiling (USP) by gas chromatography-mass spectrometry (GC-MS) 66 steroids were identified. GC-MS in patients with different adrenal diseases for detection of specific features of them.

Methods. We studied urinary steroid profiles (USP) in 166 patients with adrenal tumors: 35 patients with clinically overt adrenal Cushing's syndrome, 32 patients with mild subclinical adrenal cortisol excess, 15 with congenital adrenal hyperplasia the non-classical form, 35 with adrenocortical carcinoma (ACC) and 50 patients with adrenal adenomas without hormonal activity(AD). USP was investigated by gas chromatography-mass spectrometry on SHIMADZU GCMS QP- 2010 ULTRA. 66 steroids were identified.

Results. A decreased excretion of androgen metabolites was detected in patients with the adrenal form of Cushing's syndrome. We obtained specific profiles of USP in patients with different types of Cushing's syndrome and subclinical hypercortisolism. In patients with non-classic forms of CAH with 21-hydroxylase deficiency signs of increase 5 α -reductase activity due to evaluation of metabolite ratios, in particular, an increase of 11-OH-An / 11-OH-Et ($p = 0.026$) and allo-THB / THB ($p = 0.03$) ratios in combination with increased of 11-OH-An ($p = 0.0005$) and allo-THB ($p = 0.025$) excretion were revealed. The combination of increased excretion of THS > 900 $\mu\text{g} / 24 \text{ h}$ and / or DHEA > 2500 $\mu\text{g} / 24 \text{ h}$ in urine with detection of non-classical 5-en-pregnenes (16dP, 21dP, 21dP2, 11dP3) showed high sensitivity and specificity for differential diagnosis of ACC and ACA. These support the hypothesis about the preferential production of steroidogenesis precursors by malignant cells.

Conclusion. Urine steroid metabolomics is a powerful innovative approach for the early and differential diagnosis of adrenal diseases with a possibility to distinguish malignant and benign tumores. Defects of biosynthesis, steroid functions and new mechanisms of steroid metabolism can be recognized, which can be used for prognosing and solving fundamental problems associated with the etiology and pathogenesis of adrenal pathology. Undoubtedly, further investigations of steroid metabolome are need.

Acknowledgements. Disclosure of any conflict of interest, funding and other acknowledgement – none.

***E. coli* biofilm eradication using meropenem and *INTESTI* bacteriophage cocktail**

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Background. *E. coli* is the predominant causative agent of urinary tract infection. Recently antimicrobial resistance has become a global challenge, nevertheless other bacterial defence mechanisms have a great impact on successful treatment outcome. One such factor is bacterial biofilm. Uropathogenic *E. coli* strains are commonly strong biofilm producers. A novel approach to use bacteriophages (phages) in bacterial infection treatment and biofilm eradication has been proposed. Phages are bacterial viruses that can lyse bacteria and can eradicate biofilm as they replicate at the site of infection.

Aim. The aim of the study was to detect *INTESTI* bacteriophage cocktail and meropenem effect on *E. coli* strains and its established biofilms.

Methods. Two *E. coli* strains isolated from patients with urinary tract infection were used. Bacteriophage effect was determined using spot test method. Biofilm formation screening was done with Crystal Violet Assay. Afterwards biofilms were grown using 96 well microtiter plates with peg lids on rocking table at 170 rpm at 37°C. Biofilm formation was rechecked by viable cell count after peg sonification. A challenge plate with meropenem dilutions from 1024 mg/l until 2 mg/l and *INTESTI* phage dilutions from 1.2×10^6 until 2.35×10^3 PFU/ml were used. MIC (minimum inhibitory concentration) and MBEC (minimum biofilm eradication concentration) were determined measuring optical density with ELISA reader at 650nm, meropenem MIC breakpoint was used according to EUCAST standard V8.0.

Results. Both *E. coli* strain MICs towards meropenem was <2mg/l showing susceptibility. One *E. coli* was resistant towards *INTESTI* bacteriophage cocktail. Strong biofilm production was seen in both *E. coli* strains. Bacteriophage complete lytic effect with no cell growth was observed until 1.9×10^4 PFU/ml concentration, with lower concentration only some cell growth was detected. MBEC for meropenem was 512 mg/l that was > 256 greater than MIC. *INTESTI* MBEC was detected in all phage dilutions and was > 4 lesser than complete lytic concentration. After biofilm treatment phages were detected in all wells previously inoculated regardless dilution.

Conclusion. Although both *E. coli* strains were susceptible towards meropenem MBEC was significantly higher and achieved *in vivo* could cause lethal effect. Not always a clear phage lytic effect in planktonic cells is seen, explainable with their viral nature. Great biofilm eradicating effect can be explained by phage replication at the site of infection and longer multiplication time. Not all *E. coli* strains are susceptible to phages. To combat phage resistance various phages within phage collections should be made or bacterium-phage adaptation prior the treatment could be done.

Sepsis and septic shock in multidisciplinary hospital in Latvia

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Background. Sepsis and septic shock are life threatening emergency conditions induced by infection with increasing reported incidence, which is likely associated with greater recognition, aging population with significant comorbidities. Although true incidence is unknown estimates indicate that sepsis is a leading cause of critical illness and mortality worldwide as it is common cause of hospitalization and impose a growing burden on healthcare services. Limited data are available on characteristics and outcomes of sepsis and septic shock in Latvia.

Aim. The aim of the study was registration and analysis of sepsis and septic shock cases in Pauls Stradins Clinical University hospital (PSCUH).

Methods. In retrospective cohort study we enrolled 159 patients with sepsis-related ICD-10 codes upon discharge, admitted to PSCUH between September 2017 and February 2018. Demographic data and information on risk factors, clinical characteristics, diagnostics and mortality were collected and analysed.

Results. The hospital mortality rate was 51%, in cases of septic shock – 91%. The comorbidity score in non-survivor group was significantly higher ($p < 0.001$). Majority of patients (59%) had community-acquired sepsis with the most frequent admission diagnoses of infectious, cardiovascular diseases and neurological causes. Referrals from long-term care facilities and other hospitals were 8% and 11%, respectively. Respiratory tract infections, particularly pneumonia, urinary tract and abdominal infections were the most common sites of origin. The rate of positive blood cultures was 60% with predominance of *MS S.aureus*, being the most common microorganism in community-acquired, healthcare-associated and hospital-acquired sepsis groups, and *E.coli*. No multiresistant bacteria were detected in community-acquired sepsis patients.

Conclusion. The number of patients enrolled indicates that sepsis and septic shock cases are under-reported as mortality rates are considerably higher than estimated on a national level or demonstrated in other studies. Sepsis diagnosis should always be considered in severely ill patients if signs of infection are present. Awareness of public and medical society should be raised to facilitate the early recognition of sepsis and organ failure, thus improving outcomes.

Acknowledgements. Conflicts of interest – none to declare.

Using Liquid biopsy Technology As an Additional Method of Primary Diagnostics and Early Detection of the Disease Recurrence in Patients With Colorectal Cancer

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Background: Cancer treatment is rapidly moving from a standardized to a “personalized” treatment strategy. The development of immuno-oncology, targeted therapy and laboratory technologies makes this transition possible. Colorectal cancer is the third most common cancer in the world and the development of new effective diagnostic methods is still relevant.

Aim: To prove the possibility of using liquid biopsy as an additional method of primary diagnostics and early detection of the disease recurrence in patients with colorectal cancer.

Methods: We are planning to analyze the data from 96 patients with histologically confirmed colorectal cancer. Mutations in the KRAS, BRAF and PIK3CA genes will be initially determined in a tissue sample, after which they will be quantitatively determined in ctDNA obtained from blood samples taken at different timepoint. All patients will be divided into 3 groups according to the following criteria: group 1 - patients who are scheduled to undergo radical surgery, group 2 - adjuvant chemotherapy, group 3 - palliative chemotherapy (32 in each group). The dPCRc method with the usage of the QuantStudio3D Digital PCR System and ThermoFisherScientific kits will be used.

Results: At this stage, the data from 5 patients selected into the first group were analyzed. Blood sampling was performed before surgery, within 3 hours after surgery, 24 hours after surgery, and on the 5th and the 15th days after surgery. Of the 5 patients, KRAS blood mutation was detected in 3 patients, BRAF mutation - in 2 patients, PIK3CA mutation was not detected, which corresponds to the results from tissue samples. After comparing the data, it was found that the concentration of ctDNA with these mutations is significantly higher in the samples obtained within 3 hours after surgery (observed in all 5 samples) and significantly lower (in 2 patients) or absent (in 3 patients) in samples obtained after 24 hours. Further analysis of the data has not yet been carried out due to the insufficient number of them. It is assumed that in the samples obtained on days 5 and 15, circulating tumor DNA with the desired mutations will not be detected.

Conclusions: The results, analyzed at this stage, suggest that in order to determine of the desired mutations, the accuracy of the liquid biopsy is comparable with the tissue biopsy. This method can be used to confirm the radical nature of the surgery.

Single centre study: survival of patients with initially unresectable locally advanced stage III gastric adenocarcinoma after receiving neoadjuvant chemotherapy

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Background. Non-metastatic unresectable locally advanced gastric cancer (AGC) is quite specific group of patients, where neoadjuvant chemotherapy can be given with intent to shrink the primary tumour and therefore make it surgically resectable. Unfortunately, not all of them become resectable.

Aim. The aim of this study was to ascertain median overall survival (OS) in patients with unresectable locally AGC and to compare median OS between patients, who received surgical resection after neoadjuvant chemotherapy and who did not.

Methods. Only 26 patients of Oncology Centre of Latvia were suitable for study (in terms of stage, unresectability and treatment with neoadjuvant chemotherapy), diagnosed between 01.09.2014. and 06.09.2018. End of follow up period was 10.01.2019. Retrospectively the clinical records of patients were reviewed. Gathered data were registered using *MS Excel* and statistically analysed by *IBM SPSS 22.0*. For survival analysis, Kaplan-Meier estimate was used (p value was calculated by log rank test, where $p < 0.05$ was considered as statistically significant difference).

Results. The study included 26 patients age of 60.23 ± 10.50 (mean \pm SD) years (5 female, 21 male). 16 patients had *exitus letalis* until the end of the follow up period. Most of the patients initially had stage IIIC (20 patients) gastric cancer. 9 patients received 4 cycles of neoadjuvant chemotherapy, but 10 and 7 patients less than 4 and more than 4 cycles, respectively. 19 patients received DCF (docetaxel, cisplatin, 5-fluoruracil) regimen in neoadjuvant setting, 4 patients EOX (epirubicin, oxaliplatin, 5-fluoruracil), but 3 patients other regimens. 17 patients reached tumour shrinkage and surgery. After surgery and pathohistological investigation, 4 out of 17 patients had stage IIIC gastric cancer, but 7 patients IIIB, 2 patients IIIA, 1 patient IIB and 3 patients IIA gastric cancer.

Median OS of the study group was 60 weeks (95% CI: 46 – 74). There was statistically significant difference ($p < 0.001$) between median OS in patients, who received surgery following neoadjuvant chemotherapy and who did not receive the surgery (86 weeks (95% CI not shown) vs. 52 weeks (95% CI: 18 – 86), respectively).

Conclusion. According to this small single centre study group, most of the patients reached tumour downstaging and surgery after neoadjuvant chemotherapy and their median OS was superior, if compared to patients, whom surgery was not performed.

Acknowledgements. I have no conflict of interest and I have not received any funding in relation to this study.

Prevalence of somatic mutations and histopathological characteristics of colorectal carcinoma

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Background. Colorectal cancer (CRC) is a global burden; its incidence has increased significantly last years. Up to 1000 new cases of CRC are diagnosed every year in Latvia.

Progress in the molecular biology of cancer has led to better understanding of the mutational landscape of CRC and the possibility of developing targeted therapies. Despite the enormous progress in defining some of the common genetic and epigenetic alterations, the picture of somatic genetic changes in colorectal tumorigenesis is still under investigation.

Aim. The objective of this study was to analyze the somatic mutations and histopathological characteristics of CRC.

Materials and methods. 17 patients undergoing CRC surgical treatment in the Riga East University Hospital during 2015–2017 were enrolled in the study. The study was approved by a Central ethical committee. The histopathological characteristics of the CRC was assessed according to current *WHO* and *AJCC* 8. edition guidelines. The targeted next-generation sequencing (NGS, *Foundation One*) for 315 somatic mutations was performed on CRC formalin-fixed paraffin embedded tissue (FFPE). The correlation between genetic and histopathological data were assessed by Chi squared test.

Results. Obtained results showed that K-RAS mutation was found in all patients (100%), 7 patients had p53 and APC (41.0 %) mutations. There were 2 patients in MSI-H (microsatellite high) group, one of which had also mutations in mismatch repair genes (MSH2, MSH6). There was no significant correlation between tumour mutation burden and tumor degree of differentiation) age of patients and presence of necrosis. BRAF mutations were found in 12 patients (70.6 %). PIK3CA mutations were demonstrated in 6 patients (35.0 %)

Conclusion. CRC characterized by a complex somatic mutations, like p53, APC, PIK3CA and BRAF. Therefore, the complex assessment of somatic mutation seems beneficial in the personalized treatment and prognosis.

Acknowledgement. The study was supported by ERDF project within the framework of the Pharma and Chemistry Competence Centre of Latvia “Elaboration and standardization of novel tumour diagnostic technologies providing high quality tumour biomarker research, diagnostics and personalized treatment

The prevalence of polymorphisms of thiopurine methyltransferase gene in Latvian population of inflammatory bowel disease patients

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Background. The most common variant alleles, *TPMT*2*, *TPMT*3A*, and *TPMT*3C*, account for 95% of thiopurine methyltransferase (TPMT) deficiency. This leads to an accumulation of higher levels of cytotoxic thiopurine nucleotides in patients carrying defective TPMT alleles and subsequent severe hematological toxicity with standard doses of the parent drugs (Robert D. Nerenz, 2018). TPMT single-nucleotide polymorphisms can prospectively identify patients at higher risk for thiopurines toxicity [Paugh et al., 2011]. The frequencies of TPMT polymorphisms in the Europe population are in average 4% (*3A), 0.4% (*3C) and 0.2% (*2). *TPMT*1/*3B* allele is not common to be found in Europe population and reaches not more than 0.3% [Milek et al., 2006; Schaeffeler et al., 2004].

Aim. To identify TPMT genotype polymorphisms of selected inflammatory bowel disease (IBD) population in Latvia.

Methods. Blood samples were collected from IBD patients in Genome Database of the Latvia Population. TPMT genotyping with real-time qPCR (TaqMan Drug Metabolism Genotyping Assays) for the detection of rs1800462, rs1800460, rs1142345, respectively *TPMT*2*, *3B, *3C polymorphisms, was used. 3 TPMT alleles were obtained in 244 adults, 51% (n=124) women and 59% (n=120) men. *TPMT*2*, *3A, *3B, *3C polymorphisms found we have checked and approved with RFLP (restriction fragment length polymorphism) method. Categorical data were analyzed by the Pearson's χ^2 test; Fisher exact test was used if the number in any expected cell <5 (SPSS®23).

Results. Prospective study includes 78% (n=190) of patients with ulcerative colitis, median age 41 years (Q1-Q3=29.8-54.3) and 22% (n=54) of patients with Crohn's disease, median age 43 years (Q1-Q3=30.8-55.0), p=0.5. 93.9% were wild-type homozygous *TPMT*1/*1* genotype, 6,1 % heterozygous and had polymorphisms and 4,9% of them were ulcerative colitis patients. The most frequent polymorphisms were: 5.3% *TPMT*1/*3A* genotype, this allele contains two variants *TPMT*3B* and *TPMT*3C*. 0.4 % patients had *TPMT*1/*3C* genotype and 0.4% had *TPMT*1/*2* genotype. In our study no carriers of the *TPMT*3B* polymorphism were identified. No patients were homozygous for any mutation.

Conclusion. The homozygous wild-type *TPMT*1/*1* genotype was the most frequent genotype in both groups of IBD patients. Distributions of TPMT genotype and allele frequency in Latvian population are slightly different from Europe population. We have identified *TPMT*3A* as the most prevalent polymorphisms in Latvian population, but also the exceptional presence of *TPMT*2* polymorphism and the absence of *TPMT*3B* polymorphism. *TPMT*2*, *3A, *3B, *3C polymorphisms were approved with both real-time qPCR and RFLP methods.

High-risk individuals for gastric cancer would be missed for surveillance without subtyping of intestinal metaplasia

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Background. European guidelines are recommending surveillance of patients with intestinal metaplasia (IM) to detect gastric cancer at early stage when complete cure is possible. However, definition of lesions that should be surveyed remains controversial. It has been suggested that only patients staged III-IV according to the OLGA or OLGIM staging systems require surveillance.

Purpose. The aim of our study was to analyze the prevalence of IM subtypes and relation to the gastritis OLGIM stages in healthy adult individuals. This study was conducted in Kazakhstan, a country in Central Asia with high burden of gastric cancer.

Materials and methods. Healthy adult volunteers aged 40-64 years were referred for upper endoscopy within the regional GISTAR pilot study in Kazakhstan (n=166). Five gastric biopsies according to the updated Sydney system were obtained from each study subject. Four-micron-thick sections were stained with haematoxylin and eosin (H&E), Periodic acid-Schiff-Alcian blue (PAS-AB) staining and high iron diamine-alcian blue (HID-AB) for the subtyping of IM. Precancerous lesions (based on IM) were stratified according to the OLGIM staging system.

Results. Overall 46.0% IM prevalence was revealed. Incomplete IM was present in 48.0% (type II in 22.0% and type III in 26.0%), whereas complete IM was found in 52.0% of individuals. Extensive IM (in both antrum and corpus) was observed in 13.3%. The prevalence of OLGIM I and II stage was 85.0% and 10.0%, respectively, whereas OLGIM III was observed in 5.0%. The prevalence of incomplete IM in patients with OLGIM I was 32.0% (type II in 18.0% and type III in 14.0%).

Conclusion. High prevalence of incomplete IM was revealed not only in subjects with extensive IM, but also in those stratified OLGIM I stage. Without IM subtyping, up to 32.0% of the patients with high risk of gastric cancer development would be missed for surveillance. Subtyping of IM is important for proper gastric cancer risk stratification.

Acknowledgement. The work was supported in part from the grant of ERDF “*H. pylori* risk stratification, optimization of management and interplay with other gastric microbiota within major cancer prevention studies of international scope” and University of Latvia grant “Development, validation and implementation of an histochemical method for gastric intestinal metaplasia subtyping to assess the risk of gastric cancer”.

Gut microbiome in diabetic patients at the risk of NAFLD-associated fibrosis

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Background. Non-alcoholic fatty liver disease (NAFLD) is the most prevalent liver disease characterised by fat accumulation in liver which in some cases progresses to non-alcoholic steatohepatitis (NASH), liver fibrosis and cirrhosis. The pathogenesis of NAFLD involves genetic susceptibility, insulin resistance and gut microbiota which might provoke inflammation and subsequent formation of fibrosis. Diabetes is well-known risk factor for developing NAFLD and increases the risk for advanced liver disease.

Aim. To evaluate the composition of faecal microbiota in patients with type 2 diabetes mellitus (T2DM) depending on BAAT score for liver fibrosis.

Methods. Data were collected retrospectively from newly diagnosed T2DM patients included in OPTIMED study from June 2015 – October 2017. Patients with chronic comorbidities, taking medications affecting microbiome or who had diarrhoea during the previous week were not included. Anthropometric measures, blood samples and faecal samples were taken. Faecal microbiota was detected with metagenome shotgun sequencing approach. Modified hepatic steatosis index (HSI) (Lee et.al. 2010) was used to evaluate the presence of liver steatosis. Fibrosis risk was assessed using BAAT score (BMI, age, ALAT, triglycerides) (Ratziu et.al. 2000). Data analysis was performed using IBM SPSS Statistics 22 and Galaxy web application.

Results. 21 patient were included in the study. After calculating modified HSI, 3 patients were excluded as having no NAFLD. 10 out of 18 patients were male, age (median± IQR) 58± 18,75 yrs, BMI 34,72± 9,34 kg/m², 3 patients had BAAT score 1 (no fibrosis); 7 patients – score 2 (indeterminate) and 8 patients – score 3 (high risk for liver fibrosis). Patients with score 3 had significantly lower bacterial diversity at phylum level (p=0,034) and higher at genus level (p=0,043) when compared to patients having score 1 and 2 (Mann-Whitney U test). They had also increased proportion of family *Lachnospiraceae*, in particular – genus *Roseburia* (*Roseburia intestinalis* and *Roseburia inulinivorans*), genus *Dorea* (*Dorea longicatena* t. GCF 000154065), species *Coprococcus comes* t. GCF 000155875 and *Ruminococcus gnavus*.

Conclusion. We demonstrated differences in bacterial composition of faecal microbiota of T2DM patients with high risk of liver fibrosis in comparison to patients with low and indeterminate risk.

Acknowledgements. The authors acknowledge the Latvian Biomedical Research and Study Centre and the Genome Database of the Latvian Population for providing infrastructure, biological material and data. Research was supported by The National Research programme „Biomedicine for Public Health” (BIOMEDICINE) Project: No 2 „Molecular Mechanisms, Pharmacogenetics and New Medicines for Treatment of Diabetes and Cardiovascular Complications”.

***TM6SF2* and *MBOAT7* gene variants are not associated with the risk of developing liver fibrosis and cirrhosis in an Eastern European population**

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Background. Previous large-scale genetic studies identified single nucleotide polymorphisms (SNPs) of the *TM6SF2* and *MBOAT7* genes as risk factors for alcoholic liver cirrhosis and non-alcoholic fatty liver disease.

Aim. In this study, we tried to evaluate the association between *TM6SF2* variant *rs58542926* and *MBOAT7* variant *rs641738* and the risk of hepatic fibrosis or liver cirrhosis of different aetiology in an Eastern European patient cohort. In parallel we also aimed to evaluate whether these two SNPs mediate the effect of *PNPLA3 rs738409* risk variant for developing hepatic fibrosis and liver cirrhosis.

Methods. The study was conducted at the Department of Gastroenterology, Lithuanian University of Health Sciences Hospital, and included 334 patients with liver cirrhosis, 128 patients with liver fibrosis, and 550 controls. SNPs were genotyped by quantitative PCR, using TaqMan allelic discrimination assays.

Results. *TM6SF2 rs58542926* and *MBOAT7 rs641738* SNPs were not associated with increased liver fibrosis or liver cirrhosis risk. In combined analyses, *MBOAT7 rs641738* variant mediated the risk of *PNPLA3 rs738409* for developing HCV induced cirrhosis ($p < 0.05$).

Conclusion. *TM6SF2 rs58542926* as well as *MBOAT7 rs641738* were not linked to hepatic fibrosis, alcohol or hepatitis C virus induced liver cirrhosis in an Eastern European population. *MBOAT7 rs641738* variant mediated *PNPLA3 rs738409* risk for developing hepatitis C virus induced liver cirrhosis.

Acknowledgements. No conflict of interest.

Prolongation of hospitalization period among malnourished patients: contributing factors

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Background. Malnourished hospitalised patients have higher mortality rate, higher prevalence of infective and non-infective complications, as well as longer hospital stay in comparison with normally nourished population. The timely screening of malnutrition and appropriate attention to factors affecting its severity improve clinical outcomes and shorten the hospitalization length. However, there is still a lack of data, which factors contribute to the prolongation.

Aim. To compare the length of hospitalization of malnourished patients and of normally nourished patients in different hospital departments, as well as to evaluate factors which affect hospitalization length.

Methods. A cross-sectional study was performed in Riga Eastern Clinical university hospital in the years 2017–2018. A questionnaire included both MUST (Malnutrition Universal Screening Tool) and NRS-2002 (Nutritional Risk Screening Tool 2002) tools, as well as questions on patients' lifestyle, blood test results, length of hospitalization and therapy tactics, were applied. Three departments were chosen for the research: departments of gastroenterology (GD), endocrinology (ED) and general surgery (SD). Visualisation tool TAG was used to determine possible links among the variables of the study. The data was statistically processed with the IBM SPSS 25.0 program.

Results. Overall, 149 patients participated. Malnutrition was found in 33.6 – 36.2% of patients. Average length of hospitalisation was 13.6 days, median was 10 days. For GD it was 19.1 days, median – 16 days (± 12.1); ED – 9.6 days, median – 8 days (± 5.9); SD – 12.7 days, median – 9 days (± 10.3 days). For NRS screening tool, a group with high-risk for malnutrition had significantly longer median length of hospitalization (18 days) than in a low-risk group (7 days), $p < 0.001$. Same results were achieved for MUST screening tool: 7 days in low-risk group versus 18.5 days in high-risk group. Hospitalization length in malnourished patients (by MUST) was significantly affected by a patient's higher age ($p = 0.02$), gender, and reduced albumin ($p = 0.068$ and 0.057 respectively). In NRS-2002, it was affected by patients' age ($p = 0.019$), weight loss ($p = 0.001$) and low albumin level ($p = 0.006$).

Conclusions. More than a third of all hospitalized patients have had a high malnutrition risk according to MUST and NRS screening tools. Malnutrition was more common among gerontological and gastroenterological patients. A statistically significant effect on increasing the risk of malnutrition was associated with higher age of the patient, uncontrolled weight loss, dietary limitations, and low albumin levels.

Acknowledgements: none.

Reliability of nutrition assessment tools in predicting prolonged hospitalization

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Background. According to the research data, malnourished hospitalized patients have higher mortality rate, higher prevalence of infective and non-infective complications, as well as longer hospitalization length in comparison to those without malnutrition. For malnutrition screening ESPEN (The European Society for Clinical Nutrition and Metabolism) recommends two comprehensive tools – MUST (Malnutrition Universal Screening Tool) or NRS-2002 (Nutritional Risk Screening Tool 2002). The NRS-2002 tool is currently considered to be the most effective and sensitive malnutrition screening instrument, however, NRS-2002 is longer, and requires more complex calculations than MUST, which makes it inferior in conditions of time deficit.

Aim: to compare the reliability of two comprehensive malnutrition screening tools (MUST and NRS-2002) in predicting the prolongation of hospitalization.

Methods. A cross-sectional study was performed in Riga East Clinical university hospital in the years 2017-2018. A questionnaire included both MUST and NRS-2002 tools, as well as questions on patients' lifestyle, blood test results, length of hospitalization, and therapy tactics were applied. Three departments were chosen for the research: departments of gastroenterology (GD), endocrinology (ED) and general surgery (SD). The data were statistically processed with the IBM SPSS 25.0 program.

Results. Overall, 149 patients participated in the study, of them, 69 (46.3%) were men. Mean age of patients was 56.3 (SD 17.6 years), median - 58.0. MUST screening results showed that 33.6% of study sample is of high malnutrition risk. The biggest part were the patients of GD: 49.0% ($p < 0.001$). According to NRS results, 54 (36.2%) were high-risk patients, of them 57.1% were GD patients. Median length of hospitalization was 10 days. For low-risk group, the median was 7 days according to MUST screening results, for high-risk group the median was 18.5 days (statistically significant difference, $p < 0.001$). The length of hospitalization assessed by NRS screening tool for a high-risk group was also significantly longer than in a low-risk group (18 days versus 7 days, respectively), $p < 0.001$. The reliability of both tests for a length of hospitalization is similarly high (Cronbach's $\alpha = 0.92$).

Conclusion. More than a third of all hospitalized patients have had a high malnutrition risk according to both MUST and NRS screening tools. Both screening tools used in the study showed a high reliability to predict increase of hospitalization length and are equally effective in detecting high-risk patients.

Acknowledgements: none.

The Prevalence of Gastroesophageal Reflux Disease and its Risk Factors in Latvia

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Background. The prevalence of gastroesophageal reflux disease (GERD) has gradually increased worldwide since the early 90s, yet no data has so far been available for Latvia. The detrimental effects of GERD can be decreased by the identification of risk factors, which can differ substantially between populations.

Aim. determine GERD prevalence and identify risk factors in Latvia.

Methods. 4417 participants (ages 40-64) selected from the general population for the GISTAR study (1) in Latvia completed a detailed questionnaire on sociodemographic, lifestyle (exercise, diet, smoking, alcohol) and medical factors (body mass index (BMI), history of disease, drugs used), and symptom based GERD (GerdQ questionnaire). Participants were divided into groups based on GerdQ score: ≥ 8 (GERD likely) and < 8 (unlikely). Odds ratios (ORs) with 95 % confidence intervals (CIs) were calculated for each factor, and the most significant thereof were included in multivariate analysis with calculation of mutually adjusted ORs (aORs).

Results. The prevalence of symptom based GERD was 15.5% (684/4417), increased with age, was more common in women and those with a low level of education. After mutual adjustment, being overweight or obese (aOR 1.31; 95% CI 1.02, 1.69; aOR 1.62; CI 1.25, 2.09), proton pump inhibitor use (aOR 3.88; CI 3.03, 4.98), history of peptic ulcer (aOR 1.55; CI 1.16, 2.07), and hypertension (aOR 1.56, CI 1.09, 2.24) were associated with increased odds, while consumption of ≥ 400 g of fresh fruit/vegetables (aOR 0.75, CI 0.62, 0.90) and 3-5 instead of 1-2 or ≥ 6 meals a day was significantly associated with decreased odds of GERD. GERD was not associated with smoking. Alcohol use was slightly lower among those with (8.7g) than those without GERD (10.3 g/week).

Conclusion. The prevalence of GERD in Latvia is comparable to the pooled prevalence reported in Northern European, North American, and Middle Eastern studies (around 15.3%). However, our results differ from the GERD-associated risk factor profile reported in meta-analysis (2). GERD does not seem to be associated with the typical risk factors widely used as the basis for clinical intervention.

Acknowledgements. The study was funded by project nr. 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" of the Latvian Council of Science.

Sociodemographic, Lifestyle and Medical Risk factors for *Helicobacter pylori* infection in the GISTAR study population in Latvia

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Background. *Helicobacter pylori* (HP) is an established risk factor for atrophic gastritis, peptic ulcers and gastric cancer. Overall, rates of *H. pylori* infection are higher in developing countries and have been linked to lower socioeconomic status. Previous research has shown a *H. pylori* infection rate of 79% in Latvia, along with high rates of gastric atrophy and gastric cancer. Given that Latvia is a developed nation with a high HP prevalence, it might provide new insight into the multifactorial nature of the global prevalence of HP infection.

Aim. Identify risk factors for HP infection in a developed nation with high HP prevalence.

Methods. 1855 participants aged 40–64 years of the “*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study” in Latvia tested for *H. pylori* IgG antibodies (Eiken Chemical, Japan) were included in the analysis. Sociodemographic, lifestyle (diet, exercise, smoking, alcohol consumption) and medical (history of disease, surgery, drugs) factors obtained by survey were compared for participants positive (HP+) and negative for HP. Logistic regression adjusted for individual-level covariates was built to assess the association between factors and HP seropositivity.

Results. 1044 (56.3%) participants were HP+. The following factors significantly associated with HP+ in univariate analysis were included in the final model: level of education, smoking (current, former), binge-drinking, consumption of ≥ 200 g of dairy, ≥ 400 g of vegetables/fruit daily, very hot food/drinks weekly, pickled products (days per week), adding extra salt to food (always, sometimes, never), history of HP eradication, peptic ulcer, thyroid and cardiovascular disease). Although HP+ was associated with low level of education (OR 1.76; 95% CI 1.08, 2.91), current smoking (OR 1.45; CI 1.15, 1.83) and binge-drinking (OR 1.45; CI 1.15, 1.81) in univariate analysis, after adjustment for covariates HP+ was significantly associated with consumption of ≥ 200 g of dairy products daily (aOR 1.35; 95% CI 1.11, 1.64), pickled products 6 to 7 days per week (aOR 1.75; CI 1.02, 3.00), very hot food/drinks weekly (aOR 1.27; CI 1.01, 1.59), addition of extra salt to already salted food (aOR 1.27; CI 1.02, 1.59), and inversely associated with consumption of ≥ 400 g of fruit/vegetables daily (aOR 0.81; CI 0.65, 0.99), self-reported history of HP eradication (aOR 0.55; CI 0.39, 0.79), and history peptic ulcer disease (aOR 0.56; CI 0.40, 0.78).

Conclusion. We found HP+ to be associated with lifestyle factors, in particular dietary factors rather than socioeconomic indicators despite socioeconomic status being an established risk factor globally.

Acknowledgements. The study was supported by project nr. lzp-2018/1-0135 of the Latvian Council of Science.

Changes in the indicators of stomach cancer in Kazakhstan

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Background. According to estimates, about 1 million new cases of stomach cancer (SC) are registered in the world every year and about 800,000 die (IARC, 2018). In this case, 75% of all cases are in Asian countries, and high standardized incidence rates are established in South Korea ($39.6^{0}/_{0000}$), and mortality in Mongolia ($25.0^{0}/_{0000}$). Despite the downward trend, the problem of the SC remains relevant.

Aim. The aim was to evaluate the tendencies in SC incidence and mortality in Kazakhstan.

Methods The material of the study was the data of the MOH Kazakhstan, concerning SC (form 35). We analyzed indicators in the period of the beginning and end of the screening program for SC (2013–2016) within the National program of cancer care development. The retrospective research using descriptive and analytical methods of epidemiology.

Results. In 2013, 2,733 people were registered with the first-ever diagnosis of SC and the incidence (crude rate, CR) was $16.2 \pm 0.3^{0}/_{0000}$. In 2016, 2,667 new cases of SC were registered (table), and the incidence decreased to $15.1 \pm 0.3^{0}/_{0000}$ ($p < 0.01$).

Table. SC in Kazakhstan, 2013–2016

Indicators	2013	2014	2015	2016
New cases	2733	2726	2828	2667
Morphological verification	2447 (89.5%)	2501 (91.7%)	2706 (95.7%)	2552 (95.7%)
I-II stage	772 (28.2%)	933 (34.2%)	1015 (35.9%)	1040 (39.0%)
III-IV stage	1952 (71.4%)	1791 (65.7%)	1795 (63.5%)	1624 (60.9%)

In dynamics, mortality (CR) decreased from $12.6 \pm 0.3^{0}/_{0000}$ in 2013 to $9.8 \pm 0.2^{0}/_{0000}$ in 2016 ($p < 0.001$). The rate of morphological verification of SC in the researched years increased from 89.7% in 2013 to 95.7% in 2016. In dynamics, the indicators of early diagnosis (I-II stage) increased from 28.2% (2013) to 39.0% in 2016, and the incidence of the population of stage I-II in these years was $4.6 \pm 0.2^{0}/_{0000}$ and $5.9 \pm 0.2^{0}/_{0000}$ ($p < 0.001$), respectively. The reduction in the patients with stage III-IV of SC from 71.4% in 2013 to 60.9% in 2016, respectively, the incidence of late stages in these years was $11.5 \pm 0.3^{0}/_{0000}$ and $9.2 \pm 0.2^{0}/_{0000}$ ($p < 0.001$).

Conclusions. In Kazakhstan occurs a global tendency to reduce the incidence of SC. 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 and mortality rates), which may be associated with the screening conducted in the country.

MENTAL HEALTH IN THE 21ST CENTURY

Medicina (Kaunas) 2017;53(Supplement 2):59

Perinatal mental disorders: diagnosis and treatment

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Perinatal mental disorders refers to psychiatric disorders that are prevalent during pregnancy and as long as 1 year after delivery. Perinatal disorders ranging from mild depression and anxiety, obsessive-compulsive, mania, to psychosis and others. Perinatal mental health problems affect between 10 to 20% of women during pregnancy and the first year after having a baby [Bauer A., 2014]. However, illness goes unrecognised, undiagnosed and untreated, leading to avoidable suffering for women and their families [Noonan M., 2016].

Any woman may develop mental health problems in perinatal period. There are several risk factors: having a partner lacking in empathy or openly antagonistic; being a victim of gender-based violence; having belligerent in-laws; being socially disadvantaged; having no reproductive autonomy; having an unintended or unwanted pregnancy; having pregnancy-related illness or disability; receiving neither emotional nor practical support from one's mother, and giving birth to a female infant [Fisher J., 2012]. Perinatal mental disorders may have consequences for children's (intra-uterine) growth and development, and have been linked to negative health-related behaviours and adverse outcomes, including poor nutrition, increased substance use, inadequate antenatal care, pre-eclampsia, low birthweight, preterm delivery, post-partum depression, and suicide [Hollins K., 2007; Nguyen T.N., 2013].

This is important, as growing evidence suggests that complications during the perinatal period may provide a window into a woman's long-term health [Saade G.R., 2009]. The physical and mental health of the mother, and the family environment during pregnancy, infancy and childhood is of fundamental importance to mental health. A parent's ability to bond with and care for their baby, their parenting style and the development of a positive relationship can predict a number of physical, social, emotional and cognitive outcomes through to adulthood [Bergner S., 2008].

The use of psychotropic medications is a cause of concern for physicians and their patients because of the potential teratogenic risk, the risk of perinatal syndromes or neonatal toxicity, and the risk for abnormal postnatal behavioral development. However, psychotropic medications are widely used in pregnancy, and as evidence mounts detailing fetal risk of untreated mental disorders, the number of women taking these medications is likely to grow [Stephenson C.P., 2013]. Women with perinatal mental disorders, including schizophrenia and other psychotic disorders, bipolar disorder and moderate to severe major depression often require long-term psychopharmacological treatments to remain well and prevent risks associated with relapse.

From a patient and clinician perspective, there is need to explore evidence for comprehensive and clinically relevant pharmacotherapy and non-pharmacological treatments guidelines for management of mental disorders in pregnancy.

Online mental health: characteristics of self-reported diagnostics claims among internet users from Latvia

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Background. About a third of the population of European countries suffers from various mental health disorders, most often anxiety and depression (Wittchen *et al.*, 2011). Due to the multiple barriers of health-care accessibility between patients and the health care system, only one-third of the cases is diagnosed.

In the last decade, various resources available online have aimed to overcome these barriers. Hitherto these online counselling resources have had promising results. Similarly, mental health professionals have involved in creating web-based tools that are foster patient involvement and self-management skills. Whilst more than 10 000 mental health web applications are available, however, the quality is often under question (Torous *et al.*, 2019).

Aim. The aims of this study were to analyse and evaluate the characteristics of the self-reported claims of the e-visit users. Specifically, the aim was to investigate the claim narrative of these e-visits and to detect any links between the self-reported claims and physicians' diagnoses.

Method. The main data source was obtained from the internet portal *www.arstipsihoterapi.lv*, using anonymous user claims. All self-reported claims regarding any mental health issues were used for this study. Claims were assessed and grouped by the main symptoms: depression, anxiety, psychotic features, substance abuse, relationship difficulties or other conditions.

Results. In total, 71,8 % of all of the e-visits (n=1031) featured reported mental health problems. Among self-reported claims, 84% (2013) and 89% (2018), respectively, constituted mental health issues. The distribution of the symptoms is summarised in table-1 below.

Table 1. Self-reported symptom distribution

Symptom	2013		2018	
Depression	n=19	15,3%	n=10	15,4%
Anxiety	n=37	29,6%	n=25	38,5%
Relationship difficulties	n=24	19,2%	n=11	16,9%
Other	n=28	22,4%	n=10	15,4%

The self-diagnosis was made by 10,83% of all users in 2013, 40% of whom received the same clinical diagnosis. Meanwhile in 2018 of the 9,4% of all users, who were self-diagnosing, only 20% had diagnosis which corresponded with the reported symptoms. Statistical analysis of self-diagnosis in the categories of Anxiety and Relationship difficulties (n=9) show agreement with a specialist in one instance. In the category of specific conditions (eating disorders, gender identity disorder etc.) (n=5) the agreement was evident in four cases. The value of the Fischer test value was statistically significant at - 0,023.

Conclusion. The most common claim among e-visit users, who reported mental health issues, was anxiety and relationship problems. The prevalence of relationship issues may suggest the presence of personality disorders in the population. Moreover, self-diagnosis may lead toward erroneous conclusions in the cases of vague anxiety symptoms. Thus, further analysis of trustworthy self-diagnostic tools should be continued.

Executive functions, rumination and depressive symptoms

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Background. Despite of broad use of modern evidence-based psycho and pharma therapies, the rate of depression is still increasing in Europe. Deeper understanding of psychoemotional processes increasing depression symptoms would help to enhance treatment. From previous studies is known that rumination predicts and prolongs depression symptoms. The executive functions are crucial for adaptation in new situations and every day functioning.

Aim. The purpose of this study is to investigate the associations between depression symptoms, rumination and executive functions in a non-clinical sample.

Methods. The study participants were students (N=125; 98 women, 27 men), ages 18 to 30 years (M=21.09, SD=2.38). They completed the Latvian version of the computerized executive functions tasks (*EXAMINER*), Depression scale of the Trauma Symptom Inventory (*TSI*), Ruminative Response scale (*RRS*).

Results. The results show that set switching scores predict brooding, an aspect of rumination, negatively, while brooding predicts depression in a positive direction.

Conclusion. The clinical implications of these results indicate that executive function and rumination will enhance a deeper understanding of the processes which may be associated with depression, and this will help to improve rehabilitation by using more precise methods in each individual case.

The Effectiveness of Social Support on the Quality of Life of People with Epilepsy

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Background. A variety of factors, apart from seizure frequency, have been shown to affect the perceived sense of well-being, or quality of life (QoL), in people with epilepsy (PWE; Yennadiou & Wolverson, 2017). However, the challenges outside of basic physical treatment are often left untreated for patients (Caller et al., 2016). Social support has been suggested as cheap but effective alternative care, as these services provide self-management techniques, social and vocational opportunities, and emotional support for the frequently stigmatised PWE (Chung et al., 2012). Thereby, service users attain coping mechanisms, which can help manage the problems they face due to their epilepsy (Ridsdale et al., 2018). Even so, fairly little is known about the challenges that PWE deal with in the UK, particularly Scotland, and the effectiveness that social support services from the voluntary sector can have in mitigating the challenges experienced by PWE.

Aim. This study aimed to discover the challenges in the lives of PWE from a local charity organisation, and investigated how support services affected the QoL of service users.

Methods. A cross-sectional mixed methods design was conducted on 30 adults with epilepsy ($N_{\text{Male}} = 11$; $N_{\text{Female}} = 19$). Participants were recruited through purposive sampling through a local social support charity in Glasgow, called Epilepsy Connections. The Quality of Life in Epilepsy (QOLIE-31-P) questionnaire was used as a measure of well-being. The 10-item Parent Stigma Scale (10-PSS) and the Centre for Epidemiologic Studies Depression Scale (CES-D) were used to screen for stigma and depression, respectively. Pearson correlations and a regression analysis were conducted. Three focus groups of fifteen participants ($N_{\text{Male}} = 6$; $N_{\text{Female}} = 9$) were held to gain a deeper understanding of the role that social support plays in the QoL of PWE. A thematic analysis was used to explore the transcripts.

Results. Our quantitative results indicated that depression and stigma represented the main psychosocial challenges to PWE, negatively affecting the QoL in PWE. Focus groups confirmed psychosocial difficulties, treatment irregularities and inefficiencies as the main challenges of PWE. Support services enabled personal growth and provided opportunities that brought about important psychological, social, structural, and emotional benefits into the lives of participants.

Conclusions. The results reveal major clinical- and public policy implications, as professional care staff is advised to work more closely with verified social support organizations to effectively alleviate the psychosocial problems that result with the development of epilepsy.

Acknowledgements. The authors have no conflict of interest and no funding was received.

Appearance concerns and the Body Dysmorphic Disorder Questionnaire rates in healthy adults

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Background. There is a society pressure on body – image and self – esteem and changing appearance demands nowadays. Normal appearance concerns should be distinguished from body dysmorphic disorder (BDD). Body Dysmorphic Disorder Questionnaire (BDDQ) is a screening tool for BDD. A positive screen requires “Yes” to the both parts of the Question 1, “No” to the Question 2, “Yes” to any of the parts of the Question 4 and \geq 1hour per day spend thinking about body defect (Question 4).

Aim. To identify the normal appearance concerns and BDDQ rates among healthy adults.

Methods. Civil servants from Ministry of Interior, who had no major health problems and were at good mental health, filled in the BDDQ (Latvian or Russian translation), while having a compulsory annual health check. BDDQ – screening rates were calculated and the disliked body parts are identified.

Results. 130 questionnaires were extended in order of attendance; 116 (89.2%) were eligible.

Demographics: aged 18 - 67, mean age 36.5 +/- 10.1 Females n=60 aged 18 - 67, mean age 36.8 +/- 11.2. Males n=56 aged 18 - 57, mean age 36.2 +/- 9.

Positive answers:

Question 1A - 76 respondents (65,5%);

Question 1A and 1B - 34 (29.3%).

Question 1A, 1B and Question 2: 21 (%) were excluded from the further testing as their main concern was being overweight.

The remain 13 respondents (11.2%) reported the disliked body parts: skin (scars, wrinkles, acne), hair, breasts, stomach and hips shape, shape or size of the nose; they spend less than 1 hour per day thinking about body defect (Question 4). Four respondents (females, aged 27 - 39) reported the impact of body defects on the quality of life (distress), two of them reported difficulties in unformal social activities as well, one respondent reported about avoiding certain situations. No impact of body defects on the formal social activities was reported.

No BDDQ positive persons were detected.

Conclusion. BDDQ screening in mentally healthy adults is negative. Normal appearance concerns are widespread and most prevalent and meaningful in females. Concerns about being overweight is the most prevalent.

Acknowledgements. We acknowledge the study participants and the Polyclinic of the Ministry of the Interior Service, which provided the opportunity for the study.

Prevalence of cigarettes, alcohol and substance use, anxiety and depression symptoms among lesbian, gay, bisexual, trans and queer community and general population in young adults

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Background. LGBTQ population is considered as a high risk population for various health-related concerns. In Lithuania LGBTQ community faces barriers in health care institutions as problems are not fully understood. Assessment of multiple health-related concerns associated with LGBTQ population is important in order for clinicians to work towards practices that would satisfy health needs of sexual minorities.

Aim. The aim of this study was to determine the prevalence and to estimate the disparities in smoking, substance abuse, depression and anxiety symptoms among Lesbian, Gay, Bisexual, Trans and Queer Community and general population in young adults.

Methods. An internet survey of LGBTQ community members and control group was conducted in 2017 in Lithuania. In total, 510 people aged 18-32 filled in the anonymous questionnaire. All participants were divided into two groups: LGBTQ group (n=274) and control group (n=236). Statistical analysis was performed using IBM SPSS Statistics 24.0 software. Results were considered to be statistically significant when $p < 0.05$.

Results. The average age of all study participants was 21.9 (SD 3.9) years. The average age among LGBTQ group was 22.7 (SD 3.9) years and 20.9 (SD 7.38) in control group ($p=0.012$). 24.7% (n=126) of all participants reported smoking every day, significantly more in LGBTQ group compared to control group (31.4% (n=68) vs. 16.9% (n=40), $p<0.05$). LGBTQ group members also were more likely to smoke a higher number of cigarettes per day than control group ($p<0.05$). Significantly more subjects in LGBTQ group used alcohol compared to control group (82.8% (n=227) vs. 80.5 (n=190), $p<0.05$). The use of all types of drugs was significantly more prevalent among LGBTQ community compared to general population ($p<0.001$). Clinical symptoms for depression were more prevalent among LGBTQ group in comparison with LGBTQ (23.0% (n=63) vs. 15.7% (n=37), $p<0.05$). Significantly more subjects in LGBTQ group had clinical symptoms for anxiety compared to control group (63.5% (n=174) vs. 51.7% (n=122), $p<0.05$).

Conclusion. This study revealed increased prevalence of nicotine, alcohol and drug use, anxiety and depression symptoms among LGBTQ community in young adults living in Lithuania compared to control group. Attempts should be made to target prevention and cessation interventions for LGBTQ community members.

Acknowledgements. We would like to express our very great appreciation to LGBTQ community in Lithuania for their assistance with the collection of our data.

Limitations to safeguard the right to health care of children and adolescents suffering from emergency psychiatric conditions in the Riga region

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Background. Right to health care of children and adolescents is a priority of states and modern health care systems. Children having an emergency mental health condition should be entitled to available, accessible, acceptable, and quality (AAAQ) mental health care. Since 2009 the Ombudsman's Office has been identifying severe infringements of children rights law in all psychiatry units of Latvia. Since psychiatric emergencies are the most challenging, in respect to implementation of all the core elements, pitfalls have been studied, specifically covering the Riga region.

Aim. To identify the pitfalls of the treatment of children in emergency psychiatric conditions in one of the largest regions of Latvia and to make a proposal to improve the regional and national situation.

Methods. Data have been retrieved from reports of the State Emergency Medical Service, the Ombudsman's Office, the Centre for Disease Prevention and Control, and other health care institutions. Analysis of these data and corresponding legislative documents was performed.

Results. Number of emergency care situations for children with mental and behavioural disorders in Latvia is growing from 2559 cases in 2015 to 2989 in 2018.

In Riga region, psychiatric emergency care is provided by 3 hospitals. The Children's Clinical University Hospital (CCUH) admits patients under 16 and older nonaggressive patients. The Riga Centre of Psychiatry and Addiction Medicine (RPNC), admits a high number of nonaggressive and aggressive adolescents aged 16 and over. The Psychiatric Hospital "Gintermuiza" in Jelgava admits patients without restrictions, but it is at least 40 minutes' drive from Riga.

In RPNC there is a lack of appropriate accommodation, care, legitimacy of admission. Adolescents are placed with adults who are charged with crimes; are exposed to smoking, denied access to education and the presence of family members during the hospital stay. There is a lack of psycho therapeutic treatment and substantial differences in the duration of hospital treatment: in RPNC it is 23–24 days, whereas in CCUH 9–10 days.

Conclusion. The research reveals several shortcomings in emergency psychiatric care for children in Riga region. There are systematic insufficiencies in accessibility, availability, acceptability and quality of psychiatric emergency care.

Understanding of the importance of studies on mental health by adolescent parents in Latvia

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Background. Adolescence is specific period in life, during it occurs not only biological, but also psychologic changes. It may result in formation of different disturbances what could affect quality of life later on. Adolescents who somatise in stressful situations are at risk of developing of depression and/or panic attacks in following 4 years. During last decades the number of adolescents with chronic fatigue and chronic pain increases dramatically. For adolescents a pharmacological treatment is less effective, therefore adolescent psychotherapy is the first line treatment. In Latvia, many parents don't understand and don't notice the mental health problems of adolescents.

Aim. The objective of the current study was to analyse the willingness and agreement to participate in mental health screening survey between parents of 9th grade studying adolescents.

Methods. Screening survey was proposed to eight schools, of them three were gymnasium, and other were regular secondary schools. Due to the attempt of suicide that took place in one of the gymnasium schools exactly before the beginning of the survey, this school was excluded from the study. Parents and adolescents received an explanation on aims of the study and its importance and should sign the informed consents form at home. Forms were collected, and descriptive statistics was calculated for invited and agreed parent-adolescent pairs. Chi-square analysis was performed to assess differences in the level of participation between adolescents that study in regular secondary schools and those study in gymnasium schools.

Results. The total amount of parent- adolescent pairs invited to participate in the study was 474 pairs. In 208 (43.9%) of them parents refused to participate. From the 266 parent- adolescent pairs that agreed to participate in the study, there were similar percent of pairs from both school types: 56.8% from regular schools, and 43.2% form gymnasium type schools. We did not find a statistically significant difference between regular secondary schools and gymnasium schools in the level of participation (Chi-square test 0.83, $p = 0.45$).

Conclusion. Approximately a half of parents don't understand the importance of mental health of their children or don't support research in this field. This percent is similar for parents of children that study in regular secondary schools and in gymnasium schools. Although one can think that the level of stress of children that study in gymnasium schools is much higher than that of children in regular secondary schools, adolescents and parents from both types of schools are equally interested in psychological help.

Affective neuroscience and interpersonal neurobiology - what it changes to doctors?

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Over the last two decades different scientific areas have evolved that allow psychotherapists and doctors to better understand how the mind, the body and the psyche of humans interact. Leading studies are:

- The neurobiology of emotional development, affect regulation theory (A.Schore)
- Human and cross-species affective neuroscience (J.Panksepp)
- Neuropsychoanalysis (M.Solms)
- Regulatory processes of the autonomic nervous system (S.W.Porge)

A.N. Schore is an author of regulation theory, a biopsychosocial model of the development, psychopathogenesis, and treatment of the implicit subjective self. The theory is grounded in integration of psychology, psychiatry, and neurosciences, and it is now used by both clinicians to update psychotherapeutic models and by researchers to generate research. The focus is on the early development of right brain, and its unique social, emotional, and survival functions, not only in infancy but across all later stages of the human life span. It also offers a scientifically testable and clinically relevant model of the development of the human unconscious mind. This theory helps to improve the doctor- patient relationship via affect regulation.

Affective neuroscience seeks to illuminate how the most powerful feelings (the primal emotional affects) arise from ancient neural networks situated in brain regions below the neocortical „thinking cup”. Panksepp has found that the ancient subcortical regions of mammalian brains contain at least seven basic affective systems: SEEKING (expectancy), FEAR (anxiety), RAGE (anger), LUST (sexual excitement), CARE (nurturance), PANIC/GRIEF (sadness), and PLAY (social joy). The basic affective systems of mammalian brains are ancient universal value structures of mammalian minds that provide evaluations of the world in the form of categories of individual affective experiences. Multiple emotional streams may cross in the thinking mind, creating an enormous variety of higher emotions that could influence the body and the mind, they are the focus in psychotherapy (pride, shame, confidence, guilt, jealousy, trust, disgust, dominance, and so forth). Without a clear vision of the primary processes the important work on higher processes remains profoundly incomplete. This view allows to reposition the psychoanalytic drives within the motivational/ emotional systems, in a context once again shared with biology. Such repositioning of drives makes possible a clinic of the “implicit” no longer based on an ineffable unconscious. Now it becomes visible, understandable and interpretable through the signs of the expressions of emotions.

Jaak Panksepp, Lucy Biven “The Archeology of Mind. Neuroevolutionary Origins of Human Emotions”
Allan N. Schore “Affect Regulation and the Origin of the Self”

Three-dimensionally printed spinal intervertebral disc model development and biocompatibility assessment for applied biomaterials

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Background. Degenerative processes in spinal intervertebral disks happens with age, but spinal intervertebral disk hernias happen after trauma or after wrong load cases. In these cases, consequences could contribute to pain and even to some organ paralysis. Three dimensional bioprinting tissue constructs could provide solution for that kind of global problem like waiting for organ transplants, and also compatible and appropriate donor implant finding. With three dimensional bioprinting help it could be possible to make biologically compatible spinal intervertebral disc transplants. Considering the properties of this technology, it would be possible to bioprint transplants, specifically to each patient. It is needed to make different biomaterial *in vitro* biocompatibility evaluations with cells to find suitable biomaterials, so that it would be possible to make biologically compatible spinal intervertebral disc transplants.

Aim. The aim of this study was to examine polycaprolactone and polysaccharide hydrogel biocompatibility, growing human osteosarcoma and chondrocyte cell lines in them to determine, whether these biomaterials are appropriate for three-dimensionally printed intervertebral disc model development.

Materials and methods. Two different three-dimensional printing biomaterials were examined in this work: polycaprolactone (PCL) and polysaccharide hydrogel that contains cellulose, sodium alginate, D-mannitol and water. Two human cell lines were tested *in vitro* on both biomaterials to test their biocompatibility. Human chondrocyte cell line C20A4 was used as a test system and after exposition their viability was tested, using flow cytometer or dyed with trypan blue dye. To determine visual growth tendencies, osteosarcoma cell line MG-63-GFP was used as an indicator cell test system. This cell line has been modified with green fluorescent protein, that allows to observe their proliferation and formed structures in fluorescence microscope.

Results. Results that were obtained in this experiment about chondrocyte viability after their exposition in polysaccharide hydrogel, showed that viability after exposition, compared to positive control, is statistically lower. Cell viability in positive control model was $87.9 \pm 5.7\%$ but in polysaccharide model was $69.7 \pm 6.4\%$ (p -value $2.81 \cdot 10^{-6}$). However, indicator cells in hydrogel in two weeks period of time proliferated and increased cell death was not observed. Results after cell exposition in PCL, showed that chondrocyte viability, compared to positive control viability, was not statistically relevant. Cell viability in positive control model was $88.6 \pm 5.0\%$ but in polysaccharide model – $88.8 \pm 3.5\%$ (p -value 0,910). Also, indicator cells showed good cell attachment and proliferation in two weeks period of time in PCL.

Conclusions. PCL matrixes are morphologically suitable for cell size, cells can proliferate and attach to them. After exposition on PCL matrices, chondrocyte viability compared to positive control, was not statistically relevant. During exposition, indicator cells continue to proliferate in polysaccharide hydrogel for 14 days and there was no relevant cell death observed. After exposition in polysaccharide hydrogel, chondrocyte viability, compared to positive control, was statistically lower, however, to make closing conclusions, further biomaterial evaluation would be needed. 3D printing technology can be applied to produce three-dimensional spinal intervertebral disc models containing live human cells.

Acknowledgements. This study was supported by grant from corporation “Sistemu Inovācijas”.

Autologous bone marrow mononuclear cell transplantation in patients with acute myocardial infarction and chronic heart failure in Latvia. Clinical follow-up data

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Background. Heart failure and acute myocardial infarction are the leading causes of morbidity and mortality worldwide. Stem cell research for regenerative medicine started novel therapies in reversing myocardial injuries and improving left ventricle ejection fraction.

Purpose. The objective of the current registry data was to evaluate whether regenerative therapy is safe and improves cardiac systolic function within one year in patients with acute coronary syndrome and chronic heart failure.

Material and Methods. Between September 2009 and April 2016 patients aged 18 to 75 years with acute myocardial infarction and successful revascularization (but with reduced LV EF 15–50% or LV apical aneurysm) or known heart failure at the Latvian Center of Cardiology were enrolled for autologous mononuclear stem cell transplantation (n=123). There were n=100 (81.3%) patients with acute myocardial infarction and n=23 (18.7%) patients with chronic heart failure. During follow-up, we analysed clinical and angiographic results such as all-cause death, cardiac death, target vessel-related myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR). We report the interim analysis of the follow-up at 3 month and 12 months after stem cell therapy. Statistical data analysis was performed with SPSS software (IBM SPSS Statistics Version 21, SPSS inc., USA).

Results. Mean population from n=123 was 112 (91.9%) at mean age 51.91±10.96 years. Previous PCI was performed in n=33 (26.8%), diabetes mellitus 9 (7.3%), arterial hypertension n=58 (47.2%), dyslipidaemia n=90 (73.2%), positive family history n=39 (31.7%), active smoking n=49 (39.8%). Mean left ventricle ejection fraction at baseline in patients with acute coronary syndrome (n=96) was 42.76±9.02%, in patients with chronic heart failure (n=21) – 27.33±9.57%. Mononuclear stem cell implantation mostly done in left anterior descending artery n=85 (86.7%). Mean implanted cell amount was 47.44±26.06 million. One year follow-up reached n=88 (71.54%), echocardiography performed 82 (93.18%), left ventricle ejection fraction in patients with acute coronary syndrome (n=70) increased significantly (from 43.94±8.23 to 48.83±11.44%, p<0.001), in patients with chronic heart failure (n=12) (from 29.83±7.83 to 35.42±10.13%, p=0.015).

Conclusions. Stem cell therapy is safe and significantly improves cardiac systolic function within three months and one year in patients with acute coronary syndrome and chronic heart failure. The study should be continued with longer follow-up up to 24 months in a larger group of patients

Acknowledgements/Funding. This registry was supported in part by Latvian National Research Program “Biomedicine for Public Health” (BIOMEDICINE) and by grant from corporation „Sistemu Inovācijas”.

Hip Joint Osteoarthritis Treatment with Bone Marrow derived mononuclear Cell Injection

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Background. The osteoarthritis (OA) characterises with degenerative changes affecting cartilage, subchondral bone and synovial tissue of a joint. The therapy, possible regenerate the joint tissue, is needed. Bone marrow derived mononuclear cells (BM MNC) could be used in osteoarthritis treatment due to the high regenerative properties of mesenchymal stem cells.

Aim

1. To observe a safety and the presence of adverse events associated with BM-MNC therapy over a period of 12 months.
2. To find out the clinical effectiveness, analyse pain and changes in OA symptoms and to evaluate the joint building tissue structural changes.
3. To compare the OA activity on the patient group treated with BM-MNC and routinely used symptomatic treatment in 12 months follow-up period.

Material and methods. In the treatment group was included 27stage II-III hip OA patients and 14 patients in the control group. The treatment group received BM MNC injections in the hip joint and were monitored for a 12-month period. Control group patients were assigned to the hip joint replacement waiting list and symptomatic nonsteroidal anti-inflammatory drug use.

Results. Positive response in therapy group was found in 89% of cases. No serious adverse reactions were observed. After 12 months the therapy group patient status improved by mean of 13.32 Harris Hip Score points. Control group patients experienced progression of OA symptoms as reflected in the reduction of HHS by 10 points. Magnetic resonance images of 17 patients were evaluated before and 6-7 months after treatment. There was found improvement of articular cartilage by 5%, bone marrow oedema decrease for 1%, subarticular cysts was progressed by 1.5% and labrum tear progression by 0.5%.

Conclusions. Intra-articular injection of the BM MNC is a safe manipulation with no side effects over a 12-month period. The single dose injections of the BM MNC reduces the symptoms of the hip joints osteoarthritis of stage II - III and partially decrease degenerative changes in the joint cartilage however the other hip joint building tissue degeneration was not impaired. OA symptoms decrease in patient group treated with BM MNC was present however on the control group the increase was observed.

Acknowledgements. To Pauls Stradins Clinical University Hospital, University of Latvia, Research Institute of Cardiology, Latvian State Hospital for Traumatology and Orthopaedics for institutional support. For financial support: "Sistēmu inovācijas", research fund and Latvian national research program "Biomedicīna sabiedrības veselībai". 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.

Dynamic of Knee Osteoarthritis Clinical Signs after Mononuclear Cell injections during 36 month's Period

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Background. The treatment of early stages of the knee joint osteoarthritis (OA) continues to present its challenges in orthopedic practice. Due to regenerative and immunomodulatory capacity of mesenchymal stem cells (MSCs) it could be used in treatment of OA. The clinical effects on knee OA symptoms and tissue structure changes after a bone marrow- derived mononuclear cell intraarticular injection were evaluated and results after 12 month's was presented earlier.

Aim. The aim of this study was to evaluate mainly the knee joint osteoarthritis, changes in patient symptoms after a single dose of bone marrow- derived mononuclear cell intra articular injection in time period of 36 months.

Methods. The group of 32 patients and 34 knee joints were analyzed. Mean age $53.96 \pm SD14.15$ years, 16 males, 16 females, Kellgren – Lawrence grade: II – 16, III – 18. The intraarticular injection of mononuclear cell suspension in average $45.56 \pm 34.94 \times 10^6$ of pure mononuclear cells was performed. The cells applied were extracted from the red bone marrow.

Results. No adverse effects after the BM-MNC injection were observed. At the time point of 12 months all subscale results had improved as compared to the starting point on 32 patients. 65% of patients at the point on 12 months still have improvement more than 10 points or minimal perceptible clinical improvement of the KOOS total score. All 32 patients are evaluated over 36 months'. On 36 months' severe increase of osteoarthritis signs were reported by 9 patients and on 7 of them total knee arthroplasty was performed. Slight increase of OA symptom was reported by 8 patients and they were successfully treated with hyaluronic injections and PRP. Without increase of OA clinical signs was 15 (48%) patients, none of them was needed additional treatment therapy.

Conclusions. The single dose mononuclear cell injection reduces the knee stage II- III osteoarthritis pain and symptoms over 12 months on all patients. On 36 month's period no further progression of OA signs of 48% of patients.

Acknowledgements. To “Sistēmu inovācijas”, research fund and Latvian national research program “Biomedicīna sabiedrības veselībai”.

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.

Evaluation of novel type optical sensor prototype for glucose monitoring *in situ*

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Background. Diverse mesenchymal stem cell use in scientific research, drug testing, cell differentiation studies and cell and tissue transplantation applications drives research towards more cost-effective, time-effective and labour-effective cell cultivation methods. The large scale cell expansion bioreactor systems are applied, however glucose level monitoring in culture media are still measured by biochemical analysis and electrochemical sensors that are time consuming and sample obtaining can result in bioreactor system contamination. To resolve these aspects this study is focusing on novel type sensor development which provides real time glucose level monitoring without direct contact with culture media.

Aim. The aim of the current study is to evaluate optical glucose sensor prototype performance during adherent cell cultivation in bioreactor system for large scale cell expansion.

Methods. Prototype of optical glucose sensor was based on multi-channel photometry. Light beam from at least one light source is targeted to culture media passing through translucent tube. Afterwards scattered light is captured with multiple photodetector channels. Signals from photodetectors are filtered electronically, amplified and repeatedly filtered to differentiate signal components that are afterwards transmitted to microprocessor to digitalise the signal and to proceed with mathematical filtering, correction and recognition algorithms. Based on mathematical analysis and physically related signal variety glucose concentration in culture media is calculated.

To evaluate the optical glucose sensor prototype performance adherent cells were cultivated in Zellwerk ZRP bioreactor system from 2.5 to 3 weeks and glucose consumption in culture media were determined by biochemical analyser and optical sensor. Obtained data were compared.

Results. Optical readings with high credibility were obtainable from 10^{-4} to 10^5 lx and no optical interference from laboratory environment was observed.

Optical glucose sensor real-time readings of glucose concentration changes in culture media were compared with biochemical analyser readings at same time points. Obtained data show that optical sensor readings reach precision of ± 0.1 mmol/l in a glucose range of 3–15 mmol/l.

Conclusion. Optical glucose sensor can be applied for real time glucose consumption monitoring without direct contact to culture media. Further studies should be made to evaluate other potential application suitable for monitoring culture media, for example, lactose.

Acknowledgements. This study was supported in part by Latvian National Research Program “Biomedicine for Public Health” (BIOMEDICINE) and by grant from corporation „Sistemu Inovācijas”.

Sea buckthorn fruit residue derived polyphenol extract effect on endothelial cell proliferation *in vitro*

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Background. Growing evidence suggests that polyphenols could be serious candidates to explain the protective effects of plant-derived nutraceuticals. Based on current studies, a general consensus has been achieved to sustain the hypothesis that the specific intake of foods and beverages containing relatively high concentrations of flavonoids may play a meaningful role in reducing cardiovascular disease (CVD) and residual risk through an improvement in vascular function and a modulation of inflammation.

The evidence that nutritional factors are central to the aetiology of cardiovascular disorders is compelling. CVDs have multiple causes, but the majority of CVD events originate from the complications of atherosclerosis, a pathophysiological process that can be prevented by nutrition. Atherosclerosis is primarily a disease of the innermost layer of arterial wall, the intima, which comprises smooth muscle cells lined by a monolayer of endothelial cells. The importance of endothelium exceeds its role as a physical barrier as endothelial cells also maintain vascular homeostasis. Polyphenols reduce the oxidation of low density lipoproteins, enhance the vascular tone by molecular activation of endothelial nitric oxide. Polyphenols inhibit tissue growth factors, expression of adhesion molecules thus reducing aggregation and thrombosis. Furthermore they inhibit cell apoptosis reducing necrotic tissue.

Aim. The aim of study was to evaluate Sea buckthorn peel derived polyphenol extract effect on human endothelial cell proliferation *in vitro*.

Methods. The proliferation assay was performed by application of RTCA xCelligence instrument (ROCHE), as test system a human endothelial cell line HBEC-5i (ATCC® CRL-3245) was used.

Results. Prior to proliferation assay HBEC-5i cell line was expanded in DMEM : F12 + FBS 10% + ECGS 3% culture media. A polyphenol solution was used for proliferation assay.

RTCA reaction plates were seeded with 2 000 cells each well and cultivated for 24h at +37°C, 5% CO₂ atmosphere for 24h. Three different extract/ cell culture solutions containing 200 µg/ml, 20 µg/ml and 2 µg/ml polyphenols were exposed to test system and proliferation was monitored for 72h. As a control wells without exposition of polyphenol solution were used.

No cytotoxic and cell growth inhibition activity were observed conducting proliferation assay. In case of 2 µg/ml polyphenol solution no statistically significant difference comparing to control was observed. Cell growth reached 101.34 ± 2.44% at 2 µg/ml concentration, beside 20 µg/ml - 111.76 ± 1.52% and 200 µg/ml - 120.09 ± 7.11%.

Conclusion. Previous study of polyphenol extraction showed high antioxidant and antiradical activity of obtained sea buckthorn peel extract and observed cell proliferation rate at this particular study (concentration 20–200 µg/ml) can be assumed as reason of observed protective activity of polyphenol solution. The study clearly shows potential of sea buckthorn peel extract to be utilized as diet supplement in order to mitigate cardiovascular disease and residual risks.

Acknowledgements. This research was funded in accordance with the contract No. 1.2.1.1/16/A/004 between “Latvian Food Sector Competence centre” 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 centre”.

Novel approach of polyphenol extraction from Sea buckthorn residues

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Background. Dietary polyphenols, along with other natural compounds occurring in fruits and vegetables, have been reported to exert beneficial effects in a multitude of disease states, including cancer, cardiovascular disease, and neurodegenerative disorders. Sea buckthorn (*Hippophae rhamnoides* L.) fruit popularity has increased in last decade due to its potential as a functional food and nutraceutical. Sea buckthorn fruit derived polyphenols are in great interest due to their possible health effects moreover their antioxidant properties and their possible effects in the prevention of various oxidative stress associated disease such as cardiovascular disease.

The two main sources of valuable products are derived from the sea buckthorn fruit, juice from the fleshy tissue and seed as a single seed from each berry. Potential processing and application of juice extraction residues (peels) are poor studied. Sea buckthorn peels beside seed separation are not considered for further processing and significant source of polyphenol extraction.

Aim. The aim of study was to develop and evaluate polyphenol extraction protocol from sea buckthorn peels, assess extract yield and antioxidant activity.

Methods. The sea buckthorn peels after juice extraction were used for polyphenol extraction. Prior extraction seeds were separated. As a solvent 70% ethanol was used. In order to promote higher polyphenol yield substrate sonification was applied. After solvent exposition it was recovered by vacuum rotatory evaporation system. Obtained polyphenol extract was assessed on total polyphenol count by Folin-Ciocalteu colorimetric method. Antioxidant activity of extract was assessed by DPPH assay.

Results. Wet sea buckthorn peels were grinded to fine particles, dried and seeds were removed and followed by 70% ethanol exposition (10:1 v/w solvent to dry weight). The extraction procedure was assisted by the application of ultrasound at 20 kHz frequency continuous mode with temperature control at +50°C set point. After exposition solid particles were removed. Same procedure was repeated for three times with fresh solvent. Solvent recovery was performed by vacuum rotatory evaporator.

The Folin-Ciocalteu colorimetric method was applied to assess total polyphenol count. Average extraction yield of total polyphenols was expressed in GAE (gallic acid equivalents) and reached 205,1±0,20 mg/100 g (fresh peels). Antiradical activity was calculated by utilization ascorbic acid, expressed in AAE (ascorbic acid equivalents) and reached in average 78,1±0,18 mg/100 g (fresh peels). The DPPH reduction ability was expressed in percentage and reached in average 82,0±1,88%.

Conclusion. The approach of conducted study lead to conclusion, that sea buckthorn peels can be assumed as source of polyphenols, but at this stage of study is not clear if extraction protocol can be easy transferred to production while development of commercially available solutions of ultrasound assisted disintegration systems are on early stages.

The study clearly shows huge potential of ultrasound utilisation in production of food supplement and nutraceutical ingredients.

Antiradical and antioxidant properties of obtained extract show that applied processing protocol is designed in an appropriate manner and do not significantly impact activity of extracted polyphenols.

Acknowledgements. This research was funded in accordance with the contract No. 1.2.1.1/16/A/004 between “Latvian Food Sector Competence centre” 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 centre”.

SURGERY, ANAESTHESIOLOGY & INTENSIVE CARE

Medicina (Kaunas) 2019;55(Supplement 1):75

Strategies for medical implant surface modification

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Background. Currently, more than 1300 types of oral implants varying in form, material, dimension, interface geometry and surface properties are commercially available. Based on the available results of randomized-controlled trials, no evidence that any particular type of dental implant showed superior long-term success. Besides other parameters, implant surface characteristics are factors affecting the rate and extent of the implant bone response as well as the mechanical quality of the bone/implant interface. Two main factors, affected postoperative success are quality of osseointegration and bacterial infection that can cause implant failure and even loss.

Aim. This review aimed to analyze strategies and method for implant surface modification for increasing success after oral implantation.

Materials. The PubMed database was used with the key words – bone implants, dental implants, surface topography, surface modification, micro-roughness, nano-roughness, osseointegration, bone integration, bacterial adhesion – used in different combinations. Both experimental and clinical studies included into analysis.

Results. Two main strategies currently used for surface modification – mechanical and chemical treatment. The first one aimed to make roughness on micro- and nanolevel. Chemical strategy tries to mimic the extracellular matrix of bone and at the same time prevent bacterial adhesion. Major experimental and review articles have been shown importance of surface roughness on a micrometer to cell and tissue response, but pointed high bacterial viability on such type of surface. Machining/micromachining, sandblasting, acid etching, electropolishing, anodic oxidation, and plasma spraying currently used for commercial implant system with high clinical success, but with up to 10% of postoperative complication, including bacterial infection. Possible influence of nanostructured surface has been indicated but still not published any clinical evidence of nano-roughness success. Despite the micro-roughness, nano-level modification can prevent bacterial adhesion and biofilm formation with good biocompatibility and cell response. Chemical modification includes deposition of inorganic (Ca and P) and organic components of bone matrix as well as including some molecules that prevent bacterial adhesion. The main problem for development effective coating – the same mechanism in adhesion for prokaryotic and eukaryotic cells. Other way – including of active antibacterial agent and nanoparticles that will inhibit pathogen growth but will not affect osteoblast proliferation.

Conclusion. Commercially available dental implants have good clinical success but postoperative complications push scientists for developing new effective surfaces that increase osseointegration and prevent bacterial adhesion.

Acknowledgements. This research supported by H2020 Marie Skłodowska-Curie Actions (NanoSurf 777926) and grant POIR.01.01.02-00-0022/16.

Carotid plaque instability and neovascularisation assessment using Contrast-Enhanced Ultrasound (CEUS) and Superb Micro-Vascular Imaging (SMI)

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Background. There are several causes of cerebral ischaemia and if risk factors are diagnosed timely, the risk of stroke can be significantly reduced. One of the main risk factors of cerebral ischaemia is the unstable atherosclerotic plaque in the arteries.

Aim. The purpose of the study was to analyse multi-parametric US techniques ability to confirm the plaque's instability more precisely than the baseline investigation of Duplex US and find out correlation between the new multi-parametric US techniques results and histological findings.

Methods. During the prospective research, conducted in the period from 2017 to 2018, 38 patients with unstable plaque detected with duplex US, were included. Every patient was analysed with CEUS, SMI and CTA methods and in 22 cases the histology of the atherosclerotic plaques was done.

Results. Unstable plaque was diagnosed in 38 patients using Duplex US method and in 37 patients using CT method. Comparing both methods statistically significant correlation was found ($r_s = 0,781$; $p = 0,0001$). The neovascularization was diagnosed in 12 (31.6%) patients by SMI method and in 19 (47.5%) patients by CEUS - in 11 cases (57.9%) plaques showed neovascularization grade 1 and in 8 cases (42.1%) grade 2 plaques were detected. Using SMI method neovascularization were found in 12 (29.3%) patients, with statistically significant correlation between CEUS and SMI ($r_s = 0,801$; $p = 0,0001$). Comparing CEUS method and results of histology statistically significant correlation between CEUS and SMI ($r_s = 0,801$; $p = 0,0001$). Comparing CEUS method and results of histology statistically significant correlation was found ($r_s = 0,624$; $p = 0,002$).

Conclusion. New ultrasound methods such as CEUS and SMI provide additional information to the atherosclerotic plaque instability and vasa vasorum detecting, with positive correlation to the grade of stenosis and histological results.

Acknowledgements. Limiting factors identified during the study were: calcinated atherosclerotic plaque and worth hemodynamcs; however further evaluation in following studies is mandatory.

“Fast-track” surgery and early rehabilitation for total hip replacement

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Background. Total hip arthroplasty (THA) is a replacement of damaged parts of the hip joint with a prosthesis. Average length of stay (LOS) after these operations is 8 days. Prolonged LOS is associated with greater hospital infection risk, and it increases expenses. The “fast-track” principle is used to accelerate patient recovery, reduce risk of dysfunction and complications. An important part is early mobilization that, until now, was initiated only on the first postoperative day (POD1) due to pain and long-acting spinal anesthesia (SA).

Aim. The aim of the study is to investigate the effects of early patient mobilization on postoperative pain, adverse events, complications and LOS after primary THA using intermediate length acting local anesthetics (LA) in SA.

Methods. A prospective, randomized study was conducted at the Hospital of Traumatology and Orthopedics from September 2017 until March 2018. The study included 46 patients, who had primary THA surgery. Patients were divided into control and study groups. The study group(P) received 70 mg of prilocaine and control group(B) received 18 mg of bupivacaine in SA. Both groups received multimodal analgesia. Patients started mobilization on the day of surgery(P) or on POD1(B). Data was collected about pain while stationary and in motion using the Numeric Pain Rating Scale (NPRS), adverse reactions, blood loss, and LOS. Patients were contacted one week after their discharge, and their pain levels, ability to use the stairs, and self-care skills were assessed. Statistical analysis was done using SPSS Statistics V.25.0, with Chi-squared test, Cramer’s V correlation coefficient, Mann-Whitney test and Eta correlation coefficient.

Results. There was statistically significant reduction ($P_{MV} = 4.95 \times 10^{-2}$) of LOS for patients in P group by ~1 day (6.91 days, SD=1.41 days) compared to B group (8.00 days, SD=1.79 days). Mean NPRS score was lower in P group (2.00, Median 2.00, IQR 3.00) than in B group (3.33, Median 3.00, IQR 3.00 B) in POD1 during motion. Ability to ensure self-care was better in P group (90.91% positive), than B group (62.50% positive). Result was close to statistical significance ($P_{\chi} = 0.07$), and there was strong correlation ($V = 0.34$) between use of prilocaine and better self-care.

Conclusion. The use of intermediate length acting LA in SA with same-day rehabilitation is a safe method, which can be used to reduce the postoperative pain during movement, the length of stay, as well as to improve patient self-care abilities after discharge.

Acknowledgements. There are no conflicts of interest.

The efficacy of the endovascular transvenous bypass in the treatment of long lesions of the femoral artery

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Background. The PQ Bypass DETOUR System is a novel, investigational approach to fully-percutaneous femoral-popliteal bypass. Using fluoroscopic guidance, a series of stent grafts are deployed from the popliteal artery into the femoral vein, and from the femoral vein into the superficial femoral artery through two independent anastomoses.

Aim. The aim of this study is to demonstrate that the endovascular transvenous bypass (ETB) provides equal patency rates compared to the surgical femoral-popliteal bypass (SFB).

Methods. Data from 86 patients with PAD and long femoral occlusions were collected. Two treatment arms (above-the-knee): SFB ($n = 36$) and ETB ($n = 50$). A retrospective review was performed. All analyses were performed in IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, N.Y., USA).

Results. Mean age was 64.9 ± 7.4 years (88 % - men). The operations' lengths were $1.72 \text{ h} \pm 0.56 \text{ h}$ (SFB) and $1.71 \text{ h} \pm 0.82 \text{ h}$ (ETB) ($p = 0.966$). The mean lesion length was $23.48 \text{ cm} \pm 7.62 \text{ cm}$ with no difference between the groups ($p = 0.437$). The most frequent Rutherford grade among the groups was III (87.8 %). At 1 year the ankle-brachial index improved from 0.57 ± 0.13 to 0.88 ± 0.19 in SFB and from 0.61 ± 0.13 to 0.96 ± 0.23 in ETB ($p = 0.690$), at 2 years it improved from 0.58 ± 0.1 to 0.90 ± 0.17 and from 0.59 ± 0.14 to 0.92 ± 0.16 , respectively ($p = 0.864$). At 1 year the primary patency rates were 88.9 % ($n = 36$) and 76 % ($n = 50$) (95 % CI, 10.23 – 11.55; $p = 0.144$; HR, 0.445), at 2 years they were 78.9 % ($n = 20$) and 57.6 % ($n = 33$), respectively (95 % CI, 17.34 – 21.79; $p = 0.118$; HR, 0.179). The freedom from clinically driven target lesion revascularization at 1 year was 91.7 % and 82.0 % (95 % CI, 10.79 – 11.83; $p = 0.222$; HR, 0.455), at 2 years it was 80.0 % and 63.6 %, respectively (95 % CI, 18.13 – 22.31; $p = 0.254$; HR, 0.528). At 1 year Rutherford grade improved to I (42.9 %) and 0 (80.0 %), at 2 years it improved to I (35.0 %) and 0 (90.6 %), respectively.

Conclusions. PQ Bypass achieves an excellent primary patency and is a good alternative to SFB. Optimal stent deployment remains critical to the performance of this stent device.

Evaluation of International Ovarian Tumour Analysis Logistic Regression Model 2 and Risk Malignancy Index in the preoperative prediction of malignancy in women with adnexal masses in Latvia

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Background. In Latvia in some cases patients with benign ovarian tumors are sent to a specialized oncology-gynecology department for operative therapy and reversly – some patients with ovarian cancer are routinely operated in gynecological departments not in radical techniques, which later require repeated surgery. The results of the study will help to better identify the nature of ovarian tumor in the outpatient phase and to direct patients to a stationary profile - resulting in reduced non-radical surgery in ovarian cancer. At present, none of the protocols for prediction of malignancy risk is used in Latvia.

Aim. The aim of this study was to compare International Ovarian Tumour Analysis Logistic Regression model 2 (IOTA LR2) and Risk Malignancy Index (RMI) in predicting malignant ovarian tumor

Methods. This was a prospective study of women with an ultrasound diagnosis of an adnexal tumor. In all women the possibility of the adnexal mass being malignant was calculated using the IOTA LR2 and RMI protocols. All women underwent surgery and the ultrasound findings were compared with final histological diagnosis.

Results. The study included 35 patients with adnexal masses. 16 (45.7 %) tumors were histologically diagnosed as malignant (including 6 borderline) and 19 (54.3%) tumors as benign. Sensitivity of IOTA LR2 for predicting malignant tumors 87.5 % (95% CI 57 – 98 %) , was significantly higher than that of RMI 62.5 % (95% CI 38 – 88%), but specificity of IOTA LR2 63.2% (95% CI 43 – 85%) was relatively lower than that of RMI 73.7% (95% CI 46 – 88%).

Conclusion:

1. The study shows that IOTA LR2 and RMI are applicable models for use in ambulatory setting and should be used to select patients with adnexal masses for specialised oncology care in Latvia.
2. Considering higher IOTA LR2 model sensitivity in predicting malignant adnexal tumours, it should be recommended as the protocol of choice.
3. Considering relatively low specificity of both models the second stage test to reduce false positive findings should be created and introduced in future.

Acknowledgements. The authors thank all participating centres, the study participants for their contribution. There is no conflict of interest regarding the publication of this article.

Optimization of early medical rehabilitation of patients after hip arthroplasty

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Background. The problem of medical rehabilitation of patients after hip arthroplasty is very important. Total hip arthroplasty is the method of choice for various diseases of the hip joint. This operation improves the quality of life of patients because it reduces pain and increases movement in the joint. But only timely initiated medical rehabilitation measures allow to consolidate the results of the operation, which is one of the stages of the treatment process.

Aim. The aim of the current study was to improve the results of treating patients after hip arthroplasty by developing and optimizing a medical rehabilitation scheme.

Methods. Altogether 228 patients aged from 36 to 86 years patients were enrolled in the study. Of these, 152 women and 76 men. Depending on the method of fixation: non-cemented: 122 patients, 78 patients cemented. Two groups were identified: main and control. The main group included 148 patients. The control group consisted of 80 patients. A standard clinical examination was conducted, and the results were used to quantify the functional status of the hip joint using the method proposed by Harris. The patients of the control group underwent a course of medical rehabilitation in the early postoperative period in the usual way. Patients of the main group were given early medical rehabilitation from the first day after the operation and included an individual motor regimen, a complex of medical gymnastics, kinesiological recordings, and massage. The engine mode was prescribed individually depending on the method of fixing the endoprosthesis, the patient's body weight, the biomechanics of the musculoskeletal system and associated diseases. Also, patients were taught the correct behavior after hip arthroplasty.

Results. The patients were re-examined by us at the medium-term rehabilitation stage and the following results were identified. In the main group, the average on the Harris scale before the operation was 28.39 points, after the operation in the medium-term stage of rehabilitation it rose to 90.77 points. In the control group, the indicator was 28.45 before the operation and 80.55 after the operation.

Conclusion. Early medical rehabilitation should be started from the first day after surgery. The motor mode after surgery is prescribed individually and depends on the method of fixation of the prosthesis, taking into account the individual characteristics of the patient. Early medical rehabilitation should include elements of patient education.

Acknowledgements. No conflict of interest was declared.

The difference of body mass index between different age groups and specific types of urinary incontinence

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Background. Urinary incontinence (UI), defined as the involuntary leakage of urine, is a common problem, particularly in the female population. UI can be divided into stress urinary incontinence (SUI), urgency urinary incontinence (UUI), and mixed urinary incontinence (MixUI). BMI is important independent risk factor for the development of UI.

Aim. To analyze the difference of BMI between UI specific types: SUI, UUI and MixUI in different age groups.

Methods. The cross-sectional study was performed in Pauls Stradins Clinical University hospital. Based of patient history and questionnaires they were divided into 3 groups: SUI, MixUI, UUI. MixUI was further divided in SUI or UUI predominant forms.

Results. There were 806 women included in the study. Patients with SUI - 189 (23.5%), MixUI - 512 (63.5%) and UUI - 105 (13.0%). Statistical analysis revealed that patients with SUI had lower mean BMI, when compared to patients with MixUI and UUI, 27.4, 29.8 and 28.7 kg/m² respectively ($p < 0.001$).

Table 1. Mean BMI in different UI types and age groups.

AGE	SUI*	MixUI*	UUI*
18-44	24.9±4.7	26.7±8.6	25.4±4.5
45-65	27.7±4.6	30.3±5.9	29.8±6.9
>65	29.8±5.3	30.0±5.0	28.6±4.4

*Values are given as kg/m² mean±SD.

When patients are analysed in different age groups, statistically significant difference in BMI was found only in 45-65 age group ($p < 0.001$), while in other age groups there were no significant difference between BMI (Age group 18-44 $p = 0.609$ and in group >65 $p = 0.192$). In this age group, BMI of patients with SUI was smaller than in both other types ($p < 0.001$ and $p < 0.05$, respectively). There was no difference between BMI of MixUI and UUI in 45-65 group or any other age group.

When different types of MixUI are considered, statistically significant difference in BMI was seen only in 45-65 age group: MixUI with predominant SUI 29.6±5.3 and MixUI with predominant UUI 31.4±6.8 ($p < 0.05$).

Conclusions. Patients with MixUI and UUI had statistically higher BMI than SUI. However, when subdivided into different age groups, statistical difference was observed only in 45-65 group. There was no significant difference between MixUI and UUI in any age groups.

Weight reduction is recommended as first-line treatment of SUI and since MixUI is partly explained by SUI symptoms, weight loss might also be helpful in this group of patients.

Ruptured abdominal aortic aneurysm management: Single center experience

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Background. Abdominal aneurysm is focal dilatation of aorta >50% of normal diameter. Aneurysms are usually asymptomatic until rapidly enlarge or rupture. Worldwide aneurysm prevalence is 4–8%. Rupture is life-threatening condition, with half of patients die before arriving at hospital. If not treated properly associated with 90% mortality. Therefore it is important to recognize condition and emergently done the repair to give patient the best chance for survival.

Aim. To find out the factors which influence the choice of treatment approach and mortality.

Methods. Retrospective analysis of all ruptured abdominal aortic aneurysms treated Pauls Stradins Clinical University Hospital from 2015 till 2018. Patient hospital notes at emergency room (ER) and vascular department were analyzed.

Results. 40 patients have been included into the study. ER triage first priority was 17.5% (n=7), second 35.0% (n=14), third 42.5% (n=17), fourth 5.0% (n=2). Total patient survival was 33% (n=13); died after operation 15% (n=6), with palliative treatment 33% (n=13), died in ER 20% (n=8). 48% (n=19) patients underwent surgery with 68% (n=13) survive rate. Average age for survivors 68 years (IQR80.50–60.50), for all death cases 82 years (IQR87–75.00), $p=0.004$. Time until hospital: for operated patients 43 min (IQR64.50–14.50), for palliative patients 50.5 min (IQR70.25–28.50), $p=0.41$. Average age: for operated patients 71 year (IQR81.00–65.00), for palliative patients 84 years (IQR88–77.50), $p=0.006$. Moderate correlation between age and palliative approach ($p=0.017$; $r+0.38$). Size of aneurysm: for operated patients 7.74cm (95% CI 6.71–8.77), for palliative patients 9.29cm (95% CI 7.46–11.12), $p=0.09$. Weak correlation between aneurysm size and palliative approach ($p=0.056$; $r+0.34$). Time until senior-surgeons visit: for operated patients 21min (IQR 42.50–8.00), for palliative patients 57min (IQR85.50–5.50), $p=0.40$. GFR at ER: for survivors 87.10 ml/min (IQR 100.70–38.80), for all death cases 41.80 ml/min (IQR 57.60–30.00), $p=0.006$. GFR at ER: for operated patients 75.70 ml/min (IQR94.25–41.00), for palliative patients 41.80 ml/min (IQR 49.35–25.70), for patients who died in ER 33.60 ml/min (IQR43.63–30.83), $p=0.003$. Moderate correlation between GFR and operative approach ($p<0.001$; $r+0.56$). Moderate correlation between GFR and all death cases ($p=0.004$; $r-0.45$). Weak correlation between GFR and death in ER ($p=0.043$; $r-0.33$). Moderate correlation between second priority and palliative approach ($p=0.014$; $r+0.39$).

Conclusion. Increased age and size of aneurysm, lower GFR are associated with more frequent mortality and choice of palliative approach. No statistical difference in time until hospital or senior-surgeons visit between operated and palliative patient groups has been found. For second priority patients more frequent choice is palliative approach.

Trauma mechanism and blood lactate level impact on mortality in polytrauma patients

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Background: the polytrauma mechanism and blood lactate level at admission are two important determinants of the outcome. According to our observation, frequent trauma mechanisms are road traffic accidents and unintentional falls.

Aim: to perform the analysis of the polytrauma mechanism, lactate level at admission and their possible association with mortality.

Methods: the analysis of the data collected prospectively from January 2017 to October 2018 at the tertiary reference center Riga East University Hospital “Gailezers”. The trauma mechanism was recorded secondary to the ambulance service report form during the primary assessment, all the blood samples for laboratory investigation were taken parallel to the severity assessment. Medical records were compiled in a uniform trauma report form and resuscitation took place according to ABCDE principles.

Results: in total, 579 patients were assessed according to the polytrauma protocol. The most frequent trauma mechanism was a pedestrian struck by a vehicle in 29.7% of cases, and falling from a height of over 2 m in 27.3% of cases. From all included patients, 18 died (7 females vs. 12 males). The most common cause of death was associated with fall from a height of over 2 m and pedestrian struck by a vehicle, 5.1% and 2.3% of cases accordingly. The median lactate level in survivors was 1.7 mmol/l (IQR 1.1–2.7) vs. 2.6 mmol/l (IQR 1.6–6.7) in non-survivors, $p=0,006$. Even though lactate level under the 2 mmol/l is considered to be safe, 7 non-survivors had lactate level under 2.0 mmol/l (median of 1.4 mmol/l, IQR 1.2–1.7) and 11 had over 2.0 mmol/l (median of 4 mmol/l, IQR 3.1–7.2). The highest blood lactate level was observed in patients struck by a train, a median of 3.1 mmol/l (IQR 1.9–3.9), and in criminal trauma victims, a median of 3.0 mmol/l (IQR 2.3–3.6). Blood lactate concentration in patients with the ISS=0–15 was a median of 1.5 mmol/l (IQR 1.04–2.3), in ISS= 15–50 – a median of 2.0 mmol/l (IQR 1.25–2.9), and in ISS>50 – a median of 2.4 mmol/l (IQR 1.2–7.4).

Conclusions: blood lactate level can be used as a prognostic factor to determine the risk of mortality in polytrauma patients. The most common cause of death is associated with a fall from a height of over 2 m and pedestrians struck by a vehicle. The ISS score >50 is associated with critically increased blood lactate level, however in this study we found no significant evidence between the lactate level and trauma mechanism.

Effect of perioperative Ketamine application on postoperative pain and neurocognitive function

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Background. Pain and depressed mood have negative impact on patient recovery. Ketamine(K) has obvious, persistent antidepressant and analgesic, and immunomodulation effects. All this effects of K are necessary in case of large traumatic surgeries such as spine fusion surgery there big doses of opiates are used and early mobilisation is crucial.

Aim. The aim of the current study was to determine effect of ketamine on postoperative pain, opiate consumption and patient neurocognitive function in patients undergoing spine fusion surgery.

Methods. Two patients(ASA grade I-II) were observed. Both had anterior lumbar interbody fusion(ALIF) approach combined with posterior transpedicular fixation(TPF) due to lumbar part spondylarthrosis with spinal stenosis, spondylolisthesis. Ketamine 0.5 mg/kg was given at induction of anaesthesia and 0.25 mg/kg before extubation, followed by 0.15-0.35 mg/kg/h continuous infusion postoperatively up to 32 hours (h). Visual Analogue Scale(VAS) was used for pain, Mini-Mental State Examination(MMSE) for neurocognitive assessment preoperatively, 1, 6, 24 h after surgery and at discharge. Depression level were assessed by Patient Health Questionnaire(PHQ-9) preoperatively, on the first, fifth day after surgery and at discharge.

Results. Both patients (A and B) had similar demographics and were 43 and 55 Years old with preoperative pain score 6 and 8 for >3 months. Patient A received Trimeperidine 20mg IM before surgery. MMSE showed score >24 points reflecting normal cognition. In both PHQ-9 presented moderate level of depression.

Postoperative consumption of opioids were reduced significantly with no need in opioids in the day of surgery. Patient A received K for 14 h, B for 32 h. K presented excellent analgesic effect in low doses, respectively, patient A had 4, 2, 1 VAS score 1, 6, 24 h postoperatively with K dose 0.2 mg/kg/h, while patient B had VAS 6, 1, 1 in a dose 0.1-0.15 mg/kg/h. Both in the operation day evening required Diazepam IV. Both patients received only two injections of Trimeperidine 20 mg in the first two postoperative days. At discharge VAS score was 1 and 2 for A and B patient respectively.

MMSE showed no changes in neurocognitive function. In opposite, PHQ-9 score was reduced significantly 1(A) and 2(B) points and showed absence of depression already in the first postoperative day and 0(A) and 1(B) at discharge.

Conclusion. Perioperative application of ketamine was associated with improved scores for pain, reduce opiate consumption and improve neurocognitive function in patients undergoing elective spinal fusion surgery.

Acknowledgements. No conflict of interest to declare.

The efficiency of continuous wound infusion of local anaesthetics after gastrectomy. Pilot study

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Background. Partial and total gastrectomy is indicated to patient with active stomach ulcer or malignant tumour. First few days after the surgery the patient is experiencing severe pain. Opioids are regularly used to decrease pain in the first few days. We believe that continuous wound infusion (CWI) of *Bupivacaine* is the first 48 hours as additional analgesia allows effectively reduce pain and decrease the amount of opioids.

Aim. To evaluate the efficiency of CWI to reduce pain after gastrectomy and determine the necessary amount of opioids, combined with CWI.

Methods. The following pilot study results for period from October to January are presented here. Two groups of people participate in the study: CWI group (7 patients), which is given CWI in combination with opioids, and Control (9 patients) – where pain is reduced by opioid only. Patient is being catheterized in preperitoneal space under *m. rectus abdominis* of surgical wound, 3 – 4 cm from the edges: both catheters are used to infiltrate by perfusor of *Bupivacain* 10 mg/h to the wound during to the first 48 hours. The patients are asked to evaluate the intensity of pain according to Numeric Pain Scale (NPS) in the first 3 days. The amount of opioids also is being calculated

Results. Pain after gastrectomy, according NPS (median): day 1: CWI group – 3 (IQR 2, 5 – 7,5), control group – 5 (IQR 4 – 6); day 2: CWI group – 3 (IQR 2.5 – 3.5), control group – 5 (IQR 3 – 6); day 3: CWI group – 1 (IQR 1 – 2.5), control group – 2 (IQR 1 – 5). Opioids, during the hospital stay (median): *Sol. Phentanyli* 0,005%: CWI group – 0.5 mg (IQR 0 – 0.75), control group – 2 mg (IQR 1,5 – 3). *Sol. Trimeperidini hydrochloridum* 2 %: CWI group – 20 mg (IQR 0 – 40); control group – 80 mg (IQR 40 – 100). Complications: CWI group – 1 wound bleeding (local haemostasis), control group – 1 dehiscence and peritonitis (additional laparotomy). Side effects from the use of *Bupivacaine* have not been found. Patient mobilization: CWI group – 4 (IQR 3, 5 – 4,5); control group – 4 (IQR 3 – 5).

Conclusion. In our pilot study we observe the tendencies that the patients in CWI have less pain in the first 3 days after surgery, as well as, they get less common amount of opioids during the whole hospital stay. Only further research can demonstrate the efficiency of the CWI of local anaesthetics.

Acknowledgements. University of Latvia.

Poster presentations

Medicina (Kaunas) 2017;53(Supplement 2):1

BRAF V600 mutational status in melanoma Correlates with tumour histopathological characteristics

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Background. Melanoma is a fifth most common malignancy for men and sixth for women, and it may occur at any age. The incidence and mortality rates of melanoma increased during last years. Despite recent advancements in understanding of the mutational landscape of melanomas, there still exists a divide between the genetic and morphologic correlates.

Aim. The objective of the current study was to compare the BRAF mutational status with histopathological characteristics of melanoma.

Methods. Altogether, 35 patients undergoing melanoma surgical treatment at Riga East University Hospital in 2012-2014 were retrospectively enrolled to the study. The study was approved by the Central ethical committee. The histopathological characteristics were assessed according to the current WHO and AJCC 8. 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'-GGCCAAAATTTAATCAGTGA-3'.

Results. Thirty-five patients were enrolled in the study (10 patients were males and 25 were females). The mean age was 61 years (Min/Max 24– 83).

The BRAF mutation was observed in 15 patients (42.0%). BRAF exon 15 c.1799T>A V600E mutation was observed in 14 patients (40.0%) and BRAF exon 15 c.1801A>G V601E mutation was observed in one patient (2.0%).

Obtained results showed that BRAF mutation was observed predominantly in nodular melanoma (73.0%) compared to superficial spreading melanoma (24.0%).

83% of BRAF mutation cases was found on the trunk. The significant correlation between BRAF mutational status and Breslow thickness was observed ($Rho=+0.49$; $p=0.003$). In addition, BRAF mutational status correlated with T stage ($\chi^2=10.055$; $p=0.04$). However, the correlation between BRAF mutational status and Clark level, ulceration, lymphovascular invasion, mitotic count, peritumoral lymphocytic infiltration was not found.

Conclusion. Melanoma BRAF mutational status correlated with the tumour nodular type, high T stage and Breslow thickness. The BRAF mutation assessment for the potential personalized treatment should be based not only on clinical, but also on histopathological characteristics.

Endothelial microvesicles as biomarkers of oxidative stress

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Background. Endothelial injury is a crucial step in atherosclerosis and it is observed in acute myocardial infarction. Endothelial microvesicles were found to be potential biomarkers for acute myocardial infarction yet differences in their release in post myocardial infarction and association with oxidative stress largely was not studied.

Aim. The objective was to determine the differences in EMV numbers after myocardial infarction and their association with oxidative stress in comparison to healthy controls.

Methods. We included 15 myocardial infarction patients and 28 healthy controls. Blood plasma samples were tested using BD Fortessa cytometer (BD, San Jose). We examined two endothelial microvesicle populations: 1) CD144+, CD42a-, CD61- and 2) CD105+, CD42a-, CD61- and determined a percentage of EMV, expressing CD62e. Malondialdehyde concentration was determined by a Nexera X2 UHPLC system (Shimadzu, Japan).

Results. The overall median concentration of CD105 + endothelial microparticles was higher in the patient group (10.91 versus 33.68 microvesicles / μ l, $P = 0.006$). The median concentration of CD144 + microparticles was higher in the control group (487.7 versus 300.88 microvesicles / μ l, $P = 0.02$). CD62e levels were higher in patients with CD105 + population (14.8 versus 1.35%, $P < 0.001$). In the CD144 + population, the amount of this marker was higher in the control group (7.05 versus 1.8%, $P = 0.012$). The total amount of CD144 + microparticles correlated with the concentration of malondialdehyde (MDA) in the controls ($P = 0.03$, $R = 0.42$). CD62e expression in the CD105 + population was associated with MDA concentration in the control group ($P = 0.012$, $R = 0.466$).

Conclusion. In conclusion the present study shows amount changes of distinct EMV populations in post myocardial infarction period. Counts of circulating EMV populations and their CD62e expression were associated with oxidative stress.

Acknowledgements. This work was financed by PhD studies program of Vilnius University.

Hexose transporters in ostriches intestinal epithelium in the first postnatal week

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Background. Though carbohydrates are the main energy source of food the information about the localization of glucose transporters in different species is valuable. Until now there is few information about glucose transporters in birds intestinal epithelium in their first postnatal week.

Aim. The aim of the investigation was to carry out the immunohistochemical study of integral membrane proteins glucose transporter-2 and -5 (GLUT-2 and GLUT-5) that facilitate the transport of hexoses across epithelial cell layers on intestinal epithelial cells of ostriches chicken during their first postnatal week.

Methods. Material from duodenum and terminal part of ileum was collected from 9 ostrich's chicken (*Struthio camelus var. Domesticus*) divided into three age groups, three birds in each group: chicken immediately after hatching, 3 days old ostriches and 7 days old chicken. The material was fixed with 10% formalin, embedded into paraffin, slices 7µm thick were cut followed by immunohistochemical staining with polyclonal primary antibodies Rabbit anti-GLUT-2 and Rabbit anti-GLUT-5, carried out according to the manufacturers guidelines (IHC kit, Abcam, UK).

Results. The obtained results showed the immunohistochemical expression of GLUT-2 and -5 in the duodenal and ileal epithelial cells of ostriches in different age groups. In the groups of chicken after hatching and 3 days old ostriches in duodenal epithelium enterocytes were mostly unstained and goblet cells were mostly stained weakly for both antibodies. Weak staining of enterocytes and goblet cells was noted also in the ileal epithelium of the chicken after hatching. Some moderate staining of goblet cells was noted in the 3 days old chicken ileal epithelium. In 7 days old ostriches the expression of both antibodies was weak in duodenal, but moderate in ileal epithelial cells.

Conclusion. The revealed pattern of immunohistochemical expression of GLUT-2 and GLUT-5 in ostriches intestinal epithelial cells confirms the hypothesis that the gastrointestinal tract of ostriches immediately after hatching is not yet entirely capable of transportation of hexoses and the current study showed that the transportation is completing gradually during the first postnatal week.

Acknowledgements. The authors wish to thank Mrs. Mare Tamm for her laboratory assistance.

Involvement of KV7 and BKCa channels in GYY4137 and sodium hydrogen sulfide relaxation of rat mesenteric small arteries

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Background. Hydrogen sulphide (H₂S) is considered an important signaling molecule in the cardiovascular and nervous systems (Szabó, 2007), (Sun, Tang, DU, & Jin, 2011), (Wallace, Vaughan, Dickey, MacNaughton, & de Nucci, 2018) and a variety of pathophysiological changes including cancer, glycometabolic disorders, diabetes, and sepsis are associated with altered endogenous levels of H₂S (Kang, Neill, & Xian, 2017), (Yang et al., 2017). In the cardiovascular system endogenous H₂S can lead to both vasodilatation and vasoconstriction (Hedegaard, Gouliava, et al., 2016), (S. Li, Ping, Cao, Mi, & Cao, 2015), (Gheibi, Jeddi, Kashfi, & Ghasemi, 2018). Different types of K channels are involved in H₂S vasodilatation including ATP-sensitive K channels (KATP), voltage-gated K channels (KV7, KCNQ) and large conductance calcium-dependent potassium channels (BKCa) (Cacanyiova, Berenyiova, & Kristek, 2016).

Aim. The aim of the current study was to investigate the K channel subtypes involved in the relaxations.

Methods. Third branch mesenteric arteries were dissected from the mesenteric vascular bed, and mounted on 40-µm steel wires in microvascular myographs (Danish Myotechnology, Aarhus, Denmark) for isometric tension recording as previously described (Mulvany and Halpern, 1976). Data were presented as mean±S.E.M. with a significance level of p<0.05. The two-way analysis of variance (ANOVA) was used to compare the different conditions affecting release of sulfide species from GYY4137 and concentration-response curves obtained in functional studies of isolated mesenteric arteries. The graphs and statistical analyses were performed using GraphPad Prism 7.0 (GraphPad Software, La Jolla, CA).

Results. The preparations were incubated with a blocker of ATP-sensitive K channels, glibenclamide (1 µM), that decreased Na₂S relaxation, while GYY4137 relaxation was unaltered in U46619-contracted arteries (Fig. 6A, B). Blockers of BKCa, iberiotoxin and of KV7 channels, XE991 decreased significantly relaxations induced by both Na₂S and GYY4137 (Fig. 6C-F).

Conclusion. We have shown that Kv7 and BKCa channels are involved in the mechanism of Na₂S and GYY4137 induced vascular relaxation.

Acknowledgements. No conflict of interests to declare.

Loss of DNA mismatch repair proteins characterises Grade group 3–5 prostate carcinoma and did not correlate with serum PSA level

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Background. DNA mismatch repair (MMR) is integral to the maintenance of genetic stability. MMR can influence the regulation of tumour development in various cancers but their role on prostate cancer was controversial.

Aim of the study. The objective of the current study was to compare the expression of MSH2, MSH6, MLH1, and PMS2 by immunohistochemistry (IHC) in the tissue of patients with prostate cancer and benign hyperplasia.

Material and Methods. The study was retrospective. Altogether, 30 patients with prostate acinar adenocarcinoma and 10 patients with prostate benign hyperplasia were enrolled in the study. The patients underwent surgical treatment at Riga East University hospital at 2014. The MSH2, MSH6, MLH1, and PMS2 expression was analysed by immunohistochemistry. The Mann-Whitney U test was used to assess the differences between the groups. The p value < 0.05 was considered as statistical significant.

Results. Obtained results showed that MMR was absent in 10 patients (two patients with Grade group 3, five patients with Grade group 4 and three patients with Grade group 5).

6 cases showed IHC–Absent (IHC–A) in both MSH2 and MSH6, in 2 cases both MLH1 and PMS2 had negative staining, and just in two cases MSH6 was defective.

The loss of MSH2, MSH6, MLH1, and PMS2 was characteristics in high Grade cancer (Grade group 3, 4 and 5). In addition, the loss of MSH2, MSH6, MLH1, and PMS2 was not observed in patients with Grade group 1–2. The loss of MSH2, MSH6, MLH1, and PMS2 did not correlated with serum PSA level. MMR was present in all cases of benign prostate hyperplasia (mild to moderate staining).

Conclusions. Loss of mismatch repair proteins is characteristic in high grade prostate cancer (Grade group 3–5). The loss of MMR did not correlate with serum PSA level. The PD-1 inhibitors in prostate cancer personalized treatment seem to be beneficial in the Grade group 3–5 patients.

Acknowledgements. No conflicts of interest.

Quantification of immunohistochemical FANCM protein expression in prostate cancer stroma by using freeware image analysis programs

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Background. Increasing evidence suggests prostate adenocarcinoma (AC) is recruiting various cells from non-cancerous stroma, and by inducing their phenotypic transformations, forms a reactive tumor stroma, collectively termed as carcinoma-associated fibroblasts (CAFs). The regulatory importance of CAFs in AC progression has led to emerging of new stromal markers. The Fanconi anemia DNA repair pathway has received considerable attention after its proteins encoding gene alterations have been associated with cancer susceptibility.

Purpose. The study was designed to estimate the FANCM immunohistochemical expression in normal prostate and to compare the values with AC depending on the grade of differentiation. A reliable digital analyzing method for estimating stromal staining index (SSI) had to be worked out.

Material and Methods. The material comprised 50 radical prostatectomy specimen in which the patterns of AC were divided into 5 grade groups (GG) according to suggestions by the 2014 ISUP consensus. To identify site-specific expression of FANCM protein, the anti-human FANCM primary antibody (Novus biologicals, Abingdon, UK) diluted 1:2000, for 24 min at 37°C was applied in BenchMark Ultra automated stainer (Ventana, AZ, USA). All slides were scanned in digital slide scanner and for estimating FANCM stromal staining index (SSI) a reproducible method was worked out based on open-source freeware of Qu-Path and ImageJ.

Results. We detected strong diffusely positive FANCM staining of normal smooth muscle rich prostate stroma, mean SSI 39.82 (95% CI 38.53 - 41.12) and also in the walls of blood vessels. The stroma between cancerous glands appeared to be notably less positive compared to the normal control. Most significant decline of mean FANCM SSI was apparent already in the lowest GG1 (mean 17.97, 95% CI 16.82 - 19.13, $P < 0.0001$), and dropping continuously with each higher GG value (in GG2 mean 14.33, 95% CI 12.86 - 15.80, $P < 0.01$; in GG3 mean 11.87, 95% CI 11.32 - 12.41, $P < 0.01$; in GG4 mean 9.86, 95% CI 8.56 - 11.17, $P < 0.1$ and in GG5 mean 7.35, 95% CI 6.42 - 8.28, $P < 0.05$).

Conclusions. The reactive stroma of prostate AC shows grade-dependent decline of immunohistochemical FANCM expression compared to the normal control. This change is in accordance with the phenotypic shift from smooth muscle to CAF type cells in tumor stroma and could potentially serve as a stromal marker.

Acknowledgements/Funding. Georgi Džaparidze is supported by the “Higher education specialty scholarship in smart specialization growth areas” granted by SA Archimedes. The authors declare there are no conflicts of interest.

The interface between platelet membrane fatty acid composition, blood serum malondialdehyde and percentage of platelet-leukocyte aggregates formation in healthy men

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Background. Platelet membrane is extremely susceptible to peroxidation, providing a verity of lipid peroxides including malondialdehyde (MDA), which has been implicated in the ethiology of cardiovascular diseases. Moreover, platelet-leukocyte aggregates (PLAs) are known to contribute to advanced endothelial injury and atherogenesis.

Aim. To assess the relation between changes in the composition of the platelet phospholipid membrane fatty acids (FA), blood serum MDA concentration and PLAs formation.

Methods. FA methyl esters of platelet membrane of 79 apparently healthy men without any acute clinical condition at the time of the study were identified by GC/MS. MDA was measured by HPLC in blood serum, while PLAs were analyzed by whole blood flow cytometry. Individuals were divided into quartiles according to MDA concentration and percentage of PLAs formation. The composition of platelet membrane FA was compared to MDA concentration and percentage of PLAs formation of apparently healthy individuals.

Results. The total sum in percentage of saturated fatty acids was lower compared to the lowest and the highest levels of MDA concentration and percentage of platelet-monocyte aggregates (PMAs) formation (Median: 73.42 vs. 65.95, $p=0.607$; 77.45 vs. 73.04, $p=0.696$). Whereas the level of monounsaturated fatty acids (MUFAs) (14.54 vs. 16.99, $p=0.77$; 13.33 vs. 15.16, $p=0.942$) and polyunsaturated fatty acids (PUFAs) (9.80 vs. 13.09, $p=0.33$; 9.51 vs. 11.47, $p=0.633$) was higher.

Conclusion. MDA and formation of PMAs stimulate the incorporation of MUFAs, PUFAs in platelet phospholipid membrane, that may be a hallmark for increased level of biologically active compounds (eicosanoids/docosanoids), required for the future platelet activation.

Acknowledgements. The study was supported by the Research Council of Lithuania (Grant No. MIP-050/2015). The authors declare no conflict of interest.

Analysis of circulating tumor DNA in patients with locally advanced breast cancer

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Background. Despite the fact that breast tumors belong to visual localizations, neglected cases account for about a quarter of all cases of the disease. Meanwhile, an X-ray examination or tissue biopsy cannot always be reflective of the cancer dynamics or disease recurrence. Taking the above into consideration, the use of non-invasive analysis of circulating tumor DNA (ctDNA) can be an alternative method for cancer diagnostics and prognosis.

Aim. The aim of our research is to investigate and analyze the ctDNA count changes in patients with locally advanced breast cancer (BC) during different treatment stages.

Methods. The study includes 31 patients with a locally advanced form of breast cancer. The examination, which included a standard clinical, laboratory and X-ray examination, computer tomography (CT) was performed for all patients. All patients signed an informed consent to participate in research. The blood was taken via vein puncture directly into Vacutainer plastic blood collection tube with an anticoagulant, and the tube was centrifuged at room temperature. The plasma was pipetted into sterile test tubes per 1 ml each and labeled. All samples were placed in a -20 °C freezer. Blood samples have been taken according to the following schedule: during neoadjuvant chemotherapy, before and after surgery and during adjuvant chemotherapy. The analysis of ctDNA was performed using the QuantStudio 3D Digital PCR System.

Results. To date, quantitative detection of mutations in the PIK3CA and TP53 genes was performed for 9 patients and showed that 3 patients had PIK3CA mutation, 2 patients had TP53 mutation. PIK3CA or TP53 mutations were not detected in 4 patients. For patients with PIK3CA and TP53 mutations, was determined a decrease in ctDNA count during all cycles of neoadjuvant chemotherapy and the lowest concentration was observed prior to surgery. The results of ctDNA determination corresponded to the dynamics of the tumor process on CT scans. Further analysis of mutations will be performed for samples taken after surgery. We are expected to obtain the complete disappearance of ctDNA.

Conclusions. At this step, research results indicate the possibility of using ctDNA in monitoring of treatment he efficacy and confirm the correlation of ctDNA determination with CT scan data at the neo-adjuvant treatment stage.

Acknowledgements. This research has been performed with the financial support of grants of the Ministry of Education and Science of Ukraine No. 0118U003570 “The efficiency of “liquid biopsy” and tissue biopsy in the diagnosis and treatment of malignant tumors”.

Susceptibility of gram-negative rods to metallic nanoparticles

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Background. Nowadays nosocomial infections caused by multi-drug-resistant microorganisms have become the most urgent problem of public health. Gram-negative rods such as *E. coli*, *K. pneumoniae*, *P. vulgaris*, *P. aeruginosa* are major causes of hospital-acquired infections. Due to dramatic increase of antibiotic resistance among these pathogens the innovative approaches in the development of antimicrobial agents play crucial role in solving this problem.

Aim. In order to search new effective substance with antibacterial activity we have analyzed susceptibility of gram negative bacilli isolated from patients to silver and cooper nanoparticles alone as well as in their combination.

Methods. Cu and Ag nanoparticles were synthesized with use PVP. X-ray diffraction, transmission electron microscopy, UV-VIS spectroscopy and inductive-coupled plasma atomic spectrometry used for nanoparticle characterization. Clinical strains of *E. coli*, *K. pneumoniae*, *P. vulgaris*, *P. aeruginosa* were isolated from patient. In-vitro investigation of the antimicrobial agent's activity was performed by tube serial dilution method to determine the minimal inhibitory concentration.

Results. All species except *E. coli* that was less sensitive were inhibited with Ag NPs at concentration 25 µg/ml. Antibacterial activity of Cu NPs varied from 125 µg/ml against *E. coli* to 1000 µg/ml against *K. pneumoniae*, *P. aeruginosa* and *P. vulgaris*. In order to evaluate impact of ultrasound on the Ag NPs and Cu NPs antimicrobial efficiency we sonicated them before their use. It was found ultrasound treatment improves silver and copper nanoparticles antibacterial activity at least two times in all cases. Mixture of the Ag and Cu NPs led to sharp increasing of their antibacterial activity. Minimal inhibitory concentration of both components dropped more than 100 times for all types of microorganisms.

Conclusions. Silver and cooper nanoparticles possess antimicrobial activity against *E. coli*, *K. pneumoniae*, *P. vulgaris*, *P. aeruginosa*. Sonication and combination of nanoparticles improve their antimicrobial effectiveness.

Acknowledgements. This research supported by H2020 Marie Skłodowska-Curie Actions (NanoSurf 777926) and grants of the Ministry of Education and Science of Ukraine No. 0118U003577 "Antimicrobial effectiveness of nano-complexes (Chitosan-nanometals) against the multi-resistant clinical strains".

The effect of prostatic stones on the immunophenotype of prostate cancer cells

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Background. Prostate cancer (PGC) is leading the way in the structure of cancer morbidity around the world. The presence of prostatic concretions (PC) and skeletal metastases significantly reduces the patients' life quality and worsens the prognosis of the disease. However, the phenomenon of osteotropic tumor metastases is not sufficiently studied.

Aim. To define the impact of PC on the development of prostate cancer metastasis to the bones.

Methods. 10 samples of PGC with PC, 10 intact PGC specimens, and PGC metastasis tissue to lymph node were analysed. Histology (staining with hematoxylin-eosin), histochemistry (von Kossa reaction, alizarin red), immunohistochemistry (OSN, Col I, Col II, Bax, Casp3, MPO, CD68), SEM, EDS.

Results. All PC samples had the calcium hydroxyapatite origin with a slight deviation from the stoichiometric composition and admixture of extraneous elements. Assessment of apoptotic potential (Bax and Casp3) and inflammatory infiltration (MPO and CD68) revealed the significantly higher rates of these processes in PGC tissue with PC ($p < 0.01$). We suggest that the combined effect of these factors predetermines the development of a specific phenotype of cancer cells. This phenomena is manifested by the significantly higher OSN and Col I osteoblastic markers expression in PGC with PC and metastatic tissue ($p < 0.05$).

Conclusions. The determination of osteoblastic markers expression in PGC can be used as criterion for evaluation of probability of bone metastases development. The presence of PC in PGC tissue can be an important prognostic information for clinicians.

The presence of these pathological inclusions, namely the PC, promotes the expression of osteoblastic markers in PGC tissue, which helps the tumor cells to recognize a favorable microenvironment.

Acknowledgments. This research has been performed with the financial support of grants of the Ministry of Education and Science of Ukraine No. 0117U003937 "The development of tumor diagnosis method of reproductive system organs using cellular adhesion molecules of cancer-embryonic antigen" and No. 0118U003570 "The efficiency of "liquid biopsy" and tissue biopsy in the diagnosis and treatment of malignant tumors".

Apigenin extraction from fresh *Elsholtzia ciliata* herb

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Background. Polyphenols have gained a significant importance as bioactive compounds with substantial health benefits. The main properties of polyphenols are anti-diabetic, cardioprotective, anti-aging, neuroprotective, anti-inflammatory, antioxidative effects. The genus *Elsholtzia* from *Lamiaceae* family is rich in phenolic compounds. *Elsholtzia ciliata* is an annual aromatic plant used as a spice in cuisine and as a remedy in folk medicine.

Aim. The aim of this study was to increase the extraction efficiency of apigenin from *E. ciliata* fresh herb.

Methods. Extracts of fresh *E. ciliata* herb were produced using 96, 90 and 70% ethanol by ultrasound-assisted (UAE) (10 min, 25 °C), heat-reflux (HRE) (6 h, 95°C), continuous stirring (CSE) (24 h, 25 °C), percolation (PE) (48 h, 25 °C) and maceration (ME) (48 h, 25 °C) methods. HPLC analyses have been carried out using Waters 2695 chromatography system (Waters, Milford, CT), equipped with Waters 996 PDA detector. For analysis an ACE 5 C₁₈ 250 x 4.6 mm (Waters, Milford, USA) column was used. The mobile phase consisted of solvent A (phosphoric acid/acetonitrile/water) (1:19:80 V/V/V) and solvent B (phosphoric acid/methanol/acetonitrile) (1:40:59 V/V/V). The linear gradient elution profile was as follows: 100 % A – at 0 min, 55 % A/45% B – at 20 min, 100 % B at 25 – to 26 min, 100 % A – at 30 – to 31 min. The flow rate was 1.2 mL/min and injection volume was 10 µL. Absorption was measured at 330 nm. Quantification of apigenin was performed using reference standard of apigenin. The linear calibration curve were constructed (R² = 0.999979).

Results. The lowest content of apigenin was obtained by ME and PE using 96% ethanol (141.06±1.7 and 161.51±1.43 µg/g, respectively). The highest content of apigenin (855.54±5.75 µg/g) was obtained by UAE, using 70% ethanol. During CSE, the content of apigenin depended on the solvent concentration used: 96 % ethanol was more effective compare with 90 and 70% ethanol (532.88±7.66, 194.39±5.84 and 272.06±63.23 µg/g, respectively).

Table 1. Content of apigenin in *E. ciliata* extracts obtained by different extraction methods.

Extraction methods	Ethanol concentration, %	Apigenin, µg/g
Ultrasound-assisted	96	490.95±5.81 ^{bedf}
	90	538±8.92 ^{bedf}
	70	855.54±5.75 ^{bedf}
Heat-reflux	96	380.04±4.59 ^{acdf}
	90	310.34±0.98 ^{acdf}
	70	528.07±28.65 ^{acdf}
Continuous stirring	96	532.88±7.66 ^{abdf}
	90	194.39±5.84 ^{abdf}
	70	272.06±63.23 ^{ab}
Maceration	96	141.06±1.7 ^{abcf}
	90	218.50±0.86 ^{abcf}
	70	227.38±1.09 ^{ab}
Percolation	96	161.51±1.43 ^{abcd}
	90	243.42±1.71 ^{abcd}
	70	225.07±0.95 ^{ab}

^ap<0.05 vs ultrasound-assisted, ^bp<0.05 vs heat-reflux, ^cp<0.05 vs continuous stirring, ^dp<0.05 vs maceration, ^fp<0.05 vs percolation.

Conclusion. The highest content of apigenin was obtained using UAE method and 70% ethanol.

Acknowledgements. The authors are thankful for financial support provided by Science Foundation of Lithuanian University of Health Sciences.

Efficacy of storing of isolated porcine kidneys with *Biolasol* solution modified with the addition of prolactin

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Background. *Biolasol* is a newly developed fluid for perfusion and preservation of organs intended for transplantation. It allows the storage of the heart, liver, pancreas and kidneys by using a method of simple hypothermia. A number of our research indicates its high effectiveness in maintaining the structural and functional integrity of the graft prior to its transplantation. We confirmed that the modification of the liquid with the addition of vitamin C (0.5 mmol/l) and prolactin (1 µg/l) determines the stability of kidney cell membranes.

Aim. The aim of the current study was to analyze the effectiveness of *Biolasol* fluid modified with the addition of vitamin C and prolactin at various concentrations. The effectiveness of the obtained fluids in the protection of isolated porcine kidney nephrons was evaluated based on analysis of biochemical parameters.

Methods. In the studies *Biolasol* fluid (FZNP “Biocheffa”, Poland) modified with the addition of ascorbic acid (0.5 mmol/l) as well as porcine prolactin in concentrations of 1 µg/l, 10 µg/l and 100 µg/l was used. Thirty kidneys from adult Great White Poland pigs were used for the study. After collection, the kidneys were cannulated and stored in parallel in solutions: *Biolasol*+vitamin C+1 µg/l PRL, *Biolasol*+vitamin C+10 µg/l PRL, *Biolasol*+vitamin C+100 µg/l PRL at 4°C for 2 hours. The kidneys were then rinsed and the perfusate samples were collected from the kidney vein at 0 and 30 minutes of perfusion. After 30 minutes, the kidneys were cooled and placed in a sterile bag filled with 500 ml of appropriate preservative fluid for 48 hours. After this time, activities related to renal perfusion were repeated. The activity of the released indicator enzymes: AST (aspartate aminotransferase), ALT (alanine aminotransferase), LDH (lactate dehydrogenase) was determined in the perfusate samples.

Results. The obtained results suggest that *Biolasol* modified with the addition of vitamin C (0.5 mmol/l) and prolactin at various concentrations, i.e. 1 µg/l, 10 µg/l and 100 µg/l, determines the integrity and stability of cell membranes. After 48 hours of storage, the lowest ALT and AST activity was observed in *Biolasol*+vitamin C+100 µg/l PRL fluid perfusates, while the lowest LDH activity was found in *Biolasol*+vitamin C+1 µg/l fluid perfusates.

Conclusion. The addition of prolactin to *Biolasol* fluid affects the maintenance of the normal cytoskeleton of the stored graft, and thus the proper functioning of the organ after transplantation.

Acknowledgements. The study was supported by the SUM statutory agreement No. KNW-1-118/N/8/O.

***In vitro* antimicrobial activity of *Tuttha Bhasma* in comparison with Gentamicin and Amphotericin B**

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Background. The three great treatise of Ayurveda like *Caraka Samhita*, *Sushruta Samhita* and *Ash-tanga Hridaya* describe *Tuttha* (Copper Sulphate/Blue Vitriol), an alchemical mineral for various disorders including *kushta*, *svitra*, *vicarcika* (various skin ailments). Such a time tested, potent and low cost drug requires wider application for its anti-microbial effect either as an individual medicament or as adjuvant therapy through proper scientific validation.

Aim. The aim of this study was to evaluate antimicrobial activity of *Tuttha bhasma* on two gram-positive (S.aureus; B. subtilis); two gram-negative; (S.typhi; E.coli) and two fungi (C. albicans; T. rubrum) in comparison with Gentamicin and Amphotericin B.

Methods. The anti-microbial (antibacterial and antifungal) activity of traditionally prepared *Tuttha bhasma*, converted to solution (1mg/1ml; vortexed in distilled water) at the concentration of 1mg, 5mg, 10mg and 20mg/microliter was carried out. It was determined through Minimum Inhibitory Concentration (MIC) by Broth dilution method (Andrews JM, 2001). The experiment was carried out at T- Stanes and company Limited (DSIR approved, ISO certified R & D centre), Coimbatore.

Results. In 20 mg concentration, the antibacterial activity of *Tuttha bhasma* was equivalent to the inhibition shown by 1 mg of Gentamicin and a better antibacterial result against *Staphylococcus aureus* compared to other organisms.

Conclusion. Present experiment shows that *Tuttha bhasma* has potential anti-microbial with better antifungal activity compared to antibacterial effect. Further evaluation on various microorganisms is necessary before clinical trials.

Acknowledgements. The authors wish to thank Dr.K.Latha, Project Director, T-Stanes and company Limited, Coimbatore for her invaluable guidance in this antimicrobial study.

Pharmaceutical availability of liposomal vitamin C incorporated into hydrogel formulations for topical application

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Background. Specific structure of liposomes, which are spherical vesicles consisted of an outer phospholipid bilayer and aqueous phase inside enables to encapsulate various active substances, both hydrophobic and hydrophilic. Liposomes are suggested to be non-toxic and have potential to cross *stratum corneum* which is poorly permeable to many substances applied to the skin. L-ascorbic acid (vitamin C) was a model substance in this study due to its crucial role in number of biologically important pathways as well as its beneficial effects on the skin e.g. role in collagen synthesis or protection against UV rays.

Aim. The aim of the current study was to obtain liposomes containing vitamin C using a method of dry lipid film hydration, suspend them into two types of hydrogel bases and analysis of pharmaceutical availability of such formulations.

Methods. Azolectin, a dry soybean extract containing lecithin, cephalin and phosphatidyl inositol was dissolved in chloroform with its subsequent evaporation and obtained dry lipid film was then hydrated with 20% vitamin C solution. Prepared liposomes were subsequently suspended in two types of hydrogel bases: glycerol ointment and hypromellose gel (10%HPMC). The size of liposomes was measured with optical microscope. Rheological properties of the obtained formulations were performed in a reometer while spreadability - using an extensometer. The pharmaceutical availability was analysed with extraction cells in the paddle apparatus through the dialysis membrane Spectra/Por 2. Statistical analyses were made using Statistica 12.0 software.

Results. Statistical differences in size and surface area between liposomes with vitamin C suspended in glycerol ointment and those suspended in 10%HPMC gel were observed. The formulation containing liposomes with vitamin C suspended in 10%HPMC was characterized by higher viscosity as well as spreadability than glycerol ointment. The analysis of pharmaceutical availability shows that 82.7% and 89.9% of vitamin C released from glycerol ointment and 10%HPMC gel, respectively after 6 hours of test. The results for liposomal vitamin C incorporated into glycerol ointment were found to be significantly lower compared to the amount of vitamin C released from reference formulation (95.75%).

Conclusion. Using liposomes as a carrier of vitamin C may slow significantly its release and in turn it may prolong action of vitamin C in the deeper layers of the skin. Selection of hydrogel type may also influence the pharmaceutical availability of liposomal vitamin C.

Acknowledgements. The study was funded by Medical University of Silesia in Katowice within the project KNW-1-019/N/7/O.

Mast cells–nerve interactions in gut mucosa

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Background. Over the last decades numerous efforts were undertaken to study the neuroimmune interactions in the gut. It appears that endings of extrinsic afferent nerves as well as enteric neurons are in close proximity to mast cells (MCs). Further investigations of MCs – nerve interactions are needed to provide greater understanding of how immune and nervous systems coordinate multiple aspects of homeostatic control.

Aim. The aim of this study was to examine the distribution of MCs in the gut mucosa and to estimate connections of these cells with enteric nervous system.

Material and Methods. We examined 10 duodenal bioptic specimens and material from 7 appendices from the archives of the Pathology Department, Children's Clinical University Hospital. Patients included in the study had no history of previous malignancies, the lamina propria presented mild to moderate inflammatory infiltrate, made essentially up of lymphocytes and plasma cells. Tissue sections were stained for S100 protein, calretinin, and alpha-smooth muscle actin (alpha-SMA) using immunohistochemistry. Duodenum samples were also submitted to Giemsa and HE staining.

Results. Nerve strands from the submucosal plexus penetrate the muscularis mucosae, forming the muscularis mucosae plexus. Some nerve fibers pass through the muscularis mucosae and form the mucosal nerve plexus just beneath the crypts and between the basal portion of the crypts in the close vicinity of the α -SMA – positive pericryptal fibroblast sheath. Nerve fibers, which were located in the lamina propria, stained positive for S100 and calretinin. S100-positive Schwann cells, covering the nerve fibers, were also observed. The apparent nerve density and sprouting was greater in the mucosa of the appendix than in the small bowel. Varicose enteric nerve fibers course through the lamina propria in association with the vessels and were closely apposed to calretinin-positive MCs. In the duodenum and appendix MCs density is highest in the lamina propria mucosae. An estimated 67% of intestinal mucosal MCs are in direct contact with nerves, and another 33% are within 2–5 μ m.

Conclusions. Considering a dense sensory innervation of the duodenal mucosa and mucosa of the appendix, the preferential accumulation of MCs in this area may be due to the secretion of powerful chemoattractants for MCs by Schwann cells of unmyelinated sensory fibers and by the myofibroblasts of the pericryptal fibroblast sheath. The intimate structural relationships have been found between intestinal MCs and nerve fibers, indicating that enteric nervous system and MCs may regulate one another via paracrine signaling.

Computational assessment of candidate SNP markers of proteasomal genes for multiple sclerosis association studies in Latvian population.

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Background. Case-control studies investigating associations between single nucleotide polymorphisms (SNPs) and disease (and the efficacy of certain treatments) can be useful in diagnostics for multifactorial diseases such as multiple sclerosis (MS). However, the costs in time and materials that these studies incur mean that ensuring a high likelihood of a given candidate SNP's involvement in disease is imperative.

Aim. The aim of this study is to utilize several computational and statistical methods for the effective assessment of several proteasomal gene SNPs as candidate markers for future genotyping in the Latvian population to discover medically relevant associations with MS.

Methods. Literature and sequence data were analyzed on five SNPs of proteasomal genes: PSMB8 (rs2071543, rs9357155), PSMB9 (rs17587), PSMD9 (rs74421874, rs3825172) and an intergenic SNP (rs9275596). The sequences 50 bp upstream and downstream of these SNPs were extracted and analyzed with software for SNP-dependent DNA and RNA (for SNPs in exons) secondary structure changes, alterations in DNA bending and alternate transcription binding sites.

Results. All SNPs have previously registered associations or linkage with autoimmunity, including MS, in different populations. Additionally, both the available literature and allele frequency data indicate that rs74421874 and rs3825172 exist in complete linkage disequilibrium in all populations studied thus far. The majority of SNPs studied demonstrated allele-dependent alternative simulated secondary structures. Differential structures of DNA were found for rs9357155, rs17587, rs74421874, and rs3825172, and of RNA for rs2071543 and rs17587. Marked differences in simulated DNA curvature and bendability depending on allele were observed for rs9275596, rs9357155, rs74421874, and rs3825172. The alternative alleles for each SNP also disrupted as well as created a number of potential transcription factor binding sites for each SNP, including ones potentially relevant for chromatin architecture, lymphocyte differentiation, transcriptional repression, and other functions.

Conclusion. A review of the literature on SNPs of the chosen SNPs of proteasomal genes PSMB8, PSMB9, and PSMD9 illustrate their potential utility as markers for multiple sclerosis due to existing associations or linkage with autoimmune disorders (including multiple sclerosis itself in the case of rs17587). Our computational analyses also highlight that the chosen SNPs may be functionally relevant in their corresponding genes through modulating the binding of transcription factors via structural and sequence changes.

Acknowledgements. ERAF SAM Nr. 1.1.1.1/16/A/016 project "Determination of proteasome-related genetic, epigenetic and clinical markers for multiple sclerosis"; UL research project "The study of biomarkers and natural compounds for the diagnosis and personalized treatment of acute and chronic disease".

Comparison of *VHL* gene mutational status in clear cell renal cell carcinoma primary cell cultures

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Background. Clear cell renal cell carcinoma (ccRCC) accounts for roughly 70% of renal carcinoma cases. ccRCC is characterized by resistance to traditional chemotherapy and radiation and poor overall prognosis. ccRCC cell lines are extensively used as model systems in development of therapeutics, however generation of primary patient-derived cell cultures overcomes the limitations of commercial cell lines (Lobo et al., 2016).

Inactivation of the von Hippel-Lindau (*VHL*) tumor suppressor protein either through mutation, deletion or promoter methylation occurs in up to 92% of sporadic ccRCC cases. *VHL* loss activates hypoxia-inducible factor target genes including carbonic anhydrase 9 (CA9), which is a highly expressed hypoxia marker in various cancers (Harlander et al., 2017).

Aim. The aim of this study was to determine *VHL* gene mutation status in primary ccRCC and patient-matched normal kidney epithelial cell cultures.

Materials and methods. Patient matched tumor and adjacent normal kidney tissue samples were obtained from Pauls Stradiņš Clinical University Hospital according to the local ethics committee guidelines. Tissue samples were dissociated and cells were propagated in adherent cultures. After first passage positive selection for CA9⁺ tumor cells was performed. CA9 protein expression was analyzed in two cell cultures (CA9 positively selected tumor and normal) in fourth passage using flow cytometry. DNA from CA9 positively selected tumor and normal cell cultures in fifth passage was extracted and PCR for three *VHL* exons was performed. PCR products were sequenced by Sanger sequencing, mutations were identified using 4Peaks software.

Results. Missense single nucleotide polymorphism rs35460768 was detected in *VHL* exon one. Wild-type and mutant allelic variants were observed in both CA9 positively selected and normal cell cultures, indicating either a mixed cell population or a germline *VHL* mutation.

Conclusions. Detected mutational status of *VHL* in CA9 selected tumor and normal kidney tissue cells is inconclusive, therefore transcriptional profiling would be necessary and *VHL* loss due to epigenetic silencing should be investigated for further use of the established cultures.

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.

Bacteria and yeast differentiating analysis using spectrophotometry

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Background. Examining microorganism adhesion and what factors affect it would help us to understand the pathogenesis of microorganisms better. Several studies suggest that silica or silicon dioxide is a favourable surface for microorganism adhesion and it can be used to study the attracting forces between microorganisms and inorganic surfaces.

Aim. The aim was to determine if spectrophotometry can be used to distinguish bacteria from yeast.

Methods. The study was conducted by preparing 4 McFarland unit suspensions of 13 reference cultures of bacteria and 4 pure cultures of yeast with and without silicon dioxide. The suspensions were analysed using a spectrophotometer. The *absorbance* was measured at a wavelength of 285–700 nm and 285–1100 nm. After that the measured *absorbance* of each bacteria was compared to each yeast using t-test: Two-Sample assuming unequal variances.

Results. The results show that in most comparisons it is possible to distinguish bacteria from yeast. A longer interval favoured distinguishing bacteria from yeast. Visually comparing the graphs *absorbance* for bacteria increased at a higher rate than that of yeast. And at some point the light *absorbance* units of bacteria surpassed the light *absorbance* units of yeast. At about 305 nm all microorganisms had a drastic spike in the increase of light absorption. It was more noticeable for bacteria than it was for yeast. These criteria could be used to distinguish bacteria from yeast.

Table 1. Summary of all comparisons.

Compared types of cultures	Comparisons without silicon dioxide at 285–1100 nm	Comparisons with silicon dioxide at 285–1100 nm	Comparisons without silicon dioxide at 285–700 nm	Comparisons with silicon dioxide at 285–700 nm
Yeast compared to bacteria	52/52 (100%)	52/52 (100%)	44/52 (84.6%)	44/52 (84.6%)

Conclusion. Spectrophotometry can be used to distinguish bacteria from yeast. Silicon dioxide increases the *absorbance* of bacteria at infrared wavelengths and decrease the *absorbance* of yeast at all measured wavelengths.

Acknowledgements. Dr.habil.biol., prof. Nikolajs Sjakste for the assistance with technical advices.

Changes in eye axial length one year after laser correction surgery

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Background. With the development of modern technologies, laser vision correction as a method of ametropia correction is becoming more popular, simpler, more stable and more accessible to people. Patients are increasingly opting for laser vision correction to get rid of glasses and contact lenses. The most frequently asked question from patients is whether vision will deteriorate after a laser correction surgery. The reason for myopia progression is the prolongation of the anterior-posterior axis of the eye and, according to most researchers, refraction errors are most often caused by the axial length mismatch of the eye's optical system.

Aim. The aim of the current study was to examine if the eye axial length increases after laser correction in case of myopia.

Methods. The study was based on an analysis of patients' medical records from the database of Dr. Solomatin's Eye Rehabilitation and Vision Correction Centre. It was analysed 46 patients (92 eyes); of those 35 were females and 11 - males. All the selected patients had myopia. Eye axial length was measured by IOLMaster (TM Carl Zeiss-Meditec, Jena, Germany) before and one year after operation. Subjects were selected in several groups to compare eye axial changes: sex, degree of myopia, age, method of laser surgery. Also the data were compared to control group with subjects who had no eye surgery.

Results. The length of the anterior-posterior axis was either increased or unchanged in all patients, but the results of the study did not show a statistically significant prolongation of the anterior-posterior axis of the eye for either the group of patients after laser correction or the control group comparing the measurements after one year.

Conclusion. Myopia progression and vision deterioration following laser vision correction are not related to anterior-posterior axial length increasing.

Acknowledgements. No potential conflict of interest relevant to this article was reported.

Detection of vancomycin resistance in enterococcus species isolated from clinical samples; phenotypic vs genotypic identification

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Background. Vancomycin resistant *Enterococcus* (VRE) is a cause of hospital outbreaks worldwide, which have been dramatically increased in recent years. VRE became an important nosocomial pathogen because of its rapid spread, high mortality rates associated with infections, limited options for treatment, and the risk of vancomycin resistance genes transfer to other more virulent and more prevalent pathogens such as *Staphylococcus aureus*. Thus, rapid detection of VRE strains could be of highest importance for the treatment and prevention of the associated disease.

Aim. The aim of this study was to identify *Enterococcus spp.* up to species level and to find out the correlation between the presence of vancomycin-resistance genes (*vanA*, *vanB* and *vanC1/C2*) and their expression as detected by phenotypic tests in clinical isolates.

Methods. In this study 46 isolates were identified by phenotypic identification system *Crystal*TM. The antibacterial susceptibility testing was carried out according to the Kirby-Bauer disc diffusion method. DNA strip assay (*Geno Type*TM *Enterococcus*, Hain Lifescience GmbH) was used for the simultaneous identification of enterococcal species and for detection of vancomycin resistance genes: *vanA*, *vanB*, *vanC1* and *C2/3*.

Results. Of the tested 45 enterococci isolates 25 *E. faecalis* and 16 *E. faecium* were identified without any difference by the both phenotypic and genotypic methods. Three isolates were identified as *E. faecium* by molecular method, while were identified by phenotypic method as *E. casseliflavus/gallinarum* were using BBL *Crystal*TM. All the phenotypically identified *E. casseliflavus/gallinarum* isolates showed susceptibility to vancomycin which is an indicator for inaccurate species identification.

An overall prevalence of vancomycin resistant *Enterococcus* (VRE) in the clinical samples was about 15.5%. The results showed the presence of *vanA* gene in *Enterococcus faecalis* as well as in four of *E. faecium* isolates; *vanB* and *vanC2/C3* genes were detected in two *Enterococcus casseliflavus* isolates.

Conclusion. The results shows that incorrect identification by phenotypic methods can lead to wrong diagnosis when antibiotic susceptibility testing mismatch with species identified. In these cases a molecular methods have to be applied, to increase the chance to identify enterococci species correctly and to interpret results of antibiotic susceptibility testing accordingly. *Geno Type*TM *Enterococcus* method appears to be a useful and convenient method for rapid detection and for discrimination of vancomycin-resistant *Enterococcus spp.* genotypes in the clinical laboratory.

Evaluation of dna damage in whole blood and peripheral mononuclear cells of multiple sclerosis patients

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Background. According to different studies, oxidative stress is involved in pathogenesis of neurodegenerative diseases. Reactive oxygen species can cause demyelination and axonal damage due to the oxidation of vital cellular constituents, in particular DNA. Oxidative stress may also cause an overexpression of nitric oxide (NO), however it has not been measured directly in MS patients before.

Aim. The aim of this study is to evaluate single-stranded DNA damage in whole blood and isolated peripheral blood mononuclear cells (PBMNC) and measure nitric oxide (NO) levels of multiple sclerosis patients.

Methods. DNA damage was evaluated using the single-cell gel electrophoresis (comet assay) method. Whole blood and PBMNC of 28 MS patients and 15 healthy subjects were tested. A. The results were analyzed statistically to determine the correlation between DNA breaks in both groups. 22 MS patients and 22 healthy subjects were enrolled for the NO measurements with the EPR spectroscopy.

Results and Conclusion. MS patients tend to have an increased level of DNA damage both in whole blood and PBMNC samples. MS patients also have an increased level of NO in their blood. Both studies have reached a statistically significant difference between MS groups and control groups.

Acknowledgements/funding. This work was supported by European Regional Development Fund project 1.1.1.1/16/A/016.

Expression of CA9 biomarker in patient derived clear cell renal carcinoma cells

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Background. Most common renal cell carcinoma (RCC) is clear cell renal carcinoma (ccRCC), which is 70% of all RCCs (Nickerson, et al., 2008). CcRCC and also other RCC subtypes are very hypervascular, process that is mediated by VEGF (Vascular endothelial growth factor) and its receptor expression on the cell. High VEGF expression is associated with HIF (Hypoxia inducible factors). Negative regulation of HIF is managed by von Hippel-Lindau protein (pVHL). If *VHL* is mutated, HIF levels raise and hypoxia like effects will occur. Up to 91% of ccRCC cases have genetic or epigenetic alteration of *VHL* (Nickerson et al., 2008). HIF accumulation causes activation of HIF target genes one of them being carbonic anhydrase 9 (CA9), which is upregulated in *VHL*-mutant cells.

Aim. The aim of current study was to evaluate CA9 biomarker expression in primary cells derived from patients with ccRCC.

Methods. Surgeries were performed at Pauls Stradiņš Clinical University Hospital. The study was conducted in accordance with the guidelines of the hospital ethics committee. Tissue samples were dissociated using collagenase. Patient derived cells were sorted using streptavidin beads and biotinylated anti-CA9 antibodies (RnD Systems). Cells were cultivated in IMDM with 10% FBS. CA9 expression was tested on Amnis ImageStreamxMarkII imaging flow cytometer using anti-CA9-APC antibody (RnD Systems). Anti-IgG2A-APC (RnD Systems) was used as isotype control. Data was analyzed with IDEAS 6.2 software.

Results. Seven renal cell carcinoma tissue samples and adjacent noncancerous tissue samples were acquired from patients undergoing renal surgery. Histology results revealed, that RCC04, RCC03, RCC07 are ccRCC, the rest of the samples being from different kidney cancer subtypes. After sorting RCC04, RCC03, RCC07 cells into CA9⁻ and CA9⁺ populations, they were seeded for initial cell cultivation. RCC07 proved to be faster growing cell line. Flow cytometry results showed that RCC07 primary cells don't express CA9 marker.

Conclusions. We have isolated and propagated three patient-derived renal carcinoma and normal tissue cells. Primary renal carcinoma cells do not express CA9 biomarker after 4th passage. *VHL* mutation sequencing analysis should be performed to confirm that ccRCC case is caused by *VHL* mutation. In the future, patient derived primary cell lines could be used in renal cell carcinoma research.

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.

Human eye axial length changes depending on induced short term defocus

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Background. Average eyeball length is about 24–25 millimetres [1] and it is generally assumed that axial length (AL) remains constant in adults [2]. But it is now generally accepted that the quality of the retinal image can influence axial eye growth. Australian researchers from the Contact Lens and Visual Optics Laboratory, School of Optometry, Queensland University of Technology demonstrated that axial length reduces after exposure to myopic defocus and axial length elongates after hyperopic defocus [3].

Aim. The aim of the current study was to investigate if human eye axial length (the distance between anterior cornea to retinal pigment epithelium) changes depending on induced short term monocular defocus (+3D; -3D; diffuse).

Methods. Twenty-five young adults took part in this project. Mean age 25±3,4 range 19–34 years, 16 women, 9 men. All participants had not any ocular or systemic disease and had no history of ocular surgery or trauma. Everyone were tested with three different monocular defocus for thirty minutes and one hour, each on a different day: diffuse, myopic (+3D defocus), hypermetropic (-3D defocus). Before defocus everyone were tested with auto-refractometer and ZEISS IOLMaster optical biometry where we measured eye axial length, lens thickness and anterior chamber depth.

Results. Using paired-t test AL at baseline and AL after one hour of short term monocular defocus caused small and not significant changes. Mean value of hypermetropic (-3D) defocus before and after one hour did not show any statistically significant difference in the axial length (SD=0,015; p=0,603). Mean value of diffuse defocus before and after one hour also did not show any statistically significant difference in the axial length (SD=0,127; p=0,353). Mean value of myopic (+3D) defocus before and after one hour showed statistically significant difference in the axial length (SD=0,117; p=0,000).

Conclusion. We have found statistically significant axial length changes using myopic defocus (+3D). Decreased axial length tends to partly compensate induced defocus. We observed that anatomical structures of the eye can be influenced by solely optical manipulations and that shows significant role of using appropriate optical correction method on daily basis.

Acknowledgements. This research was not financed by any company. We got practical support of Dr. Solomatin Eye Rehabilitation and Vision Correction Centre by using their equipment.

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Macular pigment optical density in school-age children

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Background. Macular pigment carotenoids lutein, zeaxanthin and meso-zeaxanthin protect the retina from oxidative stress and high-intensity blue light. These carotenoids have a dietary origin and are accumulated not only in the retina but also are stored in fat. The previous studies in adults show that there is an inverse relationship between body mass index (BMI) and macular pigment optical density (MPOD) (Hammond *et al.*, 2002; Nolan *et al.*, 2004). A little attention has been paid to paediatric population and MPOD studies and no effect of BMI on MPOD in children has been found (Zheng *et al.*, 2013).

Aim. The aim of the study was to determine macular pigment optical density in school-age children at Marupes elementary school and its relationship with body mass index and other factors such as eye iris colour and gender.

Methods. A total of 62 children from Marupes elementary school were enrolled in this study. MPOD was measured in both eyes by Macular Pigment Screener (MPSII), which is based on the method of heterochromatic flicker photometry. Children height and weight were used to calculate BMI.

Results. The pilot study results consisted of 20 children (range 7–14 years). The mean MPOD in examined children was 0.34 ± 0.15 d.u. We found no difference between both eye results (one-way ANOVA, $F=0.09$, $p=0.76$) and no effect of ocular dominance on MPOD (one-way ANOVA, $F=3.01$, $p=0.09$). There was also no significant difference between male 0.33 ± 0.19 d.u. ($n=9$) and female 0.35 ± 0.13 d.u. ($n=11$) MPOD values and there was also no effect of blue, green and brown iris colour on MPOD values. The inverse relationship between BMI and MPOD was not found, because most of the children had normal or reduced BMI and more data with higher BMI required to compare these factors.

Conclusion. This is the first study in Latvia that provides MPOD values for healthy children which can be later used as a reference point for other studies. In our study, the mean MPOD is lower than in previous studies and obtained data don't show the association between MPOD and BMI, iris colour, ocular dominance or gender. The study sample is too small, and we will continue study to get more valid data, to confirm our conclusions and to suggest MPSII as the good screening method for young children.

Acknowledgements. This research was funded by project of University of Latvia, UL Foundation, and SIA "Mikrotikls".

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One-year results of corneal collagen crosslinking for progressive keratoconus: visual acuity and keratometry changes

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Background. Keratoconus is a disorder of the eye, when cornea becomes thinner and deforms causing blurry and double vision. To stop progression of disease, corneal collagen crosslinking has been used.

Aim. The aim of the current study was to evaluate changes in keratometry (K1, K2, Kmax values) during one year after corneal collagen crosslinking (CXL) in patients with keratoconus and analyse associations of these changes with visual acuity.

Methods. For this retrospective study we investigated 49 eyes of 42 patients (41 males and 8 females, average age 29.9 ± 8.8 years) with progressive keratoconus (stage I, II, III and IV), which were treated with corneal crosslinking (Dresden protocol). Keratometry (Kmax, K1, K2) were examined by corneal topographer Oculus Pentacam before and during a 12 months follow-up after crosslinking. Uncorrected (UCVA) and best corrected (BCVA) visual acuity, and cornea keratometry were analysed.

Results. A significant change in corneal readings was observed 1 year after crosslinking ($p < 0.001$): Kmax decreased from 52.06 ± 21.29 D till 50.33 ± 20.70 D, K1 from 33.30 ± 22.92 D till 32.24 ± 22.18 D, and K2 from 41.48 ± 21.33 D till 40.41 ± 20.77 D. A significant improvement in UCVA and BCVA were noticed 1 year after CXL: 51% participants had UCVA improvement more than 2 logMAR lines and 39% participants had BCVA improvement more than 2 logMAR lines, ($p < 0.001$). The greatest changes in UCVA were observed in participants with keratoconus stage I, III and III-IV ($p < 0.05$), biggest improvement in BCVA were noticed in participants with keratoconus stage III and III-IV ($p < 0.01$).

Conclusion. Corneal crosslinking induces a reduction in corneal volume, which improves uncorrected and best corrected visual acuity.

Acknowledgements. No potential conflict of interest relevant to this article was reported.

Presence of human parvoviruses among blood donors in Latvia

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Background. Human parvovirus B19 (B19V), human bocaviruses (HBoVs) and human parvovirus 4 (hPARV4) are members of *Parvoviridae* family, which are infrequently detected in adults and there are conflicting results regarding the presence of these viruses in the blood products.

Aim. The aim of this study was to estimate the presence of B19V, HBoVs and hPARV4 infection markers in apparently healthy blood donors in Latvia.

Methods. The inclusion criteria were apparently healthy blood donors without common bloodborne pathogens including hepatitis B and C viruses, human immunodeficiency virus and human T-lymphotropic virus. IgG class antibodies against HBoV1-4 and hPARV4 antigens in all donors' cell-free blood plasma samples were measured using indirect enzyme immunoassay format using yeast-generated HBoV1-4 and hPARV4 VP2 virus-like particles. *recomWell* Parvovirus B19 IgG test kit (Microgen GmbH, Neuried, Germany) was used to test blood donors' plasma samples for antibodies against B19V. To determine the presence of HBoVs, B19V and hPARV4 genomic sequences in peripheral blood and cell free blood plasma DNA samples of blood donors (n=50) nPCRs targeting hPARV4 VP2, B19V NS1, HBoV1 NS1 and HBoV1-4 VP1/2 protein genes were used.

Results. Parvovirus-specific IgG class antibodies were detected as follows - HBoV1-4 in 58%, hPARV4 in 10% and B19V in 74% of donors' plasma samples. In 8% of donors' plasma samples none of the parvovirus-specific IgG class antibodies were detected. In total HBoVs DNA was found in 28% of blood donors, from which HBoV1 was detected in 14%, B19V - in 6%, but hPARV4 genomic sequence was not detected in any of the blood donors' DNA samples. Active parvovirus infection, defined as the presence of viral genomic sequences in cell-free blood plasma DNA, was found in 3 out of 50 (6%) donors - HBoV1 genomic sequence in 2 (4%) and B19V in 1 (2%) blood donor.

Conclusion. This is the first study showing the presence of HBoVs and hPARV4 infection markers (viral DNA and/or specific IgG class antibodies) in peripheral blood samples from blood donors in Latvia. The presence of B19V DNA and specific IgG class antibodies among blood donors is also confirmed. The possibility that human parvoviruses could threaten the safety of blood products and whether HBoVs, B19V and hPARV4 screening is necessary requires further investigation with increased sample size.

Acknowledgements. The authors declare no conflict of interest. This research was supported by the TAIWAN-LATVIA-LITHUANIA COOPERATION PROJECT 2017-2019.

PSMA6 gene expression level in multiple sclerosis patients and control individuals

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Background. Multiple sclerosis (MS) is an autoimmune inflammatory disease of the central nervous system (brain, spinal cord and optic nerves). Inflammation damages myelin, which surrounds and insulates the nerve fibres, the nerve fibres themselves, and the specialized cells that make myelin, thus leading to neurodegeneration and disabilities. Ubiquitin-proteasome system (UPS) is crucial in the regulation of the immune system; therefore, it might play a role in the development and progression of MS. Furthermore, proteasomes were shown to be major autoantigens in case of MS. Genetic variations of proteasomal genes might be involved in modulation of UPS efficiency. Susceptibility to autoimmune diseases, cardio-vascular disorders and type 2 diabetes mellitus is associated with polymorphisms in the 14q11-24 proteasomal genes. They could be also involved in the pathogenesis of MS.

Aim. The aim of the current study was to investigate *PSMA6* gene expression level in MS patients and controls.

Methods. Altogether 127 MS patients and 17 control individuals were enrolled in the study. RNA was isolated from blood and *PSMA6* gene expression was analysed with qPCR. For statistical analysis, MS patients were divided into subgroups according to *PSMA6* gene rs1048990 allele variants and sex.

Results. *PSMA6* gene expression was increased in MS patients compared to controls ($p=3.1\times 10^{-2}$). For rs1048990 rare alleles and heterozygotes, *PSMA6* gene expression was increased compared to common alleles ($p=6.4\times 10^{-3}$). When patients were divided according to their gender, for women we could see the same trend with increased expression of the gene in individuals with common alleles ($p=1.9\times 10^{-2}$), but for males the difference did not reach statistical significance.

Conclusion. Results suggest that onset of MS increases transcription of *PSMA6* gene, and *PSMA6* gene rs1048990 allele polymorphisms are associated with *PSMA6* gene expression level in MS patients.

Acknowledgements. The study was funded from the UL research project ERAF SAM No. 1.1.1.1/16/A/016 project "Determination of proteasome-related genetic, epigenetic and clinical markers for multiple sclerosis".

Studies of DNA integrity in DMT1 patient's lymphocytes

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Background. DNA double-strand breaks are one of the heaviest damage types of a DNA molecule because of a break of the whole DNA chain. The repair process can cause errors in the DNA chain that can be followed by mutations and cytotoxic processes that result in pathology development. Both physiological and pathological DNA breaks occur in the cell. The DNA repair system is constantly congested, if physiological, environmental, lifestyle DNA break enhancing factors and pathological background combine, DNA can be exposed to increased reparative stress. Considering that these factors may be combined in different ways, individual conditions may arise for the development of diseases and their complications. DMT1 is an autoimmune disease characterised by increased formation of free radicals, which results in DNA chain breaks. There are studies showing the relationship between DNA lesions in 1TCD pathogenesis and disease complications. Usually, these studies use methods that identify small DNA fragments, there are very few researches on large-scale DNA fragments.

Aim. The aim of the current study was to determine the relationship between DNA double-strand breaks, diet and lifestyle habits, as well as type 1 diabetes and its complications.

Methods. 47 participants, 40 of whom were 1TCD patients, while others belonged to the control group - without glucose tolerance disorders, were involved in this study. Lymphocytes were purified from all samples and pulse field gel electrophoresis (PFGE) was performed. The pattern of DNA breaks was analysed through the ImageJ program, creating densitograms. The statistics analysis was performed with the SPSS programme 23.0.

Results. In an analysis of the potential association for DNA breaks and alcohol use, in samples of DMT1 patients a statistically difference was found between the alcohol factor and the presence of DNA breaks, i.e. $P\chi = 0.056$, and with a strong association ($V = 0.37$). Also, an association with average age has been established ($P\chi = 4.81 \times 10^{-2}$). Relationship to gender is on the border ($P\chi = 0.057$) however, DNA ruptures were detected in two times more in males ($n = 6$) than in females ($n = 3$).

Conclusion. In the analysis of the level of DNA double-strand breaks in the DMT1 patient and control groups with different factors affecting it, it has been established that DNA breaks are more common in DMT1 patient's DNA, individuals who use alcohol frequently and male subjects.

Effects of gammapyrone on expression of proteins participating in glucose homeostasis in streptozocin-induced Alzheimer's disease model-rats

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Background. Alzheimer's disease (AD) is an irreversible, progressive brain disorder that gradually destroys neurons in hippocampus and cortex, causing cognitive impairments. In brains of sporadic AD patients, early onset pathology manifests as reduced expression of glucose transporters 1 and 3 (GLUT1 and GLUT3) and increased expression of glycogen synthase kinase-3 (GSK-3), a protein involved in glucose homeostasis in brain. Although the data on expression of these proteins in STZ-induced AD rats are controversial (Qu *et al.* 2014), drugs that regulate their expression could be promising in AD treatment. Gammapyrone, a GABA containing 1,4-dihydropyridine analogue, has previously shown neuroprotective action in AD model-rats (Pilipenko *et al.* 2019), suggesting that glucose homeostasis might be involved in this effect.

Aim. In present study, we examined effects of gammapyrone on expression of GLUT1, GLUT3 and GSK-3 proteins in non-transgenic AD model-rat brain structures: cortex and hippocampus.

Methods. Male Wistar rats (280±20 g) were used to design sporadic AD model by bilateral intracerebroventricular injection of STZ (750 µg/10 µl or artificial cerebrospinal fluid as control per rat). Intraperitoneal administration of gammapyrone (0.1 and 0.5 mg/kg) was done for 3 consecutive days prior to icv injection of STZ, as well as on experimental days 15-22. On day 23, brains were dissected for biochemical assessment, and Western blot method was performed to determine protein expression levels of GLUT1, GLUT3 and GSK-3.

Results. Administration of STZ produced a significant increase in expression of GSK-3 in both rat brain structures, and a slight decrease in hippocampal but not cortical GLUT3 expression. Gammapyrone at both doses reversed to control levels the STZ-induced increase in GSK-3 expression in both brain structures. Moreover, gammapyrone protected against STZ-induced hippocampal decrease in GLUT3 expression. Neither STZ nor gammapyrone altered GLUT1 expression in AD model-rats.

Conclusions. Obtained results show that gammapyrone normalized the STZ-increased expression of hippocampal and cortical GSK-3, a protein which is regarded as a critical molecular link between glucose homeostasis and proteopathologies in AD. Thus, one may suggest gammapyrone's therapeutic potential as GSK-3 inhibitor. Gammapyrone also slightly protected against a decrease in neuronal glucose transporter GLUT-3 expression. Although the data indicate that the neuroprotective effects of gammapyrone in AD model-rats involve regulation of glucose homeostasis, much remains to clarify about the neurobiological mechanisms of action of this compound.

Acknowledgements. The study was funded by the Student Council of the University of Latvia.

Elastase, collagenase and hyaluronidase inhibitory activity of *Vaccinium* spp. berry pomace extracts

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Background. *In vitro* and *in vivo* studies suggest natural protector use for premature skin aging. There have been many efforts to search for affordable and efficient cosmetic ingredients from natural sources, such as vegetables, berries and other plants. Flavonoids derived from plants can form complexes with metal ions which mean they have the potential to bind with metalloenzymes thus altering or inhibiting metabolic pathways. Berry pomaces are sustainable sources of bioactive compounds with uncovered possible diverse applications in pharmaceutical, food and cosmetic industries. However, berry press-residues are insufficiently studied as anti-aging means, and their bioactivities are not properly evaluated.

Aim. The aim of the current study was to study effect of five *Vaccinium* spp. pomace extracts on activities of enzymes responsible for the degradation of the main components of extracellular matrix, such as elastin, collagen and hyaluronic acid.

Methods. Cell-free enzymatic assays were used to assess elastase, hyaluronidase and collagenase inhibitory properties of blueberry, bilberry, bog cranberry, American cranberry and lingonberry pomace extracts. The spectrophotometric assays employed were based on published methods with some modifications for use in a microplate reader. Synthetic substrate *N*-[3-(2-furyl) acryloyl]-Leu-Gly-Pro-Ala (FALGPA) was used in collagenase assay, *N*-Succinyl-Ala-Ala-Ala-*p*-nitroanilide (SANA) in elastase assay and sodium hyaluronate in hyaluronidase method.

Results. All studied here berry pomace extracts inhibited elastase, collagenase and hyaluronidase activities at concentration range from 0.125 mg/ml to 1 mg/ml. The strongest inhibitory influence was observed on hyaluronidase activity. Cranberry and lingonberry extracts at concentration of 0.5 mg/ml showed 100% inhibition of hyaluronidase activity. Cranberry extract was the most potent collagenase activity inhibitor whereas lingonberry extract was the most potent elastase activity inhibitor.

Conclusion. Maintaining of collagen, elastin and hyaluronic acid molecular structures is important in preventing the skin aging therefore these berry press-residue extracts could be used as active ingredients in wrinkle-care cosmetics. The obtained results *in vitro* assays suggest direct binding of extract ingredients to active centres of enzyme molecules.

Acknowledgements. Supported by the European Regional Development Fund within the project No. 1.1.1.1/16/A/047 "Genus *Vaccinium* berry processing using "green" technologies and innovative, pharmacologically characterized biopharmaceutical products". The authors have no conflict of interest to report.

***In vitro* antioxidant and acetylcholinesterase inhibitory properties of *Vaccinium* spp. berry press-residue extracts**

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Background. Few studies have shown the beneficial effects of polyphenol-rich extracts on learning and memory. Exact mechanism is difficult to pinpoint, could be both indirect and direct effects. The existence of specific polyphenol binding sites on rat brain cell membranes has been suggested to explain a direct effect on the brain functions. Some polyphenols are found to inhibit activity of acetylcholinesterase. Acetylcholine deficiency is associated with the development of Alzheimer's disease, whereas increased activity of acetylcholinesterase is linked to increase in the number and volume of amyloid plaques. Berry pomaces contain bioactive compounds, including polyphenols, however, their effects on activity of acetylcholinesterase are insufficiently studied.

Aim. The aim was to study antioxidant effects of five *Vaccinium* spp. pomace extracts and their influence on acetylcholinesterase activity *in vitro*.

Methods. Total antioxidant potency of blueberry, bilberry, bog cranberry, American cranberry and lingonberry pomace extracts was assessed by green phosphomolybdenum complex method. The reducing capacity was examined using Fe³⁺ to Fe²⁺ reduction assay. Anti-inflammatory effects of the extracts were assessed as inhibiting of protein denaturation. Acetylcholinesterase activity was measured using Ellman's reaction. The spectrophotometric assays employed were based on published methods with some modifications for use in a microplate reader.

Results. All berry pomace extracts showed antioxidant and reducing capacity in a concentration dependant manner. Bilberry and cranberry pomace extracts showed the strongest red-oxy effects expressed as ascorbic acid equivalent µg per mg of extract. Albumin denaturation protecting effect of extracts at concentration of 0.25 mg/ml was approximately equal to that of diclofenac 0.02 mg/ml. All berry extracts inhibited activity of acetylcholinesterase at concentration of 1 mg/ml approximately on 11-20%. Synergy was observed between acetylcholinesterase reversible inhibitor neostigmine and berry extract effects. Neostigmine bromide was used as positive reference.

Conclusion. Neurodegenerative diseases are characterized by oxidative stress and neuro-inflammation in the brain, whereas Alzheimer's disease also by low level of neurotransmitter acetylcholine. Effective treatment strategies rely mostly on either enhancing the cholinergic function of the brain or inducing antioxidant and anti-inflammatory processes. Plant or plant derived compound that combine these properties could be effective for developing newer CNS drugs. We suggest further neuroprotective studies on berry press-residues *in vivo* assays.

Acknowledgements. Supported by the European Regional Development Fund within the project No. 1.1.1.1/16/A/047 "Genus *Vaccinium* berry processing using "green" technologies and innovative, pharmacologically characterized biopharmaceutical products". The authors have no conflict of interest to report.

***In vitro* study of efficacy of antimicrobials in combination with polyherbal extracts using Checkerboard method**

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Background. Due to increased resistance to conventional antimicrobials worldwide, it could be rational to study the combination or synergy therapy of individual antimicrobials with herbal alternatives, which can expand the spectrum of their activity. This effect may lead to new ways of treating nonhealing infections. An object of our study is a polyherbal formulation, *Jathyadi Thailam* (by *Yogagrantha* – a modified South Indian variant) (JT_{YG}), which is used topically in treatment for chronic wounds. The activity of the formulation in combination with antimicrobials is not studied before.

Aim. The aim of this study was to evaluate the antimicrobial activity of two JT_{YG} extracts: direct hydro-ethanol (direct- HE) and ethylacetate (EtAc) in combination with antimicrobials by Checkerboard synergy method.

Methods. The antibacterial efficacy of the JT_{YG} extracts was studied by determining the minimum inhibitory concentration (MIC) by modified broth microdilution method as described by Balouri (Balouiri *et al.*, 2016). Synergy activity was studied using Checkerboard method. Synergy was determined by fractional inhibitory index (FIC). Stock solution of gentamicin (0.4 mg/mL) and streptomycin (1 mg/mL) were used as MIC controls in each experiment according to CLSI standards CLSI-2017- M02-A12 (Clinical and Laboratory Standards Institute, 2017).

Results. The combination of JT_{YG} extracts and antimicrobials was more effective for Gram positive bacteria and the synergy effect was observed. Gentamicin in combinations with direct-HE and with EtAc was more active than Streptomycin. The lowest FIC index was obtained for *P. aeruginosa* in the combination of Gentamicin and direct-HE, followed by *K. pneumoniae* and *S. aureus*.

Conclusions. JT_{YG} extracts in combination with antimicrobials (Gentamicin) are found to have the capability of increasing synergy effect against Gram positive and Gram negative bacteria. Further study is necessary for clinical bacterial strains.

Acknowledgements. The study was funded from LU effective collaboration project No ZD2016/20226 and Arya Vaidya Chikitsalayam and Research Institute.

Incorporation of polyprenol and provitamin paste microemulsions into topical formulations and their study on healthy volunteers

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Background. Cosmeceuticals consist of ingredients which are applied topically and combine biologically active compounds and medicinal benefits. Conifer tree needles are an abundant source of bioactive lipophilic compounds such as polyprenols and provitamin paste (β -carotene, vitamins E and K, sterols). These extracts contain ingredients that can influence the biological function of the skin.

Aims. The aims of our study were to a) prepare three types of conifer containing face creams and b) determine whether the conifer ingredients can improve the appearance, texture and anti-ageing activity in the skin of volunteer subjects.

Methods. *Picea abies* (≥ 95 purity) polyprenols and provitamin paste were acquired from JSC "Biolat". Three different cream compositions were prepared and tested for physico-chemical and microbiological stability according to existing laboratory standards. A total of 25 female subjects with varying skin types took part in the study for four weeks. Multiple instrumental tests such as skin moisturizing level by Corneometer, biomechanical skin parameters by Cutometer, wrinkle length and depth by Visioline and subjective evaluation questionnaire assessment were carried out. Volunteers were instructed to regularly use the products according to the described method, exclude the use of other cosmetic products, and perform a detailed evaluation of the tested product via the received questionnaire.

Results. None of the tested creams produced allergic or irritant effects. The cream with polyprenols on average moisturized the skin by 10%, improved skin elasticity by 12% and skin firmness by 8%; it reduced wrinkle length by 7% and wrinkle depth by 4%. The cream with polyprenols and additional active ingredients on average moisturized the skin by 8%, improved skin elasticity by 14% and skin firmness by 10%; it reduced wrinkle length by 1% and wrinkle depth by 5%. The product with provitamin paste moisturized the skin by 8%, improved skin elasticity by 14% and skin firmness by 19%; it reduced wrinkle length by 7% and wrinkle depth by 6%.

Conclusions. Three new microcarrier forms for conifer extract biologically active fractions of poly-prenols and provitamin paste have been developed. All three microemulsion containing creams showed an excellent safety and tolerability profiles. All cream formulations were found to significantly improve skin parameters such as moisture level, elasticity, firmness, wrinkle length and depth to varying degree.

Acknowledgements. Project N₀ 1.2.1.1/16/A/005 "The incorporation of conifer needle extractives": polyprenols, silbiol and provitamin paste microemulsions into cosmetic formulations (P28)" in cooperation with SIA "Smart material and technology competence centre" and CFLA.

The antimicrobial activity of eight essential oils against ESBL *Escherichia coli* isolated from pigs

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Background. The emergence of bacterial resistance to the currently available antimicrobial agents is an increasing concern in recent years in the world. Agricultural farming promotes the transmission of the antibiotic resistant bacteria to humans. As an alternative strategy in pig farming is the use of essential oils (EOs) aimed to decrease possibility to contaminate environment due to antibacterial properties of the oils.

Aim. The objective of this study was to determine the antibacterial activity of 8 plant EOs against ESBL *E.coli* isolated from liquid pig manure.

Methods. The phenotypic confirmation of ESBL production in selected *E.coli* isolates was tested (CLSI, 2016) using both cefotaxime (CTX, 30µg) and ceftazidime (CAZ, 30µg) disks alone and in combination with clavulanic acid (CA, 10µg) (BD BBL). The *in vitro* antimicrobial activity of EOs was evaluated using the well diffusion technique (Tejero-Sariñena, 2012). 60µL of EOs was placed into each well. After incubation in 37°C for 18-24 h the diameter of the inhibition zone, including the well diameter, was measured. We have analyzed the original pure EOs of the following 8 plants: *Pinus sylvestris* (Pine) leaf; *Petroselinum sativum*; *Origanum vulgare*; *Juniperus Communis* fruit; *Cedrus Atlantica* Bark; *Cinnamon Bark*; *Lavandula officinalis*; *Eucalyptus globulus*. EOs were produced by “Oils4life” (UK) and by “Aromatika Ltd” (UA).

Results. The antibacterial activity of EOs tested by the well diffusion method varied at great extent. All ESBL *E.coli* isolates were sensitive to five EOs. The highest activity was observed for EOs from *Cinnamomum Zeylanicum* Bark (25 mm); *Eucalyptus globulus* (16 mm) and *Origanum vulgare* (15 mm), and, in contrary, lowest activity was detected for *Pinus sylvestris* (11 mm) and *Lavandula officinalis* (10 mm). Other 3 EOs did not exhibit the antimicrobial activity.

Conclusions. The results of our study suggest that the EOs (especially *Cinnamomum Zeylanicum* Bark oil) mostly is a potential source as antibacterial agent against antibiotic resistant Gram negative bacteria.

Age estimation from sternal end of 4th rib in the population of Latvia

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Background. Estimation of the age at death based on examination of skeletal remains of unknown individuals is required in forensic medicine. One of the most reliable methods for age determination is currently considered to be Işcan's phase method, developed by Işcan et al. in 1984 and based on component analysis using sternal end of 4th rib. Several studies approved that Işcan's method applicable in different populations, however age-related changes vary between populations, and the age of a person should be determined by population-specific standards.

Aim. To evaluate applicability of Işcan's component and Işcan's phase method for age at death estimation from sternal ends of 4th rib to the Latvian population.

Methods. Sternal ends of right 4th rib (n=61) were collected during autopsies in State Centre for Forensic Medical Examination of the Republic of Latvia from 20 female and 41 male individuals (18-96 years old) with known age and gender. Sternal ends of 4th ribs were removed 1-2 cm from costochondral junction, then boiled for 20-30 minutes, adherent soft tissue and cartilage were removed. Rib fragments were examined according to Işcan's component method evaluating features like pit depth (component I), pit shape (component II) and rim and wall configurations (component III) and according to Işcan's 9 phases. Data was analyzed statistically using IBM SPSS Statistics 22.

Results. In this study, the correlation of age with the rib phases was statistically significant ($p \leq 0,01$) and strong (male $r = 0.89$, female $r = 0.87$) in both genders. Işcan's component method had moderate correlation with age in the male group, but in the female group correlation for component I was not statistically significant. The most age-dependent factor identified by the individual components was the wall/border shape or component III. According to the Işcan's phase descriptions, bony projections were observed in both genders starting from phase 6.

Conclusion. Işcan's rib-phase method for determination of age of the person is applicable to the Latvian population, and is more effective than Işcan's component method. Although in both groups the actual age of individuals in phases 3-6 and in the male group in phase 1 was corresponding age intervals offered by Işcan, it would be necessary to examine more samples in both gender groups to determine precise age intervals for each phase.

Association between dietary factors and clinical parameters in type 1 diabetes in Latvia

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Background: Diet plays an important role in the management of type 1 diabetes. However, the association between dietary intake and health has not been extensively studied in this population.

Aims: We studied the cross-sectional association between dietary factors, clinical parameters and different complications status in patients with type 1 diabetes.

Methods: Samples and data of 267 patients with duration of type 1 diabetes of more than 1 year were analyzed. Dietary intake was assessed using a self-reported questionnaire (InterDiane) and a diet score, expressing the extent to which individuals adhered to standard dietary recommendations.

Results: We observed correlation between diet score and BMI, age, metabolic syndrome ($p < 0.001$), waist circumference, number of diabetic complications, diabetic retinopathy, level of blood pressure ($p < 0.005$), coronary heart disease, peripheral vascular disease, diabetic polyneuropathy, smoking, TG level ($p = 0.05$).

Conclusions: In type 1 diabetes, dietary habits are associated with prevalence of diabetic complications, CVD and cardiovascular risk factors. Data on association between these markers provide new knowledge about links between dietary factors and clinical parameters in type 1 diabetes. More attention should be paid to dietary counselling of patients with type 1 diabetes.

Acknowledgements: we thank Aila J. Ahola from FinnDiane group (Helsinki, Finland) and Martins Veide (University of Latvia) for counseling. This work was supported by State Genome database project, Latvian Association of Endocrinology, and a project of the University of Latvia: "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment".

Bioimpedancemetry in the practice of sports medicine doctor

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Background. There are various ways to assess the harmonious development of the body in humans. It is generally accepted that body mass index (BMI) indirectly allows you to assess whether body weight is overweight, normal or insufficient. Unfortunately, the method of calculating BMI is not always relevant in the practice of sports medicine. So, BMI indicators in athletes with pronounced muscle development may indicate overweight or obesity, which is not true. To help the practitioner of sports medicine, bio-impedance method of body composition analysis.

Aim. Evaluate the effectiveness of the bio-impedance method for the study of body composition.

Methods. A total of 45 weightlifting athletes were examined - men aged 21 to 32 years. A comparative analysis of the impedance body composition, caliperometry and BMI has been carried out. The impedance body composition was measured using the Diamant «AIST» bio-impedance device, and the classical method was used for caliperometry: folds on the chest, abdomen, and hip were measured. BMI was calculated by the formula: weight (kg) / height (m) ².

Results. Subjects had an average BMI of 27, which, in accordance with the WHO recommendations, corresponds to an overweight indicator. At the same time, caliperometry indicators are generally from 10.6 to 18%, which corresponds to a low and ideal% content of subcutaneous fat. And indicators of fat mass on the results of bio-impedance on the device Diamant “AIST” average 20% of the total mass, which also indicates the ideal value. Based on the data obtained, a Diamant «AIST +» device was created, designed specifically to study body composition in athletes.

Conclusion. In assessing the harmonious development of the body in athletes, it is necessary to take into account the specifics of the sport. And the assessment of body composition to carry out bioimpedance method.

Acknowledgements. No conflict of interest was declared.

Bronchial reactivity in adults with diabetes type 2

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Background. In the present study, we tested hypothesis that patients with type 2 diabetes have higher risk to get bronchial asthma. As bronchial hyperreactivity (BHR) is an ultimate feature of asthma, relationship between diabetes type 2 (Dt2) and bronchial reactivity (BR) was studied. We associated also these data with patients gender, body mass index (BMI) and lung function indices (FVC, FEV1 and FEV1/FVC).

The aim. Purpose of the study was to find the association between BR to methacholine and Dt2 in males and females.

Methods. We analyzed retrospectively 2781 adult people data (1908 woman and 873 man), who underwent methacholine bronchoprovocation test (BPT) to exclude possible asthma diagnosis. 104 patients had already approved Dt2 diagnosis before the testing (81 woman and 23 man). To establish the association between Dt2 and elevated bronchial reactivity we used logistic regression analysis, but to check the association of these data with gender, body mass index and lung function indices ANOVA was used.

Results. The study revealed that Dt2 patients significantly more frequently had BHR ($p=0.00239$). Such association was present both in woman ($p=0.0291$) and men ($p=0.0353$). Both gender having both BHR and Dt2 showed the highest BMI ($p<0.000001$). Patients with Dt2 and BHR had lower lung function indices compared to persons with normal BR – FVC ($p=0.000024$), FEV1 ($p<0.000001$), FEV1/FVC ($p=0.000093$). Comparing patients with Dt2 and BHR with patients having only BHR showed lower FVC ($p=0.0316$) and FEV1 ($p<0.000001$). Comparing patients with Dt2 and BHR with patients suffering only Dt2 showed significantly lower FEV1 ($p=0.00008$) and FEV1/FVC ($p=0.00007$).

Conclusions. Dt2 is positively **associated** with BHR that is characteristic for both genders. It could be explained with elevated BMI and insulin resistance. Patients with **co-existent BHR and Dt2** have more affected lung function compared to those which have only BHR or Dt2. Future studies are necessary to find out intimate mechanisms underlying association between BHR and Dt2.

Characteristics of metabolic syndrome in patients with hyperuricemia

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Background. Elevated serum uric acid (SUA) has been identified to have a relation with a number of cardiovascular conditions, including metabolic syndrome. However the association between the uric acid level and particular parameters of metabolic syndrome remains inconclusive.

Aim. The aim of this study was to compare the features of metabolic syndrome between patients with asymptomatic hyperuricemia and patients with normal serum uric acid values.

Methods. A total of 610 subjects (men aged 40–55, women aged 50–65) participating in Lithuanian High Cardiovascular Risk (LitHiR) primary prevention programme in Vilnius University Hospital Santaros Klinikos and diagnosed with metabolic syndrome according to the updated NCEP ATP III criteria were enrolled. All participants were categorised into two groups based on SUA concentration: normal SUA ≤ 357 $\mu\text{mol/L}$ for men and ≤ 428 $\mu\text{mol/L}$ for women ($n=402$) and elevated SUA >357 $\mu\text{mol/L}$ for men and >428 $\mu\text{mol/L}$ for women ($n=208$). Anthropometric parameters, parameters of lipid and glucose metabolism and blood pressure values were compared between two groups using t-test.

Results. We found statistically significant difference between means of BMI and waist circumference, with a higher values in subjects with hyperuricemia (33.47 ± 4.33 kg/m^2 vs 31.4 ± 4.32 kg/m^2 , $p < 0.001$, for BMI and 106.99 ± 9.76 cm vs 102.66 ± 11.53 cm , $p < 0.001$, for waist circumference). Mean HDL cholesterol value was lower and mean triglycerides value was higher in hyperuricemia group (1.15 ± 0.25 mmol/l vs 1.21 ± 0.29 mmol/l , $p=0.03$ for HDL-C and 2.57 ± 1.45 mmol/l vs 2.15 ± 1.64 mmol/l , $p < 0.0001$ for triglycerides). Mean serum glucose concentration was higher in hyperuricemia group (6.72 ± 1.37 mmol/l vs 6.63 ± 1.8 mmol/l , $p=0.009$), as well as mean blood pressure values for both systolic (140.71 ± 14.3 mmHg vs 137.56 ± 15.34 mmHg , $p=0.0008$) and diastolic (84 ± 9.63 mmHg vs 81.87 ± 9.31 mmHg , $p=0.014$) blood pressure.

Conclusions. Present study indicates a significant relationship between SUA and metabolic syndrome parameters. Therefore routine SUA measurement in patients with metabolic syndrome is important to prevent hyperuricemia and its complications.

Correlation between migraine and autoimmune thyroiditis

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Background. Migraine is a common neurological disease in which the patient loses his/her ability to work during the attack. Previous studies have found that migraine is common with other diseases (comorbidities) including endocrine such as autoimmune thyroiditis. Comorbidity refers to greater than coincidental association of separate conditions. The existence of an link between migraine and thyroid disorders is still a matter of debate. Epidemiological studies have shown a potential connection between plasma TSH concentrations and migraine but results are inconsistent. According to Anca Staii, et al., the prevalence of Hashimoto thyroiditis worldwide is estimated to be 0.3–1.2%.

Aim. To identify frequency of autoimmune thyroiditis and evaluate it's clinical characteristics between the patients with the diagnosis of migraine with/without aura in Latvia.

Methods. A retrospective study was performed at the Headaches Center in outpatient clinic "Veselības centrs 4". Data was gathered from medical histories including Headache Questionnaire of patients with migraine with/without aura and analyzed with IBM SPSS 22 software.

Results. The study included 50 patients, of which 44 were female (88%) and 6 male (12%). Patients ages ranging from 17 to 60 years (M=36.70; SD=11.46). Only 36% of patients had migraine with aura (n=18) and 64% presented with migraine without aura (n=32). 10 % of patients (n=5) had autoimmune thyroiditis (mean age=39.60 years; SD=9.96). All these patients were female. 40% of patients with autoimmune thyroiditis (n=2) had migraine with aura and 60% of patients (n=3) – migraine without aura. Odds ratio (OR) for patients with autoimmune thyroiditis to have migraine with aura than patients without autoimmune thyroiditis = 1.2 [95% TI: 0.18 to 8].

Conclusion. We found a high prevalence of autoimmune thyroiditis in migraine (10%), significantly higher than in the general population (0.3–1.2%), that's why autoimmune thyroiditis should be considered as migraine comorbidity. Women have a higher prevalence of autoimmune thyroiditis with migraine with/without aura than men. Also our data suggest that patients with autoimmune thyroiditis have a higher risk to have migraine with aura than patients without autoimmune thyroiditis.

Correlation of bone marrow and peripheral blood changes in lymphoma patients

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Background. Lymphoma is a malignant, heterogeneous neoplasm of the lymphatic system with two main types: Hodgkin lymphoma and Non-Hodgkin lymphoma. The most common type of Non-Hodgkin lymphoma is B-cell lymphoma 85%. It distinguished between slow-growing or low grade cancer and fast-growing or high-grade cancer. Before treatment bone marrow biopsy is used to help determine the stage of a lymphoma. In comparison with Hodgkin lymphoma bone marrow infiltration in Non-Hodgkin lymphoma is approximately 10%. Lymphoma can be disseminated into the bone marrow and influence the production of blood cells, this can lead to other complication, for example anaemia, leukopenia and thrombocytopenia.

Aim. The aim of the current study was to determine correlation of bone marrow and peripheral blood changes in lymphoma patients.

Methods. The data from histologically confirmed lymphoma were obtained from Pauls Stradins Clinical University Hospital from year 2012–2018. We analysed patient age and type of lymphoma, bone marrow biopsy results and changes in peripheral blood, such as hemoglobin, red blood cells, leukocytes, platelets and lymphocytes. We used several methods: Boxplot, histogram, a Chi-squared test and odds ration test.

Results. The study included 44 patients, 18 women and 26 men. The average age of patients was 57.6 ±16.9 years. The number of patients with Non-Hodgkin lymphoma was 36 (82%). The number of patients with Hodgkin lymphoma was 8 (18%). Bone marrow infiltration was confirmed in 10 (23%) patients. Most of them 6 (60%) patients had indolent lymphoma. In 34 (77%) cases bone marrow biopsy showed no malignant lymphoma cells. Should be noted most of the patients (94%) without bone marrow infiltration had aggressive lymphoma. The statistically significant correlation between bone marrow infiltration and anaemia ($p=0.786$), leukopenia ($p=0.213$) thrombocytopenia ($p=0.051$) and lymphocytopenia ($p=0.401$) was not observed.

Conclusion. The correlation between bone marrow infiltration and peripheral blood changes in lymphoma patients was not registered as statistically significant, possibly because of the small number of patients in the study.

Acknowledgements. None.

Diabetic retinopathy - types and association with other microvascular complications in patients with type 1 diabetes mellitus

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Background. Diabetic retinopathy is a severe complication of diabetes mellitus that can cause vision loss to people in working age. One-third of people with type 1 diabetes mellitus (T1DM) already have signs of diabetic retinopathy (DR), a further one third has vision-threatening DR (Ryan Lee et al. 2016). DR is more likely to develop in patients with T1DM (Kanski's Clinical Ophthalmology, 2016). Other microvascular complications coexist together with DR such as diabetic neuropathy and especially diabetic nephropathy (Leslie R.Dye et al., 2018).

Aim. To detect types of DR and find any association with other microvascular complications in patients with type 1 diabetes mellitus.

Methods. A retrospective study was held at Pauls Stradins Clinical University Hospital (Riga, Latvia) from January 2016 till March 2018. 79 patients (158 eyes) were enrolled in this study, and all those patients observed one particular doctor for results to be more reliable. Indirect ophthalmoscopy method was used with pupil dilatation using eye drops. IBM SPSS Statistics Version 25.0 and Microsoft Excel 2016 was used. *Kramer's V* indicator was used to find the association and the level of statistical significance (P_x) was set at < 0.05 or 5.00×10^{-2} .

Results. 79 patients were enrolled in age from 19 till 75 of which 48.10% ($n=38$) were men and 51.90% ($n=41$) were women. DR were detected in 77.22% ($n=61$) patients, 20.25% ($n=16$) have no signs of DR and 2.53% ($n=2$) were excluded for further research. From patients with any kind of DR – 29.11% ($n=23$) have PDR and 48.10% ($n=38$) have NPDR. From microvascular complications – 2.60% ($n=2$) patients have isolated nephropathy, 32.47% ($n=25$) polyneuropathy, 29.87% ($n=22$) both complications together and 35.06% ($n=27$) have no other microvascular complication. Between DR and microvascular complications strong association ($3.70 \times 10^{-4} V = 0.40$) was found with the existence of DR and even stronger ($P_x = 4.54 \times 10^{-5} V = 0.61$) with the forms of DR.

Conclusion. More than 2/3 of enrolled patients have any kind of diabetic retinopathy, mostly NPDR. Most of them have polyneuropathy separately or both – nephropathy and polyneuropathy together. In most cases are patients with NPDR. Diabetes mellitus complications have a strong association ($V = 0,40$) with the existence of DR and even stronger ($V = 0,61$) with the forms of DR.

Acknowledgements. Because of the strong association of DR and other microvascular complications, patients with diabetes should be screened regularly for retinopathy, nephropathy, and neuropathy.

Neuropeptide Y and angiotensin 2 as markers of neurovascular interplay in type 1 diabetes mellitus

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Background. Derangements in autonomous nervous system associated with DM lead to impaired vascular tone and increased production of vasoconstrictor and angiogenic mediators such as norepinephrine and neuropeptide Y (NPY), and therefore might be involved in development of endothelial dysfunction and vascular complications of T1D. Serum angiotensin 2 (ANGPT2) levels have been associated with endothelial dysfunction in type 1 diabetes mellitus (T1D).

The aim of the study was to investigate differences in ANGPT2 and NPY between T1D patients stratified according to presence of complications of T1D and possible correlation between these biomarkers.

Methods. 295 patients with T1D duration > 1 year were included. ANGPT2 was measured by Luminex technology. NPY was measured by ELISA. Statistical analysis was performed by programme R.

Results. Levels of NPY and ANGPT2 were higher in patients with diabetic nephropathy, chronic kidney disease and arterial hypertension, compared to patients without these complications. Diabetic polyneuropathy was not associated with changes in concentrations of NPY and ANGPT2. NPY, but not ANGPT2 was higher in patients with diabetic retinopathy. Oppositely, higher ANGPT2 but not NPY was associated with cardiovascular disease. We observed a positive correlation between serum ANGPT2 and NPY concentrations, as well as a negative correlation between both biomarkers and estimated glomerular filtration rate.

Conclusion. Higher concentration of NPY and ANGPT2 are associated with vascular complications of T1D. Correlation between these biomarkers indicates on association between derangements of autonomous nervous system and endothelial dysfunction in diabetes.

Acknowledgements. This work was supported by a project of the University of Latvia: "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment".

Pain in patients with *Hidradenitis suppurativa*, association with DLQI and PGA severity scale

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Introduction. *HS* is a multi-factorial, chronic disease with relapsing nature. Disease is characterized by suppurative cutaneous lesions affecting skin that bears apocrine glands. Patients disease burden includes intense pain, work disability and overall poor quality of life.

Aim. The aim of this study was to evaluate the level of pain in *HS* patients and determine pain association with life quality and severity scale according to *PGA*.

Methods. In total 22 *HS* patients were included in the study of whom all were treated in Riga 1st Hospital. Patients level of pain was evaluated using *NPRS*. Life quality was evaluated using *DLQI* questionnaire. *PGA* scale was used for disease severity evaluation. Statistical analyses were performed in RSU Statistical Laboratory using *SPSS* version 22.0 and *Microsoft Excel* version 14.

Results. According to *NPRS* 5 patients admitted that they have no pain, 12—that they have mild pain, 1 patient had moderate and 4 patient severe pain. The mean level of pain was 2.91, indicating mild pain. From all the patients 12 were women and 10 men. Mean level of pain in women group was 3.17 and in group of a men—2.60. According to *DLQI* 4 patients had no effect at all on quality of life, 7—had small effect, 3—moderate, 7—very large effect and 1—extremely large effect on his life because of *HS*. The mean *DLQI* score was 8.23, indicating a moderate effect on patients' lives. Mean impact on life quality in group of women was 10.25 and in group of men—5.80. There was a significant correlation with *NPRS* and *DLQI* scales with p value – 0.039 ($p < 0.05$).

With *PGA* scale 1 patient was in category “clear” and admitted no pain, 5 patients “minimal” with mean pain level—3.6, 6 patients “mild” with mean pain level 1.5, 10 patients “severe” with mean pain level 3.7 and no patient as “very severe”. Correlation between *PGA* and *NPRS* appeared to be 0.062 ($p > 0.05$). That means correlation is not statistically significant, but however tendency is visible.

Conclusions:

1. *NPR* scale showed that most of the patients had mild pain.
2. Results of *DLQI* questionnaire are seemingly lower than expected, this means moderate impact on the quality of life.
3. Pain and life quality level among women are significantly higher than in group of men.
4. There is no correlation with disease severity and *DLQI* or *VAS* scores.
5. There is strong correlation between *VAS* and *DLQI* score.

Prevalence of hyperuricemia and gender specifics in middle aged Lithuanian adults with metabolic syndrome

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Background. Cross-sectional studies have reported associations between serum uric acid levels and metabolic syndrome. However, gender differences of metabolic syndrome in patients with hyperuricemia are unknown.

Aim. The aim of this study was to evaluate the gender related differences in prevalence of hyperuricemia and its association with individual components of metabolic syndrome in middle aged Lithuanian adults.

Methods. A total of 610 subjects (men aged 40-55, women aged 50-65) participating in Lithuanian High Cardiovascular Risk (LitHiR) primary prevention programme in Vilnius University Hospital Santaros Klinikos and diagnosed with metabolic syndrome according to the updated NCEP ATP III criteria were enrolled. Hyperuricemia was defined as serum uric acid (SUA) >357 µmol/L for females and >428 µmol/L for males. Relationship between SUA (normal vs elevated) and metabolic syndrome parameters for both sexes was evaluated using t-test.

Results. Overall, the estimated prevalence of hyperuricemia was 57.74 %, with no statistically significant difference between females and males ($p=0.343$). Males with hyperuricemia had mean blood pressure values higher than those with normal SUA (141.1 ± 13.92 mmHg vs 136.45 ± 13.31 mmHg, $p=0.0008$ for systolic and 87.33 ± 9.74 mmHg vs 83.76 ± 8.4 mmHg, $p=0.012$ for diastolic values). No such difference was seen between female participants. Both males and females with hyperuricemia had mean BMI higher than those without elevated SUA (32.96 ± 3.91 kg/m² vs 31.24 ± 3.85 kg/m², $p=0.001$ for males and 33.79 ± 4.56 kg/m² vs 31.51 ± 4.54 kg/m², $p<0.0001$ for females). Among females, those with elevated SUA had higher mean waist circumference (105.25 ± 9.95 cm vs 100.06 ± 11.71 cm, $p<0.0001$) and glucose concentration (6.87 ± 1.52 mmol/l vs 6.61 ± 1.74 mmol/l, $p=0.006$). No such difference was observed in male participants.

Conclusion. Hyperuricemia is common among patients with metabolic syndrome and its association with various metabolic indicators showed some differences in sexes.

Quality of life in first-time rheumatic patients in Latvia

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Background. Rheumatic diseases (RD) are debilitating and progressive by their nature, therefore, they influence different areas of a patient's life: physical, psychological and social. Due to the significant increase in RD worldwide, it is essential to assess the impact of these disorders on health related quality of life (HRQoL).

Aim. The aim of the study was to analyze the impact of RD on the quality of life (QoL) of the first-time rheumatic patients.

Methods. Patients who presented to a rheumatologist as out-patients for the first time in their lives were asked to complete the standardized EuroQol questionnaire EQ-5D-5L and to answer questions related to their medical history and sociodemographic characteristics. Descriptive statistics and nonparametric tests were used to determine the possible differences in HRQoL by gender, education and clinical diagnosis.

Results. 45 out-patients (34 female, 11 male) completed the questionnaires. The mean age was 56.4 (SD 10.8) years. Out of five EQ-5D-5L items "pain/discomfort" section received the lowest ratings – 13.3% reported having severe pain or discomfort, 4.4% reported having extreme pain or discomfort. The mean EQ VAS value was 56.2 (SD 17.6) for all patients. Based on EQ VAS values, 2.2% evaluated their overall health as very poor, but 51.1% - poor. The median HRQoL value was 0.683 (IQR 0.520-0.802), osteoarthritis (OA) group had the lowest HRQoL – 0.619 (IQR 0.433-0.788), both values represent poor HRQoL assessment. However, no statistically significant relationships were found in HRQoL value by gender ($p=0.606$), education ($p=0.351$) and clinical diagnosis ($p=0.462$).

Conclusion. RD are associated with impaired QoL. Patients with OA and systemic inflammatory rheumatic diseases have similar HRQoL impairment. In other words, the QoL is not contingent on aetiology. The main goal of any treatment procedure should be the improvement of HRQoL.

The choice of treatment and neurological outcomes for patients after acute cerebral infarct in *a. cerebri media*

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Background. Stroke is the third most common cause of disability and second most common cause of death worldwide. All of strokes approximately 80% are ischemic. It's important to detect best choice of treatment for patient with acute ischemic stroke to maintain patients' quality of life.

Aim. To find out the best therapy for patients with acute cerebral stroke based on neurological outcomes after used treatment.

Methods. A retrospective study includes patients with cerebral stroke in Pauls Stradins Clinical University Hospital. Data were collected from January till April 2017. Patients were included based on including criteria: stroke in *a. cerebri media*, SKK-10 code I63.3 which refers to cerebral infarct. The obtained data were analyzed by IBM SPSS using independent t- test. We compared neurological outcome in 3 groups depending on treatment using National Institutes Health Score (NIHSS) and modified Rankin scale (mRS).

Results. There were 98 people included, 76 were analyzed for this research.

Among 76 people 39 (51,9%) were women mean age $M=76,9$ years; $SD=9,9$ and 37 (48,1%) men mean age $M=71,3$ years; $SD=8,4$. Thrombolysis was performed for 11 patients, thrombolysis with followed thrombectomy for 5 people and 60 people had conservative therapy.

Comparing neurological outcome between these groups by paired sample t- it shows that patients group who had conservative therapy neurological status using NIHSS $M=7,36$; $SD=5,5$ before and $M=5,27$; $SD=5,1$ after the treatment. Second group having thrombolysis has their NIHSS $M=9,36$; $SD=3,9$ and after treatment $M=5,27$; $SD=5,9$ respectively ($P<0,05$). Third group having thrombolysis and thrombectomy had NIHSS $M=14,4$; $SD=2,7$ before and $M=4,00$; $SD=8$ after treatment ($p<0,05$).

To detect neurological outcomes comparing mRS scale, it shows that group who neither have thrombolysis nor thrombectomy their mRS were $M=3,93$; $SD=1,2$ before and $M=3,18$; $SD=1,56$ after the treatment ($p<0,0001$). The group of patients who had thrombolysis mean mRS were $M=4,45$; $SD=0,93$ before and $M=2,91$; $SD=1,37$ after ($p<0,0001$). Patient group who had thrombolysis and thrombectomy mean mRS were $M=4,60$; $SD=0,5$ before and $M=2,60$; $SD=0,89$ after ($p<0,0001$).

Conclusions. Thrombolysis with following thrombectomy shows best neurological outcomes. Results shows that there is best neurological improvement in patients after thrombolysis itself and thrombolysis followed by thrombectomy but analysis shows that all three groups have statistical improvement.

Thrombocytosis in non-small cell lung cancer patients

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Background. Thrombocytosis is a common entity in cancer patients and is often associated with reduced life expectancy. Non-small cell lung cancer (NSCLC), with 5 year survival rate of only 22%, is responsible for up to 85% of lung cancer cases. Taking that in consideration, there are conducted numerous studies in the search for cheap along with easily available prognostic and predictive biomarkers. Maraz et al in his study concluded that thrombocytosis should be considered as a possible negative independent survival factor for patients that are undergoing lung cancer resection. Furthermore, as suggested by Boddu et al paraneoplastic thrombocytosis might be useful parameter in evaluating the necessity for anti-cytokine therapies alongside chemotherapy. In addition to prognostic significance of thrombocytosis in NSCLC, it could also be a useful and inexpensive laboratory marker in helping to identify a certain malignancies, such as NSCLC, in otherwise healthy individuals.

Aim. The main objective of this research was to find out if there is any association between thrombocytosis and newly diagnosed non small cell lung cancer patients variable factors, such as age, gender, tumour histopathological type of cancer, stage and blood count values.

Methods. We retrospectively reviewed 96 medical records of newly diagnosed primary non small lung cell carcinoma patients, whose diagnosis was confirmed with biopsy in year 2017 at the Pauls Stradins Clinical University Hospital Oncology clinic in Riga, Latvia. Counts of platelet (P), leukocyte (L), erythrocyte (E) as well as the concentration of C-reactive protein (CRP) and haemoglobin (HB) were analysed. In addition, patients age, gender, pathological, histological variables were recorded and assessed. The Pearson chi-squared test (χ^2) was used to compare the distribution of categorical variables. Statistical significance was determined at $p < 0.05$.

Results. Of 96 newly diagnosed NSCLC patients, 20 were female and 76 male, mean (SD) age 69.30 (9.27) and 66.68 [8.71] years respectively. Squamous cell carcinoma was diagnosed in 49 patients (51.0%); adenocarcinoma, in 47 (49%). Elevated platelet count was found in 21 (21.9%) patients, of whom 71.4% had stage III-IV NSCLC (χ^2 , $p=0.20$); 66.7% leucocytosis (Pearson chi square, $p=0.26$); 71.4% anaemia (χ^2 , $p=0.40$); 57.1% of patients with thrombocytosis had squamous cell carcinoma, but 42.9% adenocarcinoma (χ^2 , $p=0.81$). 85.7% of man and 14.3% of woman had thrombocytosis (χ^2 , $p=0.09$).

Conclusion. Our results show that thrombocytosis is often observed in NSCLC patients and is associated with the higher stage of disease, anaemia, leucocytosis and male gender.

Acknowledgements. None.

Labor planning management for HIV positive patients in Latvia: type of labor depending on viral load, vertical transmission prevention

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Background. The HIV virus multiplies in the cells of the immune system, affecting the body's defences against infectious diseases. WHO statistics show: 36.9 million HIV infected in 2017, only 59% (21.7 million) receiving ART. CDC of Latvia data: 19.0 cases of HIV per 100,000 registered in 2017; 2016 - 18.5 per 100 000, compared to European CDC: 5.9 cases per 100,000 in EU / EEA countries in 2016. HIV diagnosis during pregnancy is associated with the need to initiate therapy, adequate provision, control of viral load, prevention of complications for the patient and reduction vertical transmission risks to the child. Vertical HIV transmission is the most common cause of HIV infection in children worldwide. ART reduces the viral load in blood, secretions and prevents pre-exposure (transplacental) of the child. Post-exposure prevention: ART after birth. Guidelines suggest, if viral load >10E³ ml, an elective cesarean section is performed (38 weeks of gestation) to avoid premature rupture of membranes and the onset of labor. Zidovudine is administered intravenously prior to surgery. For viral load <5E1 ml, delivery is planned through natural delivery routes. In cases of non-detectable viral load after 34-36 weeks of pregnancy, the risk of transmission is 0-0.5%.

Aim: to study labor planning management for HIV positive pregnant women depending on therapy, viral load, other infections.

Materials and methods. Retrospective study was performed from November 2016 to December 2018. The study included pregnant women diagnosed with HIV infection, who were hospitalized to provide labor assistance at Riga Maternity Hospital. Patient medical records were used for data collection. Data statistically analysed. Patient sensitive data have not been disclosed.

Results. 116 patients were analysed. 31% (n = 35) have had vaginal deliveries, 69% (n = 81) operative, 14% (n = 16) of those had co-infection with HCV. Post-exposure prophylaxis in neonates given in 100% (n = 116) of cases. Treatment during pregnancy: regular 67% (n = 78), irregular or no treatment: 33% (38). Non-observed patients 8% (n = 9). The data is in the process of obtaining and processing, and it is not possible to present the results fully at the time of the abstract submission. Preliminary research data will be presented at the conference.

Conclusions. The most common problems leading to poor infection control include: late diagnosis, and patient inequality in the use of medication and outpatient care.

The spectrum of clinical manifestations of syphilis monoinfection and other sexually transmitted diseases coinfection patients

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Background. In general, sexually transmitted infections constitute a serious health problem either in young people, as well as in adults. Despite the fact, that the number of patients infected with syphilis is decreased, it remains a great risk factor for developing serious complications in patient future life if they stay untreated. Syphilis has a plenty of clinical manifestations, and its symptoms may look like many other diseases. However, typically infection follows a progression of stages that can last for weeks and even years.

Aim. The aim of the study was to detect the most common and otherwise rare clinical features of syphilis.

Methods. In study were included 107 patients (34 male and 73 female, 17-72 years old), diagnosed with syphilis at Riga 1st Hospital from January 2016 to December 2017. Surveillance data was mapped to symptoms according to syndrome groups (cutaneous, mucous, lymphatic, neurologic), disease stages and STD coinfection groups.

Results. *Lues primaria* was diagnosed in 7.5% of patients (n=8), *lues secundaria* in 24.3% (n=26), *lues latens praecox* in 23.4% (n=25), *lues latens tarda* in 8.4% (n=9), *neurolyues* in 7.5% (n=8) and *lues in anamnesis* in 28.9% (n=31). More than half of patients were without any clinical signs of disease (55 patients were asymptomatic, 52 symptomatic), furthermore the main part of women was pregnant (n=42; 57.5%). The most frequent cutaneous sign was trunk roseolas (n=13; 12.1%), then trunk papules (n=7; 6.5%), palmo-plantar papules (n=5; 4.7%) and the rarest feature was *leukoderma* (n=1; 0.9%). Mucous manifestations were: oral papules (n=9; 8.4%), genital papules (n=6; 5.6%), genital ulcer (n=6; 5.6%), *condylomata lata* (n=3; 2.8%), oral ulcer (n=2; 1.9%). The main part of patients had syphilis monoinfection (n=77; 71.9%), but 28.1% of patients had STD coinfections: HIV in 4.7%, Ureaplasmosis in 9.3%, Mycoplasmosis in 1.9%, both Ureaplasmosis and Mycoplasmosis in 5.6%, VHC in 4.7% and both HIV and VHC in 1.9%.

Conclusions.

1) There was no statistically significant difference among syphilis monoinfection and other STD coinfection cases, but HIV infected individuals had an increased incidence of development of neurological complications such as headaches (42.9%) and diplopia (14.3%).

2) Early recognition and reporting can minimize the spread of disease to healthy persons and prevent complications by ordinating adequate treatment for infected persons.

Acknowledgements. Study is accomplished with support of my supervisor, Professor Ilona Hartmane, Head of Clinical Centre of Skin and Sexually Transmitted Diseases, Riga 1st Hospital, Latvia.

Urinary catheter use in University Hospital in Latvia

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Background. Catheter associated urinary tract infections (CAUTI) are one of the most common types of hospital-acquired infections (HAIs). The CAUTI contributes to a prolonged hospitalization, increased antibacterial resistance and healthcare costs. The greatest risk-factor for acquiring the CAUTI is the use of urinary catheter. The CAUTIs can be avoided if a bundle of preventive strategies in the clinical routine are implemented.

Aim. To assess and reduce cases of unjustifiable use of urinary catheters in University Hospital in Latvia.

Methods. Prospective interventional study was performed in Pauls Stradins Clinical University Hospital (PSCUH) in the period between December 2017 and December 2018. To assess the frequency and the objective need in catheterization patient files in 26 PSCUH departments were surveyed in December 2017. Study protocol was based on the European Center for Disease Prevention and Control Point Prevalance Survey protocol. Four departments with a high urinary catheter use were selected for participation in the current study: a department of urology, neurology, neurosurgery and kidney transplantation. Interventive methods, mainly focused on educating the medical staff, were implemented. In December 2018 a repeated PPS was performed in selected wards. Furthermore, an additional survey was carried out in the period from August 2018 to December 2018, when the number of the catheterized patients and all new catheterization cases were documented on a daily basis.

Results. The first PPS involved 609 patients, 107 (17.6%) of whom had an indwelling urinary catheter. The second PPS in four selected wards involved 107 patients. There was observed a reduction in a number of catheterized patients comparing to the years of 2017 and 2018, when 25 (43.1%) had a urinary catheter in 2017 and 19 (13.9%) - in 2018. The indication for placement of the urinary catheter was appropriately stated in 17% of cases in 2017 and 21.1% in 2018 in the selected departments. Since August 2018, catheter-days per patient-days had reduced in the neurosurgery and neurology departments in the range from 0.13 to 0.07 and 0.27 to 0.17, respectively. New cases of catheterisations per 1000 patient-days decreased in both departments: from 55.1 to 43.8 in neurosurgery and from 27.8 to 21.7 in neurology.

Conclusion. The frequency of patient catheterization in PSCUH was not higher compared to the scientifically observed data. An interventional approach revealed successful outcomes when unjustifiable catheter use frequency and length decreased. We can recommend that interventions should be continued.

Acute kidney injury association to creatinine and high-sensitivity troponin measurement changes after cardiac surgery

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Background. Acute kidney injury (AKI) is common clinical syndrome that increases mortality, health-care expenses and overall hospital days. As well as improving patient's quality of life after cardiothoracic surgery.

Aim. To analyse the diagnostic value of high-sensitivity troponin T (hsTnT) in the settings of cardiac surgery-induced AKI. Search if there are risk factors that could affect kidney injury.

Materials and methods. A retrospective study using medical history records in Pauls Stradins Clinical University Hospital, Latvian Centre of Cardiology surgery. MDRD formula is used to calculate glomerular filtration rate. Statistical analysis is performed by Independent Samples Test, Chi-Square Tests.

Results. The study included 30 patients, 12 female and 18 male patients. Patients were classified in such groups: AKI group, non-AKI group. Patients in non-AKI group (80.0%, n = 24) mean age 65.167 (SD = 12.09). Group with AKI (20%, n = 6) mean age 63.33 (SD=10.65). In non-AKI group 9 out of 10 patients had such comorbidity as diabetes mellitus. In non-AKI group 21 out of 27 had primary hypertension, however, in AKI group the prevalence of hypertension was only 6 out of 27 (p = 0.36). Body mass index – BMI (kg/m²) in group of AKI - mean 29,47 kg/m² (SD=5.06), in non-AKI group - mean 34,43 kg/m² (SD = 9.73, p=0.089). The mean time of anaesthesia in AKI group is 264.16 minutes (SD = 69.31) in non-AKI group mean anaesthesia time is 206.04 minutes (SD = 52.27, p=0.03). Mean artificial blood circulation time in AKI group is 98,21 minutes (SD = 28.73), in non-AKI – 121.0 minutes (SD = 71.99). Post-operative atrial fibrillation was detected in non-AKI group in 6 cases out of 8 (p= 0.68). The average amount of bed days is 10.31 days (in both groups). Creatinine clearance in non-AKI group patients tended to decrease comparing to creatinine level before the surgery. In acute kidney damage group patient's creatinine clearance is increasing in dynamics, however, it's returning to creatinine baseline very slowly. Hs-Troponin T level in risk group patients is higher than in those without any risk factors. In dynamics hs-troponin T level reduced slower than in those patients who were without any risk factors. Mean hs-troponin T level in AKI is 21069 ng/L, therefore in non-AKI group – 11998 ng/L.

Conclusions. This is a pilot study. For study to be statistically reliable, there is need of more patients to be enrolled in this study.

The quality of life assessment in patients with severe (grade II-III, IV) esophageal achalasia after laparoscopic Heller myotomy and Dor fundoplication

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Background. Achalasia is a primary esophageal motility disorder characterized by the absence of esophageal peristalsis and impaired relaxation of the lower esophageal sphincter in response to swallowing. There are different treatment options for achalasia- pharmacologic treatment, pneumatic dilation, Heller myotomy (HM), peroral endoscopic myotomy, however, each method has different long term treatment efficiency.

Aim. The aim of the current study was to evaluate the quality of life (QL) in patients with severe (grade II-III, IV) esophageal achalasia after laparoscopic HM and Dor fundoplication (DF).

Methods. Four patients who underwent surgical treatment from 2015 to 2018 were enrolled in the study. Three patients had grade IV, one patient- grade II- III achalasia. A standardized quality of life assessment questionnaire (GQLI) which contained 36 questions with 5- point Lickert scale (0- 1- 2- 3- 4), each with a score of 0- 4 points was used. Calculation of the score: most desirable option- 4 points, least desirable option- 0 points; GQLI score: sum of the points. Global score: 0- 144 points; higher score= better QL; normal= 125 points. The intensity of the most common symptoms of achalasia (heartburn, vomiting, regurgitation, dysphagia, retrosternal oppression, stagnation) using the numeric rating scale (0- 10)- 0: none, 10: maximum possible- postoperatively was also assessed.

Results. GQLI scores for patients were 114 (9% less than normal quality of life score (NQLS)), 130 (4% above NQLS), 115 (8% less than NQLS) and 106 (15% less than NQLS). One patient didn't have trouble with swallowing food, other three had it a little. Two patients didn't have nausea, other two had it a little. Two patients didn't have regurgitation, one had it a little, one- some of the time. Postoperatively none of the patients had evaluated heartburning intensity by more than moderate (score 5). Three patients had evaluated vomiting intensity as score 0 (none). Two patients never had regurgitation, dysphagia and stagnation postoperatively.

Conclusions. Patient QL has been demonstrated to be improved after laparoscopic HM and DF. All patients had almost normal or above normal GQLI (85- 104%). None of the patients had the intensity of any of the most common symptoms of achalasia more than moderate. Three patients had none or minimal intensity (0- 2) of these symptoms. Patients with severe achalasia demonstrated good GQLI after laparoscopic HM and DF.

Acknowledgements. This research received no specific grant. The authors declare that there is no conflict of interest.

Accuracy of the serum biomarkers in the detection of atrophic gastritis in Kazakhstan population

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Background. Serum pepsinogens (Pg) detection is the best available non-invasive method for non-invasive detection of gastric corpus mucosal atrophy. Very limited numbers of studies so far have been performed in Kazakhstan and other Central Asian countries.

Aim. To estimate the adherence of Kazakhstan individuals to serum pepsinogen test and its accuracy in the detection of gastric atrophy.

Methods. Pepsinogens were detected by latex agglutination method (Eiken Chemical., Tokyo, Japan). Two cut off values were used: to define decreased Pg values - $\text{Pgl/PgII} \leq 3$ and $\text{Pgl} \leq 70$ ng/mL; for severely decreased Pgs - $\text{Pgl/PgII} \leq 2$ and $\text{Pgl} \leq 30$ ng/mL. Biopsies for histopathology were obtained according to the updated Sydney system; corpus moderate to severe atrophy was considered for the current analysis.

Results. Data from altogether 157 individuals were available for the current analysis. Moderate to severe corpus atrophy was present only in 2 cases (1.3% of the study subjects). In 42 cases $\text{Pgl/PgII} \leq 3$ and $\text{Pgl} \leq 70$ ng/mL was identified, the sensitivity of Pg test with this cut-off value was 28.9%, specificity 86.4%, overall accuracy 36.9% for detection of moderate to severe atrophy in the corpus; 15 subjects had $\text{Pgl/PgII} \leq 2$ and $\text{Pgl} \leq 30$ ng/mL, the sensitivity of the Pg test was 11.1%, specificity 100.0%, overall accuracy 23.4% with this cut-off values.

Conclusions. Histologically confirmed moderate to severe atrophic gastritis was identified only in a few cases, while decreased Pg values were identified in a substantially larger study population. The current study suggests that pepsinogen testing could be performing worse in Central Asian populations than in similar study populations in Europe and East Asia.

Acknowledgements. The work was supported in part by the ERDF project in Latvia “*H.pylori* risk stratification, optimization of management and interplay with other gastric microbiota within international research activities”

Cholelithiasis in Kazakhstan: some incidence aspects

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Background. Cholelithiasis at the present stage is considered as an interdisciplinary problem and a polyetiological incidence, many factors influences in the development: genetic aberrations, eating habits, disturbance hormone metabolism, cholesterol and other causes. Despite the high level of diagnosis and treatment of cholelithiasis, the for many years study of its clinical and epidemiological features doesn't lose its relevance.

Aim. The purpose of the research is to study the incidence of cholelithiasis in Kazakhstan.

Materials. Analyzed the accounting and reporting data of the Ministry of Health of the Republic of Kazakhstan (Form 12) on new cases of cholelithiasis (ICD 10 - K80) in the republic as a whole for 2006-2015. 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. In Kazakhstan, 115,817 new cases of cholelithiasis were registered, of which in children (under 15) – 4,318 (3.7%), in adolescent (15-17) – 2,546 (2.2%) and adults (18+) – 108,953 (94.1%) (table).

Table. Cholelithiasis in Kazakhstan (2007-2016)

Age group	Number (%)	P±m	95% CI	T, %
Children under 15 years	4,318 (3.7)	10.9±1.7	7.5-14.2	-9.4
Adolescent (15-17)	2,546 (2.2)	30.6±2.3	26.1-35.2	-5.1
Adults (18+)	108,953 (94.1)	94.8±4.9	85.1-104.4	+4.6
Total	115,817 (100.0)	70.7±3.2	64.4-77.0	+3.7

The average annual incidence of cholelithiasis among the entire population of the republic was $70.7 \pm 3.2^0/_{0000}$ and in dynamics had tendency to increase from $68.5 \pm 0.7^0/_{0000}$ (2006) to 87.9 ± 0.7 in 2015, and the average annual growth rate of the equal indicator was $T = +3.7\%$.

Among the studied population groups, the high incidence of cholelithiasis was detected in adults – $94.8^0/_{0000}$ (95% CI=85.1-104.4 $^0/_{0000}$), while the incidence in children under 15 years and adolescent was statistically significantly lower and amounted to $10.9^0/_{0000}$ and $30.6^0/_{0000}$ respectively. In dynamics, the indicators tended to increase ($T = +4.6\%$) in adults, and the incidence trends in children decreased (table).

Conclusion. Thus, the analysis of the incidence of cholelithiasis in Kazakhstan shows a steady increase trend, both in general and in the older age group. The obtained data require further immersed study and are recommended for monitoring and evaluating prophylaxis, early diagnosis and treatment.

Acknowledgements. The study supported by public association «Central Asian Cancer Institute».

Clinical indicator association with severity of acute and acute recurrent pancreatitis, preliminary data

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Background. Acute pancreatitis (AP) is inflammation of the pancreas that can cause local pancreatic complications: necrosis, abscess, or pseudocysts, systemic organ dysfunction, or both. The incidence of AP ranges 5 – 30/100,000. Considering the potential complications of AP, the total mortality rate is 5%.

Aim. The aim of the current study was to determine the prevalence of moderate severe and severe AP and identify the association of the clinical data (etiological factors, Neu/Ly, Plt/Ly, CRO/albumin ratio, levels of lipids, co-morbidity and medication used before, previously known recurrent acute pancreatitis) with severity grades of AP as in future possible predictive factors.

Methods. The study is a prospective cross-sectional study that included 18 patients till now (11 males), mean age 55 years (range 18 – 86) from Pauls Stradins Clinical University Hospitals gastroenterology, hepatology and nutrition therapy center. Inclusion criteria: patients signed agreement to participate, ≥18 years old, with at least 2 out of 3 criteria for diagnosis AP: typical abdominal pain; elevated serum amylase/lipase >3 times upper limit; typical changes in examination in imaging. A pre-developed questionnaire was used to collect the results of patients' clinical parameters. Severity of AP were evaluated by imaging data and Ranson's criteria. The collected data were analyzed using SPSS Statistics 22. Tests used in analysis – Chi-square, one-way ANOVA for univariate analysis, logistic regression for multivariate analysis to evaluate the association between risk factors and severity of AP.

Results. From all 18 patients moderate severe grade had 40% (n=7), severe 0,06% (n=1), other 59,94% (n=10) were mild AP. No cases of mortality were reported. Such factors as etiology, BMI, previously statins receiving, Charlson's Comorbidity index, levels of parameters: total cholesterol, ratio between Neu/Ly, Plt/Ly, CRO/albumin ratio did not show significant association with severity grades of AP. In univariate analysis only reported recurrent AP showed significant result (p=0,07). From 7 moderate severe AP 5 patient previously already had AP episodes. In multivariate analysis were included such factors as recurrent AP, total cholesterol level and Neu/Ly, Plt/Ly, CRO/albumin ratio. Still no clinical parameter showed significant level, excluding recurrent pancreatitis (p=0,03).

Conclusions. The results of our study present high prevalence of moderate severe grade AP in small cohort of patients. Previously reported AP episodes were significantly associated with moderate severe grade of AP. No other clinical parameters showed significant association with more severe AP.

Epidemiologic features of prevalence of colorectal cancer in big cities in Kazakhstan

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Background. Epidemiological study features incidence of colorectal cancer (CRC) and attempts to find reasons of differences of its occurrence rate ensure extension of knowledge in the field of etiology and development of preventive actions in fighting this pathology. Malignant tumors are one of the most important and most complicated problems of modern public health sector; namely, colorectal cancer belongs to commonly encountered tumors. This research is dedicated to study of specific features of prevalence of CRC in big cities in Kazakhstan.

Aim: Study prevalence of colorectal cancer in big cities in Kazakhstan.

Materials. Materials of the research are data of cancer care facilities of the country related to new cases of CRC. The research is retrospective for 2007–2016. Extensive, crude rate (CR) and age-standardized rate (ASR, world) of prevalence have been calculated according to conventional methods of medical statistics. Annual average values (M) and annual average rate of growth/decrease ($T_{gr/dec}$, %) have been defined.

Results and discussions – Over the period of study 27,252 cases of CRC were registered in Kazakhstan. Average age of patients with colorectal cancer is 64.3 ± 0.2 , while annual average rate of growth is $T_{gr} = +0.5\%$. Annual average RG of prevalence of CRC equals to $16.4 \pm 0.04\%$ ($T = +1.7\%$).

In comparison of standardized indicators of prevalence in big cities of the country, the maximum prevalence was revealed in Astana (26.3 ± 1.8) and had a tendency to growth ($T = +7.3\%$), while in Almaty (22.4 ± 0.7) it tends to reduction ($T = -1.1\%$). However, when comparing population size a difference by 2.5 times in Almaty (3,257) and in Astana (1,257) is indicated (Table).

Table. Colorectal cancer in Kazakhstan (2007–2016)

Indicators	Kazakhstan	Almaty	Astana
Amount (%)	27,252 (100%)	3,257 (11.9%)	1,257 (4.6%)
Average age (T, %)	64.3 ± 0.2 ($T = +0.5\%$)	65.7 ± 0.2 ($T = +0.1\%$)	63.6 ± 0.4 ($T = +0.1\%$)
CR (T, %)	16.4 ± 0.4 ($T = +1.7\%$)	22.5 ± 0.6 ($T = -1.8\%$)	17.3 ± 0.9 ($T = +5.8\%$)
ASR (T, %)	17.7 ± 0.4 ($T = +1.4\%$)	22.4 ± 0.7 ($T = -1.1\%$)	26.3 ± 1.8 ($T = +7.3\%$)

Conclusion – Thus, some epidemiologic features of prevalence of malignant tumors of colorectal cancer over the last years in big cities in Kazakhstan were identified, which are recommended to use in monitoring and evaluation of cancer activities.

Acknowledgements. The study supported by public association «Central Asian Cancer Institute».

Spacio-temporal epidemiological aspects of esophageal cancer development in Kazakhstan

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Background. The research of the regional characteristics of the disease development is highly important due to the practical needs of incidence data among the population in different regions. The studies in this area indicate higher geographic variability and trend movement. The issues of esophageal cancer (EC) are relevant worldwide. EC is the eighth most common cause of cancer in the world, which leads to approximately 400,000 deaths per year. There is a high scientific and practical interest to study this issue in Kazakhstan, especially from the regional perspective given the trends.

Methods. Provided data on new cases of EC for the period 2007–2016. A retrospective study with descriptive and analytical methods of epidemiology used as the main research approach.

Results. There were 13,204 new registered cases of EC in Kazakhstan within the abovementioned period. The average age of EC patient within the country was 66.9 years. The average annual age-standardized incidence rate (ASR) of the overall population in Kazakhstan was 8.8 ± 0.2 , and it tended to decline (Table).

Table. Incidence rates of EC, 2007–2016

Region	Number(%)	ASR, ⁰ / ₀₀₀₀	95%CI	T, %
Low level regions:Almaty city	617(4.7)	4.3±0.3	3.8–4.9	–5.6
Medium level regions:Jambyl	735(5.6)	9.3±0.3	8.7–9.8	–0.9
High level regions:Kyzylorda	1115(8.4)	25.8±2.7	20.6–31.1	–9.5
Kazakhstan	13204(100)	8.8±0.2	8.3–9.2	–2.3

The detailed regional research of EC ASR shows that the maximum incidence rate of the EC was set in the Kyzylorda region of $25.8^0/_{0000}$. The minimum incidence of esophageal cancer is registered in Almaty $4.3^0/_{0000}$.

The analysis of EC incidence in dynamics reveals higher indicators, while the overall increase in 2016 compared with 2007 is $T = -2.3\%$.

Conclusion. The detailed regional EC incidence analysis has revealed areas with highest and lowest rates of disease spread and location – incidence control. The results enable the organizers of the health service to obtain an objective picture of regional EC incidence rate. It makes possible to organize events aimed at the prevention and early detection of EC cases, as well as to organize measures to reduce the influence of risk factors.

Acknowledgements. The study supported by public association “Central Asian Cancer Institute”.

Experience of using fecal immunochemical tests (FIT) in local group of patients with high-risk of colorectal cancer (CRC)

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Background. CRC is the third most common cancer worldwide. Incidence of CRC has been increasing steadily in recent years in Russia (in 2016 – 44.6 per 100 thousand persons). In the Yaroslavl Region in 2016 this index constituted 65,7 per 100 thousand persons. Today immunochemical FOBTs are the most reliable tests for detecting colorectal neoplasia.

Aim. The aim of the current study was to examine the possibilities of using FIT in a local group (employees of the petrol plant) who have the high risk of CRC.

Methods. For carrying out screening 885 workers have been invited (aged 40 and over), everyone was surveyed so that risk factors of CRC could be detected. The test «Colon View» Hb and Hb/Hp) was done 3 times among 849 employees (95.9%). The rate of the Hb and Hb/Hp level was below 40 mkg/l (according to the instruction). The statistical analysis was made by MedCalc V12.6.1.0.

Results. 237 (27.9%) persons were FIT - positive. The median level Hb in all tests (94.5) was higher than level of Hb/Hp (62.1) ($P < 0.05$). The median level Hb in all tests was higher among employees at the age of 50-59 (119.1) than in the groups aged 40-49: (78,2) and aged 60 and over: (57.4) ($P < 0.05$). All FIT-positive patients were referred to colonoscopy that was performed among 118 (49.8%) individuals. Hyperplastic polyps were identified in 22 (18.6%) cases, adenoma – in 32 (27.1%), diverticulosis in 7 (5,9%), hemorrhoid – in 15 (12.7%), colitis - in 7 (5.9%), colorectal cancer in 5 (4.2%) cases and in 30 (25.4%) cases the colon pathology was absent. With the aim of diagnosing adenoma and CRC test sensitivity (Se) when applying Hb analysis constituted 75.4%, specificity (Sp) constituted 52.1%, although the best indexes of Se and Sp were observed while using the threshold level of Hb - 200 and over: Se –80.9% и Sp – 60.0%, AUC 0.763 (CI 0.690-0.851).

Conclusion. High prevalence of FIT-positive patients detected at the local refinery is likely to be associated with the high risk of developing CRC in this particular category of people that are due to undergo colonoscopy as the next stage of investigation, especially the group aged 50-59, in which Hb levels were the highest. The carried-out colonoscopy taped high percent of precancerous pathology of colon. Two-stage screening of CRC allows to reduce the number of unreasonably conducted colonoscopies.

Acknowledgements. Nothing to disclose.

Cartogram of liver cancer incidence in Kazakhstan

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Background. The necessity of medical and geographical description is due to practical needs in the data of sanitary condition of various regions, population sickness rates and spreading of disease. Medical geographical maps are perspective method of interconnection establishment between factors of geographical environment and human health condition, occurrence and dynamics of various diseases. According to IACR there are about 841,000 new cases of liver cancer (LC) registered in the world in 2018, and age-standardized rate is 9.3 per 100,000.

Indicators of LC incidence were defined in connection with administrative-territorial division of regions. In the investigation, we drew up a cartogram of LC incidence in Kazakhstan.

Aim. to draw the medical graphical map of liver cancer incidence in Kazakhstan.

Methods. Primary data were for registered patients with liver cancer (ICD 10 – C22) in the whole country during the period of 2007–2016. The data of the Statistics Committee of the Ministry of National Economy of the Republic of Kazakhstan of the total population of the republic were used. Age-standardized incidence rates of 10 years (2007–2016) were used in drawing up of diagram. It was applied method of diagram drawing up proposed in 1974 by Igissinov S.I. based on indication of average quadrant decline (σ) from average (\bar{x}).

Results. On the basis of abovementioned accounts, the diagram of liver cancer incidence in various medical geographical zones of Republic was drawn up. In this connection the following groups of regions were defined:

1. Regions with low degrees ($\bullet 9.2^0/_{0000}$) – Northern Kazakhstan (5.0), Kostanay (5.9), Almaty (8.0), Karagandy (8.2), Akmola (9.0). In completely 5 regions.
2. Regions with average degrees ($9.2-12.7^0/_{0000}$) – Eastern Kazakhstan (9.4), Zhambyl and Aktobe (10.4 and 10.5), Almaty city (10.7), Southern Kazakhstan (11.4), Pavlodar (11.6), Atyrau (12.4). Overall 7 regions;
3. Regions with high degrees ($\geq 12.7^0/_{0000}$) – Mangystau (13.8), Astana city (14.6), Western Kazakhstan (15.2), and Kyzylorda (18.6). In total 4 region.

Conclusion. In the result of drawn up graphical map of LC incidence with territorial differentiation were underlined “locuses” with low and high degrees. Received results allows to organizers of health service to acquire distinctive picture relatively to liver cancer incidence, level of sickness rate which gives the opportunity for acceptance of organized methodical activities according to earlier and prevention of LC and also organization of measures on decrease of risk factors influence power.

Acknowledgements. The study supported by public association «Central Asian Cancer Institute».

The assessment of malnutrition in inflammatory bowel disease patients

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Background: Inflammatory bowel disease (IBD) keeps rising over 21st century, reaching prevalence of 0,3%, with highest rates in Europe [Ng, S.C., et al., 2017]. Patients with IBD are at greater risk of malnutrition, with higher prevalence in Crohn's disease (CD) than ulcerative colitis (UC). Malnutrition correlates with increased rates of hospital admission, length of stay and therefore costs of treatment [Nguyen, G.C., et al., 2008]. In order to improve treatment outcomes in patients with IBD it is crucial to set proper nutritional support, therefore adequate screening is essential [Forbes, A. et al. 2017].

Aim: To evaluate a risk of malnutrition and nutritional assessment in IBD patients.

Methods: Our prospective pilot study was performed from September 2018 to January 2019. In total 30 patients aged ≥ 18 years were screened using Malnutrition Universal Screening Tool (MUST). MUST assesses body mass index (BMI), weight loss in last 3–6 months and severity of disease. 28 of patients also were evaluated by Bioelectrical impedance analysis (BIA)

Results: We assessed 30 patients, 13 (43%) females and 17 (57%) males, between age of 18 to 85 years, with average 42. Hospitalized were 13 patients. 15 (50%) of them had UC with average Mayo score 4.5 and 15 (50%) had CD with average Crohn's disease activity index (CDAI) 155. According to screening tool MUST, 15 (50%) of patients were at high risk of malnutrition (score ≥ 2) and they needed nutritional support, 11 (73%) of them received it. All 11 patients received enteral feeding, 3 patients had additional parenteral peripheral feeding and 1 parenteral central feeding. 2 (7%) patients were at medium risk (score 1) which requires observation and 12 (40%) at low risk group (score 0). BIA analyze found that 14 (52%) patients had reduced optimal body weight and soft lean mass (SLM), 12 had also reduced body fat. 4 of them had MUST ≤ 1 and 10 had MUST score ≥ 2 , but 2 patients with MUST ≥ 2 , did not show significant changes in BIA. 12 (73%) of CD patients and 6 (40%) of UC patients had reduced SLM.

Conclusions: Screening system MUST appears to be effective for evaluation of necessity for nutritional support. IBD patients with increased disease activity had higher MUST score and reduced muscle and fat mass in BIA. Additionally, BIA can be helpful for detection of unrecognized body composition disbalance for IBD patients in remission, with higher risk of malnutrition in CD patients.

Next generation sequencing derived miRNA signatures for active ulcerative colitis

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Background. MicroRNAs (miRNAs) are short non-coding RNAs that regulate gene expression. Growing number of studies have shown that miRNAs are highly involved in different inflammatory diseases including ulcerative colitis (UC). To date, miRNA deregulation profiles in active UC have not been fully explored.

Aim. The aim of this study was to evaluate and compare miRNA profiles in tissues of active UC, UC in remission (inactive UC) and healthy controls.

Methods. In the initial stage, miRNAs were sequenced in tissue samples of 32 healthy controls, 23 active UC and 21 sample of UC in remission using next generation sequencing platform. Most deregulated miRNAs were further validated in a second cohort of individuals with 38 healthy controls, 38 active UC and 36 inactive UC patients using RT-PCR based arrays. Statistical analysis was performed by using HTqPCR package. In order to identify the overall similarity structure of the miRNA expression profiles, a multidimensional scaling (MDS) analysis using Spearman's correlation distance (1-correlation coefficient) was performed.

Results. Next generation sequencing results of tissue samples from patients with active UC and healthy controls revealed 108 differentially expressed miRNAs, while 74 miRNAs were deregulated comparing active UC and UC in remission. Interestingly, only 31 deregulated miRNAs were found comparing healthy control and inactive UC tissues. In the validation phase, eight miRNAs (hsa-miR-223-3p, hsa-miR-155-5p, hsa-miR-146a-5p, hsa-miR-431-5p, hsa-miR-146b-3p, hsa-miR-493-3p, hsa-miR-1180-3p and hsa-miR-424-3p) have been confirmed as consistently deregulated when comparing active UC and healthy controls. In parallel, only three miRNAs (hsa-miR-223-3p, hsa-miR-431-5p and hsa-miR-1180-3p) were confirmed as deregulated between healthy controls and inactive UC tissues.

Conclusion. Ulcerative colitis has unique miRNA signatures in colon tissues comparing active disease stage and disease in remission, which also differ from healthy controls. Furthermore, individuals with UC in remission have a more comparable miRNA expression profile with healthy controls than with active UC.

Acknowledgements. The authors declare no conflicts of interest.

Prevalence of liver steatosis and its association with severity of chronic pancreatitis.

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Background. Chronic pancreatitis (CP) is complicated inflammatory disease which leads to pancreas functional insufficiencies and often pronounced pain syndrome. Less data can be found in literature about fatty liver disease in this population. Still alcohol abuse is often as etiological factor, as well part of patients has diabetes mellitus and dyslipidemia. We hypothesized that fatty liver disease is often found and affect grade of CP severity.

Aim. To analyze liver steatosis prevalence in CP patients and to evaluate its association with chronic pancreatitis severity.

Methods. Study was carried out as cross-sectional research in Gastroenterology, hepatology and nutrition Centre Pauls Stradins Clinical University hospital during year 2016–2019. The clinical parameter (like demographic data, etiological factors, endocrine, exocrine insufficiency, pain syndrome) and abdominal computed tomography (CT) scan images of patients were collected. The severity of CP disease was assessed by M-MANNHEIM classification. Unenhanced abdominal CT scans, which were done due to clinical state of patients, were reevaluated retrospectively. Liver and spleen attenuation were measured in Hounsfield units (HU) to diagnose liver steatoses (liver attenuation <10HU than the spleen was criteria). The collected data were analyzed using SPSS Statistics 22. Tests used were Chi square, Kruskal's-Wallis and logistic regression. Results were considered statistically significant at $p < 0.05$.

Results. 73 CP patients were included (54 males; mean age 51 years within range 29–86). Mean BMI was 23.3 cm/m² (± 4.48 cm/m²).

30% as etiological factor was alcohol abuse, 10% nicotine, 22% both, 30% other causes. 23% no chronic pain reported, 47% had pancreatitis relapses, 30% had chronic pain syndrome.

48% had exocrine insufficiency, 27% diabetes mellitus (mean HbA1c level 7,2% \pm 2.2%). ALT mean level was 57.5 (\pm 51.12) U/l, total cholesterol 4.67 (\pm 1.11) mmol/l.

By CT scans measurements 60% of included CP patients had liver steatosis. No significant association was found between steatosis and HP severity grade.

In univariate analysis was found association between CP severity and with such factors as exocrine insufficiency ($p < 0.001$), chronic pain syndrome ($p = 0.02$), decreased BMI ≤ 18.5 cm/m² ($p = 0.007$) and calcificates in pancreas ($p = 0.036$).

Steatosis was significantly associated with pancreatitis relapses episodes in CP (OR 7.5; CI (95%) 1.445–8.862; $p = 0.016$). 63% (n=19) patients with pancreatitis relapses history had liver steatosis.

Conclusion. We reported prevalence of liver steatosis in CP 60%. No significant association with severity of CP was found. Still, steatosis in our study was associated with increased risk of pancreatitis' relapses in CP.

Association Between Gastroesophageal Reflux Disease, Gastric atrophy and *Helicobacter pylori* Infection in Latvia

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Background. General trends show a decrease in the overall prevalence of *Helicobacter pylori* infection (HP) and increase in gastroesophageal reflux disease (GERD) and complications worldwide. The prevalence of both GERD and HP can vary substantially by population. Studies reporting lower prevalence of HP in patients with than without GERD have caused much debate.

Aim. Aim: analyse GERD in relation to the prevalence of HP and gastric atrophy in Latvia (HP prevalence 79%).

Methods. 1879 participants (ages 40–64) selected from the general population for the GISTAR study (1) in Latvia completed a detailed questionnaire (sociodemographic, lifestyle, medical data) and were screened for HP IgG and pepsinogens (Pg). Gastric atrophy was defined as PGI/PgII \leq 3 and PGI \leq 70 ng/ml. Participants were divided into two groups based on GerdQ score: \geq 8 (GERD likely) and $<$ 8 (unlikely). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for GERD and HP, and atrophy; adjusted ORs (aORs) were calculated after adjusting for previously identified GERD risk factors.

Results. The prevalence of GERD was 15.4% (289), HP infection 55.5% (1042) and atrophy 7.2% (136/1879). HP was positive in 52.6% of those with and 56.0% of those without GERD ($p=0.29$), while atrophy in 3.1% of those with and 8.0% without GERD ($p<0.01$). GERD was inversely and significantly associated with atrophy (OR 0.37; CI 0.19, 0.74) but not significantly with HP (OR 0.87; CI 0.68, 1.12). After adjusting for GERD risk factors identified previously (gender, income, body mass index, consumption of \geq 400g fruits and vegetables daily, meals per day, proton pump inhibitor use, history of peptic ulcer disease, arterial hypertension), GERD remained inversely associated with atrophy (aOR 0.31; CI 0.14, 0.68), while HP remained not significant (aOR 0.91; 0.68, 1.21).

Conclusion. Our results show an inverse association between gastric atrophy and GERD. There also seems to be an inverse trend between GERD and HP, possibly as a result of gastric mucosal atrophy. More research is necessary to determine the clinical significance thereof.

Acknowledgements. The study was funded by project nr. 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” of the Latvian Council of Science.

Views of Family Physicians on Follow-up Care of Colorectal Cancer Patients

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Background. Family physicians (FPs) are involved in the care of colorectal cancer patients, but the role of FPs is not defined in Latvia, and it remains unclear for how long colorectal cancer patients should be followed up, what tests should be done, and who should be conducting the follow-up.

Aim. Therefore, FPs' were surveyed about their role, comfort and confidence in the follow-up care of colorectal cancer patients and elicited opinions on improving the transfer of care from oncology specialists to FPs.

Methods. 62 FPs registered in Latvia were interviewed or answers were got by email using 16-point questionnaire form that addressed their comfort and confidence regarding surveillance for colorectal cancer recurrence, evaluation of the transfer of care from oncology specialists, access to palliative care, and suggestions for improving these processes.

Results. 54,8% of FPs were comfortable for surveillance of cancer recurrence, 59,7% rated the current transfer of care from oncology specialist to FP as poor or unsatisfactory. The most common problems identified were uncertainty regarding the colorectal cancer markers (45,2%), frequency (71,0%), and duration (77,4%) of surveillance testing, uncertainty about whether the patient's oncologist is providing preventive health care or FP (53,2%), and the access level to palliative care was not sufficient (80,6%). During interviews 54,8% of FPs mentioned the necessity and potential benefit of markers' reimbursement in the primary care setting.

Conclusion. Study results suggest that levels of comfort and confidence of Family physicians on follow-up care of colorectal cancer patients were generally low. FPs need more specific guidance or recommendations regarding surveillance for colorectal cancer recurrence. There is a need for better communication and information exchange between oncology specialists and FPs regarding their patients. Discussions on the necessity of reimbursement of markers in the primary care setting and improved access to palliative health care could be beneficial for patients.

Acknowledgements. No conflicts of interest to declare and no specific funding for this work.

Diastolic dysfunction of the left ventricle in the development of chronic heart failure

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Background. Diastolic dysfunction of the left ventricle is one of the leading mechanisms for the formation of chronic heart failure.

Aim. The aim of the current study was identified factors of risk for the development of chronic heart failure.

Methods. A clinical and instrumental study of 333 patients aged 39–86 years was performed. The grounds for inclusion in the study were sinus rhythm, essential arterial hypertension, chronic ischemic heart disease, chronic heart failure, myocardial infarction in the past, after which at least six months passed. Statistical data processing was performed using Statistica v 6.0, the results were evaluated using non-parametric methods. Comparison of groups was performed by constructing tables according to the Pearson method. Spearman correlation coefficient was calculated. The method of multiple regression analysis was used to analyze the dependencies of the studied parameters.

Results. Diastolic dysfunction of the left ventricle (DDLV) type I (impaired LV relaxation) was diagnosed in 31.8% of patients, DDLV type II (pseudonormal filling) was diagnosed in 26.7%, DDLV type III (restrictive LV filling) was diagnosed in 5.1%; chronic heart failure (HF) occurred at 51.1%. Patients with various types of DDLV differed significantly in frequency of HF and NYHA classes of HF ($p < 0.001$). Chronic HF of NYHA classes I-II occurred in 30.2% of patients with DDLV type I. In patients with DDLV types II and III, chronic HF was diagnosed in 100% of cases. Patients with DDLV types II had HF of NYHA classes II and III. Patients with DDLV types III had HF of NYHA classes III and IV. A statistically significant strong relationship was found between DDLV and NYHA classes of chronic HF (Spearman $R=0.66$, $p=0.001$). Multiple regression analysis showed that the most significant risk factors for the development of chronic HF of high NYHA classes are DDLV and ischemic heart disease (IHD). The regression equation was as follows: $Y = -0.54 + 0.52 \times \text{DDLV} + 0.41 \times \text{CHD}$, $R^2 0.60$, $F 251.84$, $p < 0.001$, $SE 0.79$.

Conclusion. Diastolic dysfunction of the left ventricle is a predictor of the development of chronic heart failure. Diastolic dysfunction type II and type III is a significant risk factor for the development of chronic heart failure of high functional class NYHA.

Acknowledgements. No.

Differences in stress, anxiety and depression by gender and age of cardiovascular patients in Latvia

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Background. Associations have long been established between cardiovascular disease and a wide variety of risk factors, including non-modifiable variables such as age, sex, and family history, and modifiable atherosclerotic risk factors. The most important determinant of cardiovascular health is a person's age.

Depression, anxiety and stress are risk factors for several cardiovascular diseases. Psychological disorders and cardiovascular events share some disturbances of inflammatory, hemostatic, and autonomic processes, thus suggesting fundamental pathways linking these different diseases. They affect the cardiovascular system through immune, neuroendocrine and behavioral pathways.

Aim. To investigate the level of stress, anxiety and depression in hospitalized cardiovascular patients by gender and age.

Methods. Cross-section study was performed in Pauls Stradins Clinical University Hospital (PSCUH) and Riga East University hospital (REUH) between March 2017 – July 2018. Study questionnaire contained 90 items, of them 23 were related stress, anxiety and depression and were further grouped in categories of levels. Patients from PSCUH and REUH were enrolled in the study. All patients were with cardiovascular diagnoses, 18-80 years old. Chi-square test was performed for the investigation of differences between genders in levels of stress, depression and anxiety of patients. Differences between ages were investigated using ANOVA test. We considered the level of significance as 0.05.

Results. Study sample included 948 patients, of them 418 from PSCUH and 530 from REUH, 547 (57.7%) of them were men. The mean age of patients was 65.9, SD=10.2 (range 18-80). The main diagnoses of patients were acute coronary syndrome 30.1%, atrial fibrillation/flutter 35.9%, planned coronary angiography and percutaneous coronary intervention 15.2%. We observed statistically significant differences between genders concerning levels of stress ($p = 0.03$) and anxiety ($p < 0.01$), but not in the level of depression ($p = 0.15$). Women displayed higher levels of medium and high levels of stress (60.3% versus 50.7%) and subclinical and significant levels of anxiety than men (22.6% versus 15.3%). There were no statistical differences in levels of stress, anxiety and depression between different ages of patients ($p = 0.27$, $p = 0.24$, and $p = 0.95$, respectively).

Conclusions. Hospitalized women with cardiovascular diseases should be more attended to reduce their level of psychological disorders. Probably there is a reason to propose help of professional psychologist or psychotherapists, especially for women.

Acknowledgements. No conflict of interest

Evaluation of clinical outcomes of surgical treatment of atrial fibrillation at the time of concomitant cardiac surgery in Paula Stradins Clinical University Hospital

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Background. Atrial fibrillation is common heart disease. Some forms of atrial fibrillation are persistent to treatment and last for years. Doctors can use another kind of treatment, such as surgical cardiac ablation to restore patients normal heart rhythm.

Aim. The aim of the study is to evaluate patients with atrial fibrillation, to find out the effectiveness of surgical cardiac ablation and to estimate the duration of the cardiac surgery.

Methods. A prospective retrospective study of patients after surgical treatment of atrial fibrillation at the time of concomitant cardiac surgery during the period from July 19, 2018 to July 19, 2019 in Paula Stradins CUH. Seven patients were observed.

Results. During the period from July 19, 2018 to December 30, 2018, 7 patients were observed and followed up after 3 months. The mean age is 65.86 +/- 14,17 years. All patients had congenital heart disease stage 2 by NYHA and atrial fibrillation (persistent form (n= 4, 57,14 %) and long persistent form (n= 3, 42,86%)) directly before surgery. The mean CHA₂DS₂ - VASc score was 2,71 +/- 1,38 (median-2 points, max-5). Stroke risk valued as high. No previous cardio-vascular event was found.

Two types of energy were used in procedures: extreme cold (cryoablation) and heat (radiofrequency). Full cryoablation (n=1, 14,29%), biatrial cryoablation (n=1, 14,29%), full left atrial cryoablation (n=1, 14,29%) and radiofrequency catheter ablation (n=4, 57,14%) were performed at the time of concomitant cardiac surgery – aortic valve replacement (n=3, 42,86%), mitral valve replacement (n=1, 14,28%) and repair (n=1, 14,28%), tricuspidal valve repair (n=2, 28,57%).

The mean cardiopulmonary bypass time was 120,42 +/- 30,59 minutes (median 121 minutes). The mean cardiopulmonary bypass time during aortic valve replacement was 92,67 +/- 15,27 (median 96 minutes), during mitral valve replacement -130 minutes, mitral valve repair - 151 minutes and tricuspidal valve repair – 148 +/- 16,70 minutes (median 151 minutes).

Six patients were discharged from the hospital with sinus rhythm and all patients were without any complications. The mean duration of hospital stay was 10,43 days +/- 3,2 (median 9 days).

After 3 months follow up, 6 patients (85,71%) had sinus rhythm, 6 patients (85,71%) were receiving rhythm control therapy, 4 patients (57,14%) were using peroral anticoagulants.

Conclusion. Concomitant surgical ablation of the atrial fibrillation during cardiac surgery has high effectiveness. The mean cardiopulmonary bypass time during surgical treatment of atrial fibrillation at the time of concomitant cardiac surgery was 120,42 minutes.

The effect of radiofrequency catheter ablation of premature ventricular complexes

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Background. Frequent idiopathic premature ventricular complexes (PVCs) can result in PVC-induced cardiomyopathy. Radiofrequency catheter ablation (RFA) is a way to treat medication resistant PVCs, fluoroscopy must be used during this procedure, therefore causing radioactive exposure to all participants.

Aim. The aim of this study was to assess the effectiveness of radiofrequency catheter ablation in patients with premature ventricular complexes.

Methods. The study included 72 patients who underwent RFA for the treatment of symptomatic frequent PVCs in Vilnius University hospital Santaros clinics between 2013 and 2017. The analysis was done using Microsoft Excel and SPSS statistical software.

Results. The study group consisted of 72 patients, 46 (63.9 %) women and 26 men (36.1 %). The mean age – 45.7 ± 17.4 years. 81.9 % of patients were symptomatic, most common symptom – heart palpitation (70.8%). 12.5% of patients suffered from syncope. Resistance to drugs was observed in 62 (87.3%) patients. The frequency of arterial hypertension – 30/72 (41.7 %), coronary heart disease – 7/72 (9.9 %), cardiomyopathy – 22/72 (30.6%), 23/72 (31.9 %) – heart failure. In 69.4 % of patients, 3D mapping system was used. 41.7 % of the procedures were performed manually, 58.3 % using magnetic Stereotaxis system. Mean duration of RFA procedure – 56.3 ± 25.8 min, mean fluoroscopy duration – 3.8 ± 6.9 min. Mean fluoroscopy duration in RFA guided by EAM (electroanatomic mapping) was 2.18 ± 2.98 min, and in RFA guided without EAM – 7.92 ± 11.2 min, $p < 0.05$. 51.4 % of all patients, the right ventricular outflow tract was the origin of the PVCs. 67 (93.1 %) patients had a positive effect after RFA, for 5 (6.9 %) patients RFA wasn't successful, $p < 0.05$. There was none of complications and procedure-related mortality.

Conclusion. Most common site of RFA for PVCs was right ventricle outflow tract. The use of electroanatomic mapping may reduce the fluoroscopy duration in the RFA of PVCs. According to our data RFA is effective and low risk treatment for pharmacological resistant PVCs.

Evaluation of cognitive disorders in patients with cardiovascular diseases

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Background. It is well documented that cardiovascular disease (CVD) can result in cognitive impairment, but it is becoming increasingly clearer that traditional risk factors for CVD, such as high blood pressure, diabetes, and dislipidemia are also associated with alterations to brain structure and cognition. CVD risk can lead to further functional debilitating changes, including cerebrovascular disease and dementia.

Aim. To investigate the association between a cardiovascular diagnoses and cognitive impairment.

Methods. Cross-section study was performed in Pauls Stradins Clinical University Hospital (PSCUH) and Riga East University hospital (REUH) between March 2017 – July 2018. All patients were with cardiovascular diagnoses, categorized in 8 groups, 18–80 years old, screened by Montreal Cognitive Assessment test (MoCA), with cutoff <26 for cognitive impairment. Quantitative data were reported as mean value and standard deviation (SD), in the analysis of two groups the t-test of independent selection was used. Qualitative data were displayed as number and percentage (n,%). In this study we considered the level of significance as 0.05.

Results. Study sample included 948 patients, of them 418 from PSCUH and 530 from REUH, 547 (57.7%) of them were men. The mean age of patients was 65.9±10.2 (range 18–80). The mean value of MoCA scale was 24.27 points, indicating mild cognitive impairment. There were 63.7% (n=604) of patients, whose MoCA scale was < 26 points. Statistically significantly higher MoCA score results were observed in 3 cardiovascular disease groups: atrial fibrillation/flutter, ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI), in patients whose education was <12 years (23.8±3.9) and in patients whose education was ≥12 years (24.6±2.9) (p<0.001). There was found statistically significant negative correlation between the age of patients and cognition (r=-0.34; p<0.001).

Conclusions. There is an association between particular cardiovascular diagnoses and cognitive functions. Two thirds of cardiovascular patients have light cognitive impairment. It is important to consider cognitive factors in the cardiovascular patients, and routine cognitive screening should be considered in higher risk patient subgroups.

Acknowledgements. No conflict of interest.

FFR_{CT} Potential in Preoperative Evaluation of Patients Undergoing Elective Carotid Artery Surgery

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Background. Patients undergoing elective carotid artery surgery are at increased risk for perioperative myocardial infarction and death due to earlier undiagnosed and untreated coronary artery disease (CAD) even if they have no previous clinical cardiac history. FFR_{CT} analysis (computed tomography derived fractional flow reserve) is noninvasive method to reveal CAD and influence of coronary artery stenosis to myocardium. FFR usage during invasive coronary angiography (ICA) improve patients' event-free survival.

Aim. To reveal and treat functionally significant CAD in patients without cardiac history who undergo elective carotid artery surgery, a strategy which may improve clinical outcomes.

Methods. We conducted prospective study at Pauls Stradins Clinical University Hospital, Riga, Latvia. Patients undergoing elective carotid artery surgery without history of clinically manifest CAD and previous coronary angiography or coronary revascularization were included. All patients received peri-operative management as recommended by current guidelines plus standard CT-scan. Acquired CT-scan images were sent to HeartFlow to design individual 3D coronary artery model and to calculate FFR_{CT}. Patients with FFR_{CT} of ≤ 0.80 in a major coronary artery were referred to ICA and potential coronary revascularization. Gender, age, weight, height, creatinine, comorbidities and used medicines, vital signs were recorded, and statistical analysis was performed by MS Excel and SPSS Statistics.

Results. Study included 44 patients. Majority were men ($n=34$, 77.3%), and mean age (\pm SD) was 68.8 ± 7.8 years. Prevalence of other risk factors and prehospital treatments was as follows: active smoking ($n=13$, 29.5%), hypertension ($n=37$, 84.1%), diabetes ($n=4$, 9.1%), antihypertensive therapy ($n=32$, 72.7%), statins 18, 40.9%) and anti-platelets ($n=24$, 54.5%). FFR_{CT} analysis revealed hemodynamically significant CAD in 32 (72.7%) patients. The therapy was optimized for all these patients which included statins, low-dose aspirin daily, ACE inhibitors in presence of arterial hypertension and lifestyle recommendations. Thirteen (40.6%) patients were scheduled for ICA, and 2 (6.2%) were continued on optimal medical therapy, 8 (25%) underwent percutaneous coronary intervention and the investigation is pending in 3 (9.4%) patients.

Conclusion. Patients without CAD history who are undergoing elective carotid artery surgery have high prevalence of undiagnosed hemodynamically significant CAD. Knowledge of the presence and severity of CAD may change patient management. Further studies are required to determine impact of this strategy on perioperative and long-term cardiovascular outcomes.

Acknowledgements. FFR_{CT} analysis is funded by Heartflow. This project is supported by University of Latvia Donor SIA "Mikrotikls". Foundation of the University of Latvia is administrator of this donation.

Predictors of acute kidney failure after open-heart surgery on infrarenal aorta

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Background. At this point, the question about reduction of the lethality in open surgical intervention on infrarenal aorta remains in connection with some of the risks of postoperative complications (from 18% to 55%). Acute kidney failure (AKF) ranks third among them.

Aim. The aim of the current study was to detect risk factors of AKF after open surgical intervention on infrarenal aorta.

Methods. We studied 26 patients, who had been operated on for Leriche syndrome and infrarenal aortic aneurysms. The results of our observing formed the basis of this work. 7 patients became the study group because they had been suffered from postoperative complications with acute kidney failure. 19 patients were shaped in the control group as they did not have AKF in postoperative period.

Nature of aorta's injury, existence of cardiovascular diseases and previous surgical intervention, laboratory and instrumental results and arterial hypertension were assessed during our work.

The results of our research were classified on the average value scale (mean) \pm standard deviation (SD). The non-parametric Mann-Whitney test was used to compare the average value groups. The difference in the categorical variables was also reviewed by the use of Pearson's χ^2 and the Fisher index. The differences were considered statistically significant at $p < 0,05$. Mathematical processing was conducted using software packages STATISTICA 10.

Results. Reliable connection was found between increasing risk of developing AKF and a high atherogenic coefficient as indicator of broke lipid metabolism ($p < 0,05$). All the patients in the study group were overweight ($p < 0,05$). Heart attack and other cardiovascular diseases were observed in a half of all cases in anamnesis ($p < 0,05$). There was hypotonic version of hemodynamic instability during peri-operative period ($p < 0,05$) in the study group. Bleeding was spotted at more than a half of all the patients also during peri-operative period ($p < 0,05$).

Conclusion. The results of surgical treatment considerably get worse in conditions of development of kidney failure that means necessary to count all the risk factors, including bleeding, peri-operative hypotension and source change of myocardium.

Evaluation of impact of some risk factors on severity of coronary artery disease in Ukrainian patients with STEMI

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Background. Cardiovascular diseases are the leading cause of morbidity and mortality in Europe. Recent statistics indicate a reduction in mortality from these pathologies in Western, Northern and Southern Europe over the past 30 years. But in Central and Eastern Europe, the situation is the opposite - mortality from coronary heart disease (CHD) still increase with time. The authors of the third edition of the statistics on cardiovascular morbidity and mortality in European countries illustrate the current sharp contrast between the countries of Eastern and Western Europe in the example of Ukraine, in which the mortality from CHD among males aged 65 and over is 14 times higher than in France, and among women of the same age - 25 times. The acute coronary syndrome (ACS) occupies a prominent place in the structure of cardiovascular mortality. In Ukraine over the 500 000 people died annually from CHD with mortality rate from ACS - 654 per 100 000 of population. The risk factors of ACS in Ukraine and their association with coronary artery damage severity have not been studied well.

Aim. The aim of current research was to assess association of coronary artery damage severity according to the data of coronary angiography (CAG) in patients with acute coronary syndrome with ST segment elevation with risk factors of cardio-vascular disease.

Materials and Methods. We have analysed the cases history of 112 patients with STEMI who were treated at the Sumy Regional Cardiology Hospital (Sumy, Ukraine). Association between risk factors (gender, weight, age, and the presence of arterial hypertension, family history of cardiovascular disease, smoking, diabetes and dyslipidemia) and coronary artery damage severity were assessed.

Results. Hemodynamically significant stenoses were not detected during the CAG in 14 patients, among which 9 were women. Two-vessel lesions were detected in 58 patients, in 27 - a single-vessel lesion, a three-vessel coronary artery disease was revealed in 13 patients. An association with male gender ($r=0.54$, $p=0.034$), overweight / obesity ($r=0.43$, $p=0.042$), age ($r=0.68$, $p=0.046$), and the presence of arterial hypertension ($r=0.49$, $p=0.033$) was revealed in patient with three-vessel lesions. These patients didn't have association with a family history of cardiovascular disease ($r=-0.09$, $p=0.17$) and smoking ($r=0.12$, $p=0.23$). We have found an association with type 2 diabetes ($r=0.61$, $p=0.018$) and dyslipidaemia ($r=0.43$, $p=0.041$) among patients with three-vessel lesions.

Conclusions. As primary prevention of STEMI must be measures aimed at controlling body weight, blood pressure, blood glucose levels and lipids levels.

Comparing quality of life in healthy children according to KIDSCREEN questionnaire in Latvia

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Background. When examining a child, it is crucial to ask for the subjective opinion of a child about their health. It is essential not only to gather objective information about a patient's health but also to have their attitude towards their well-being. In a normal prophylactic visit the doctor should engage with the patient asking about their personal point of view regarding their health, otherwise health problems can be misdiagnosed – such as tiredness and stress that is related to school and other activities.

Data about quality of life in healthy children in Latvia are very limited. At the same time this assessment is crucial for psychological, mental, physical and social management in schoolchildren.

Aim. The objective of the study was to analyse schoolchildren's health and well-being (health-related quality of life, HRQoL), including attitudes towards their general health, as well as the associations between age groups and different health related Quality of life dimensions.

Methods. The children group included 100 children aged 8 to 17 years at the general paediatrician's practice without chronic and congenital diseases. Participants were surveyed by a KIDSCREEN-52 questionnaire (Ravens-Sieberer U. *et al.*, 2005, The KIDSCREEN Group Europe, 2006). The questionnaire includes 10 HRQoL dimensions such as physical and psychological well-being, moods and emotions.

Patient participation was voluntary and random. SPSS Statistics 22 was used for the statistical analysis of data. Statistical analysis was performed using Spearman's correlation coefficient to evaluate any possible correlation between age and well-being, age and hopelessness, well-being and hopelessness.

Results. A total of 100 children were included in the study. The mean age of the patients was 14,5 and it ranged 7 – 17 years. Using Spearman's correlation test between age and general health or general health and hopelessness no significant correlation was found ($p > 0,05$). Using Spearman's correlation test between age and hopelessness significant correlation was found ($r_s = 0,38$, $p < 0,001$), therefore higher age comes with higher levels of hopelessness.

Conclusions. Correlation was found between age and hopelessness, but no significant correlation was found between age and general health or general health and hopelessness in children. In primary school the factor is new environment and in the teenage period one's opinion can be inflicted by relationships with other teenagers, school homework and outdoor activities. The study suggests that children growing up feel more hopeless which indicates a need for a more extensive study on the population to confirm this finding.

Frequency of colic depending on the type of feeding during the first year of life

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Background. Colic is inconsolable crying in infant that lasts many hours a day, starting in the second week of life and lasting until three months of age. Based on Wessel's Criteria – about 20–25% of babies meet the definition of “colic”. There is still no definite answer about the cause of colic. One of the reasons could be type of feeding, since formula-fed infants may be intolerant to certain proteins in formula.

Purpose. To detect the prevalence of colic and compare the frequency in respect to the feeding type of an infant.

Material and Methods. A prospective study was carried out through the internet during April, 2018 till December, 2018. Mothers of children (aged six months to seven years) were asked to answer an anonymous questionnaire about mothers age, pregnancy risk factors, gestational week and type of baby's delivery, mothers and baby chronic diseases, baby's feeding type during the first six months. The statistical analysis: χ^2 test.

Results. The total patient sample included data about 495 children; among them exclusive breast-feeding was reported in 50%(247/495), mainly breastfeeding (reported use of formula feeding only a few times) – in 7%(35/495), mixed feeding – in 37%(183/495), and only formula feeding – in 6%(30/495) of infants. In total, colic was reported in 80%(397/495) children. Among exclusively breast fed infants colic was reported in 73%(180/247) of cases, out of them: often – in 16%(39/247); sometimes – 32%(78/247); seldom – 25%(63/247) and never – in 27%(67/247). Infants, who were mainly breastfed, had colic in 86% (30/35), out of them: often – in 20%(7/35), sometimes – 40%(14/35), seldom – 26%(9/35), never – in 14%(5/35). Among infants with mixed feeding colic was reported in 87% (160/183), out of them: often – in 20%(37/183), sometimes – 43%(79/183), seldom – 24%(44/183), never - in 13% (23/183). Among formula fed infants colic was reported in 83% (25/30), out of them: often – in 33%(10/30), sometimes – 23%(7/30), seldom – 27%(8/30), and never – in 17% (5/30). The prevalence of colic was significantly lower in exclusively breast-fed infants 73%(180/247) compared to mixed 87%(160/183) and formula fed 83%(25/30) infants ($p<0.001$).

Conclusion. In the studied patient sample the prevalence of exclusive breast feeding was rather high. Exclusive breast feeding was associated with lower frequency of colic and in the majority of exclusively breast-fed children colic was reported rarely or never. Interaction of other factors (chronic diseases, mother diet etc.) associated with presence of colic should be studied further.

Dental situation according to international caries detection and assessment system of preschool children in Latvia

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Background. Dental situation in children in Latvia is poor comparing with a situation in other Europe countries. This includes insufficient hygienic and nourishing habits and resulted caries and gingivitis in early children ages. Additionally, situation may be influenced by place of living due to density of dental praxes and gap between living standards. Unfortunately, there is a lack of precise information about children oral health.

Aim. The aim of the current study was to investigate the dental situation of children in one kindergarten placed in a region with good socio-economic situation according to international caries detection and assessment system (ICDAS) which is suggested to identify restorations/sealants with the first digit, followed by the appropriate caries code.

Methods. Cross-sectional study was performed in a kindergarten in Latvia. The research population consisted of 4–7 years old children and their mothers. Children's dental situation according ICDAS codes was assessed during an examination by five dentists. Children's mothers were interviewed on their socio-demographic situation, feeding and habits of the child, and history of child diseases. Descriptive statistics was performed for all study variables, and for each surface of each primary tooth of children (ICDAS codes).

Results. The study sample comprised 182 children–mothers' pairs living in Ikšķile, Latvia. 57.7% of children were males, most of them (45.6%) aged 4 to 6. Number of missing teeth because of caries varied from one (6.6% of children) till 8 (0.5% of children). In D surface the mostly frequent ICDAS codes were 04 (for example, for one tooth in 11% of children), 05 (for one tooth in 8.8% of children), and 06 (for one tooth in 6.6% of children). In B surface the mostly frequent codes was 02 (for example, in one child there were 19 teeth with this ICDAS code). In L surface the mostly frequent code was 02 (for one tooth in 22% of children with the maximum in eight teeth). In M surface the mostly frequent code was 05 (for one tooth in 9.9% of children with the maximum in five teeth). In O surface the mostly frequent codes were 02, 03, 04, and 05 with the maximal number of five teeth with carries for 04 and 05 codes.

Conclusion. Parents should be promoted to pay attention on children's primary teeth situation, cleaning habits, diet, and regular visits to dentists.

Trends of live-born twins by gestational age and birth weight in Latvia, 2000 to 2016

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Background. One of the causes of adverse neonatal outcome, including neonatal, infant and adolescence morbidity, is preterm birth. In recent decades, the overall rate of preterm births has increased, as well as the prevalence of multiple gestations.

Aim. The aim was to examine trends in twin birth rates (TBR) by gestational week (GW) and birth weight (BW) in Latvia from 2000 to 2016.

Methods. Data from Medical Birth Register were used. Study design – retrospective cohort study. All live-born twins (n=8385) (2000 – 2016) were included in data analysis. Premature births were divided into subgroups: extremely premature birth (22-27 GW), very early (28-31 GW), premature (32-36 GW) and timely birth from 37th GW. BW was divided: extremely low (500-999 g), very low (1000-1499 g), low (1500-2499 g) and normal weight of 2500 g and more. Specific TBR according to the GW and BW were calculated.

Results. The TBR rose 87 percent from 2000 through 2016, from 17.1 (95% CI 15.4-19.0) to 29.9 (95% CI 27.7-32.3) per 1,000 live births. The average proportion of twins with BW (\leq 999g) is 1.7% (95% CI 1.4-2.0). From 1000g to 1499g is 3.8% (95% CI 3.4-4.2); 1500-2499g - 36.4% (95% CI 35.4-37.5) and more than half of twins are with BW (\geq 2500g) – 58.2% (95% CI 57.1-59.2).

A statistically significant increase in TBR by GW was observed in three groups. TBR in extremely premature birth slightly increase ($p < 0.05$) from 0.3 per 1000 live births to 0.6. In the premature (32 – 36 GW) group TRB increased ($p < 0.01$) from 5.9 to 10.9/1000 and in the timely birth group TBR increased ($p < 0.001$) from 9.8 to 17.4 in 2016. Slight increase in TBR by BW categories was observed for low (1500-2499 g) and normal BW (\geq 2500g), respectively from 6.5 to 10.3 ($p < 0.01$) and from 9.4 to 18.5 ($p < 0.001$).

17.7% (95% CI 16.7-18.8) of twins with low BW (\leq 2499g) observed in timely births (\geq 37 GW) and 29.5% (95%CI 27.8-31.1) with normal BW (\geq 2500g) in premature (32 – 36 GW) births.

Conclusion. The twin birth proportion with low BW has risen by 5.3% ($p < 0.01$) comparing year 2000 to 2016. Twin pregnancies with birth weight discordance are at higher risk of prenatal complications.

Acknowledgements. This study was supported by National Research Programme Biomedicine for Public Health (BIOMEDICINE). Research on acute and chronic diseases in a wide age-range children to develop diagnostic and therapeutic algorithms to reduce mortality, prolong survival and improve quality of life.

Physical development of premature children during the first year of life

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Introduction. An optimal nutrition of premature infants immediately after birth is a crucial factor for healthy development and steady weight gain is associated with better neurocognitive development. On the other hand, excessive weight gain can increase the risk of metabolic diseases later.

Aim. To estimate the weight and length increase of premature born children during the first corrected year of life.

Methods. Study was performed at Children's Clinical University Hospital, Latvia. We analysed data of all premature infants included into Follow-up programme in 2016. Children were divided in two groups: born \leq 29th week of gestation (1st group), \geq 30th week of gestation (2nd group). Weight and length mean percentile at the corrected age of 12 months was compared to population growth charts (percentiles) and to weight mean percentile at birth. Influence of comorbidities on growth was analysed. Statistical analyses: T-tests, Wilcoxon test.

Results. In total, 173 children (87(50.2%) boys) were included: 1st group contained 78(45%); 2nd group – 95(55%) children. Children, born small for gestational age(SGA) were 2.6%(n=2) and 4.2%(n=4) in the 1st and 2nd group, respectively. The most common morbidities were: respiratory distress(RD) (80.7%(n=63) and 51.5%(n=49)), intraventricular haemorrhage(IVH) (43.5%(n=34) and 12.6%(n=12)); sepsis (33.3%(n=26) and 10.5%(n=10)) in the 1st and 2nd group, respectively.

In the 1st group weight mean percentile in newborn and 12 months was 57.11% vs 51.08%;(p=0.15), in the 2nd group – 55.00% vs 69.50%;(p=0.03), respectively. The height mean percentile in newborn and 12 months was 67.30% vs 61.03%;(p=0.08) and 64.16% vs 67.54%;(p=0.40) in the 1st and the 2nd group, respectively. The birth weight mean percentile of SGA children was lower than at 12 months: 4.75% vs 54.00%;(p=0.04).

In the 1st group the children with RD had lower weight mean percentile at 12 months compared to birth: 47.21% vs 56.96%;(p=0.04), respectively. In the 2nd group the children without sepsis had higher weight mean percentile at 12 months compared to birth: 66.62% vs 54.66%;(p=0.01), those without IVH – 63.35% vs 52.14%;(p=0.01), respectively.

Conclusion. Generally, the weight gain of premature infants during the first year of life is not excessive thus showing that nutritional intervention during perinatal period is adequate. Since higher weight gain was observed in SGA children born till the 29th week of, possibly they should be followed further to monitor weight gain later in life. Nutritional intervention should be strictly monitored in neonates with serious diseases to promote normal development and weight gain.

Use of electronic devices at bedtime and the influence on sleep hygiene and daytime sleepiness

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Background. Behaviours before retiring may affect the quality of sleep and – therefore – daytime functioning. It is no secret that electronic devices are irreplaceable in daily lives. It is known that use of electronic devices, including smart phones, might influence nighttime sleep. Sleep Hygiene Index(SHI) was created to evaluate behaviours affecting sleep. Epworth Sleepiness Scale(ESS) was developed to measure daytime sleepiness.

Aim. To analyze the habits of using electronic devices before sleep and determine their possible effects on sleep hygiene and sleepiness during the day.

Methods. A prospective study was carried out in 2017 in 11 schools in Latvia. Adolescents attending 7th to 12th grade were included. Data were collected using questionnaire (general demographic data, pre-sleep activities, sleep hygiene index (SHI; range 15-65), Epworth sleepiness scale (ESS; range 0-24)). Statistical analysis: ANOVA, Chi-squared, Kruskal Wallis, Mann-Whitney test.

Results. The final sample consisted of 1057 respondents (41% boys) – 12 to 19 years of age (median – 15). Four hours before retiring 64.2% (637/991) of adolescents (72.9% (425/583) of the girls and 52.0% (212/408) of the boys, $p<0.05$) did homework; 23% (228/992) played sports (20.4%(119/584) of the girls, 26.7% (109/408) of the boys, $p<0.005$); 5.7% (56/989) read books (7.0% (41/582) of the girls) and 3.7% (15/407) of the boys, $p<0.05$)).

Majority of respondents (79.9% (789/987)) used electronic devices before sleep every working day, most of them (80.41% (817/1016), $p<0.0001$) one to two hours, and more often girls compared to boys (84,5% (489/579) vs 73,5% (300/408); $p=0.0004$). Children using electronic devices before sleep had higher median ESS and SHI, respectively: ESS – 9.00 (CI 8.00–9.00) vs 7.00 (CI 6.00–8.00), $p=0.001$; SHI – 20.00 (CI 20.0–21.0) vs 16.00 (CI 14.0–17.0), $p<0.0001$. Use of smart phones before sleep in working days was higher in girls compared to boys (94.7% (553/584) vs 88,5% (360/407); $p=0.0003$). However, boys used their personal computers more often (40,4% (165/408) vs 31.7% (185/584); $p=0.0045$). Median SHI was higher in children using personal computer before sleep (21.00 in users group and 19.00 in non-users group, $p=0.004$). There were no statistically significant difference in SHI and ESS in children who were watching TV or use tablet before sleep.

Conclusion. Altogether, adolescents in Latvia spend most of their time before retiring doing homework and using electronic devices – mostly smart phones. However, the use of electronic devices alone before sleep do not affect daytime sleepiness so the daytime sleepiness is caused by constellation of pre-bedtime and bedtime behaviours.

Use of smart devices in 6–36 months old children in Latvia

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Background. Electronic devices are reportedly becoming irreplaceable in our life. Nowadays, even young children use them on daily basis.

Objectives. To analyze the habits of smart device use in 6 – 36 months old children in Latvia; to analyze parental attitude towards smart device use in children.

Methods. A prospective study was carried out in 2018/2019. Parents of 6 – 36 months old children were asked to answer questions regarding their education, general demographic data of the child (sex, age), use of smart devices and parental attitude towards children using smart devices. *Statistical analysis: ANOVA, Chi-squared, Kruskal Wallis, Mann-Whitney tests.*

Results. The final sample consisted of 2385 respondents (50.1%, n=997 male) – aged 6 to 36 months (mean 21.8, median 22.0). Most of the children (69.1%, n=1364) were reported to use smart devices and 30.1% (n=311) did not use smart devices. Most of the parents (67,7%, n=607/896) thought the child didn't use smart devices too much. Furthermore, when asked about smart phones positive effects most of parents (60,3%, n=540/896) considered that the use of smart phones had positive effect. When asked to mentioned positive influence of the smart devices, 65.6% of the parents felt they were good for children due to educative possibilities (language, animals, colours, etc); 22.0% thought that the devices helped overall development (movements, social capabilities, etc); 12.4% used smart devices to distract the child or keep in touch with relatives. Vast majority (80.9%, n=725/896) thought smart phone had negative effect on the child: 34.3% said that they were bad for physical health, 63.2% thought that the smart devices were bad for emotional development, 2.4% of the parents stated that they influenced sleep.

Parents with high school degree gave smart devices to the child significantly more often than the parents with bachelors or masters degree (73% (249/338) vs 67% (869/1281), p=0,05, respectively). Smart devices were used when feeding the child.

Conclusions. Considering that the smart devices is a normal part of daily activities it is understandable that majority of children use smart devices. Most of the parents do not think that the children use them too often or too much. Although many parents think that the smart devices have both positive and negative effects on child's health, majority of parents highlight that they should be careful with daily use of smart devices due to possible negative effects on both physical and mental health.

Vaccination coverage in prematurely born and born at term children in Latvia.

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Background. Vaccination represents a crucial progress in medicine as many diseases became preventable. Preterm infants are more susceptible to infections, but their vaccinations are often delayed or cancelled. Immunization is elective in Latvia, so research reveals current patterns.

Aim. The aim of the study was to compare vaccination trends in prematurely born and born at term patients through an anonymous questionnaire for parents of children born in 2013–2018.

Methods. Parents of children up to five years filled out a survey recording the child's age, gender, birth data and health status, post-partum hospitalization length and Neonatal Intensive Care Unit (NICU) need. Opinions about vaccination, plan to follow the immunization calendar, vaccinations and adverse reactions were documented. Data were collected from GPs in Riga and the Latvian parental association of premature babies. Vaccination coverage, adverse reactions (side-effects) and complications were compared in preterm and term patients.

Results. The final sample included data about 177 patients: 25 prematurely born (mean age 29 months; 56% (14/25) males) and 152 children born at term (mean age 27 months; 55.3% (84/152) males).

Among prematurely born children, 20% (n=5) were extremely preterm; 20% (n=5) - very preterm; 60% (n=15) - moderately-late preterm, mean hospitalization time - 34 days, out of them - 64% (n=16) needed the NICU.

The mean hospitalization time in the term group was 3 days and 3.3% (n=5) required the NICU.

Among preterm patients, 84% (n=21) received at least the BCG shot, and 40% (n=10) reported a delay in BCG or complete vaccination programme; among the term group - 77.6% (n=118) were vaccinated at least with BCG and 8.6% (n=13) experienced a delay.

Prevalence of reactions to vaccination did not significantly differ in premature and term populations: fever developed among 48% (n=12) of preterm patients compared to 36.8% (n=56) of term ones (p=0.29), fussiness - among 44% (n=11) and 40.1% (n=61), respectively (p=0.22), swelling - 36% (n=9) and 30.3% (n=46); (p=0.56); screaming - 8% (n=2) and 13.2% (n=20); (p=0.47); others - among 16% (n=4) and 21.1% (n=32); (p=0.38) preterm and term patients, respectively.

Most adverse reactions occurred either after DTP or first Hexavalent shot (diphtheria-tetanus-pertussis-hepatitis-B-poliomyelitis-Haemophilus influenza-b), in 20% (n=5) prematurely born and 16.4% (n=25) term children.

Conclusion. Preliminary results revealed that prematurely born children have a rather good overall vaccination coverage although more delays were observed in those patients. The prevalence of adverse reactions was non-significantly higher in the preterm group and they mostly occurred after DTP or hexavalent vaccine in both populations.

Acknowledgements. There are no conflicts of interest, funding sources to disclose.

Forecasting of kidney damage in neonates with asphyxia

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Background. The frequency of newborn asphyxia varies from 1 to 1.5%. A disturbance of kidney function in neonates with asphyxia occurs in 45-50%.

Aim. The aim of the work is create a system of prognosis kidney damage in newborns with asphyxia.

Methods. Investigation included 200 full-term newborns with disturbance of kidney function: 100 infants who had severe asphyxia, and 100 – with moderate asphyxia. Comparison group consisted of 20 healthy children without asphyxia. Clinical and anamnesis data, as well as laboratory parameters (level of biomarkers, enzymes, cytokines, etc.), parameters of macro- and microelement homeostasis on 1-2 days of life were analyzed. Mathematical prediction performed using Wald-Genkin's sequential procedure of statistical analysis with calculation the informative level for each sign.

Results. Most indicators of obstetric anamnesis showed a high predictive informativeness ($3.0 \geq I(x_i) \geq 1.0$) and may play role as risk factors of kidney damage in newborns with asphyxia. The three signs had the high level: the fetal distress ($I(x_i) = 2.19$), the threat of abortion ($I(x_i) = 1.77$) and entanglement an umbilical cord around the neck ($I(x_i) = 1.75$). Moderate predictive significance ($1.0 > I(x_i) \geq 0.50$) was typical for urinary tract infections in the mother during pregnancy. Among the neonatal indicators, respiratory distress demonstrated the highest informative level ($I(x_i) = 6.71$). High informativeness was associated with a low Apgar score on the 1st ($I(x_i) = 4.36$) and the 5th minute ($I(x_i) = 3.62$), with male gender ($I(x_i) = 1.82$), peripheral ($I(x_i) = 1.55$) or brain edema ($I(x_i) = 1.10$). Kidney damage is also associated with: low blood pH < 7.25 ($I(x_i) = 3.00$), reduced partial pressure of oxygen in blood < 50 mm Hg ($I(x_i) = 7.06$), serum neuron-specific enolase > 56.2 ng/ml ($I(x_i) = 8.17$), serum cystatin C > 2600 ng/ml ($I(x_i) = 8.63$), urinary IL-18 > 25 pg/ml ($I(x_i) = 1.76$), serum IL-6 > 35 pg/ml ($I(x_i) = 4.13$), serum TNF α > 8.5 pg/ml ($I(x_i) = 7.21$), serum IL-10 > 10 pg/ml ($I(x_i) = 7.25$), serum gamma-glutamyl transpeptidase (GGT) > 120 nmol/l ($I(x_i) = 4.08$) urinary GGT > 47 nmol/(sec*1) ($I(x_i) = 2.20$), as well as serum K > 4.5 mmol/l ($I(x_i) = 2.68$), urinary Ca > 0.8 mmol/l ($I(x_i) = 5.69$), serum Pb > 0.200 mmol/l ($I(x_i) = 7.08$).

Conclusions. The most informative factor for prognosis of kidney damage in newborns with asphyxia is serum cystatin C. Among non-invasive markers for confirm kidney injury in newborns in critical condition due to asphyxia should recommended urinary interleukin-18, gamma-glutamyl transpeptidase and calcium.

Acknowledgements. There is no conflict of interests. This study was performed with financial support from the Sumy State University.

Assesing the risk of pelvic organ dysfunction in the postpartum period

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Background. Pelvic organ dysfunction (POD) is defined as a loss of muscle and connective tissue support of uterus, bladder and bowel; therefore, they lose their normal anatomic position and functions. There are many risk factors contributing in development of POD but the most important ones are childbirth, age and increased BMI. POD significantly influences physical, psychological and social wellbeing of patient's life, therefore, it is crucial to identify high risk groups and adapt preventive tactics.

Aim. Identify risk of developing pelvic organ dysfunction in two groups:

- 20 year risk for *primiparous* women in postpartum period
- 12 year risks for *multiparous* women in postpartum period

Methods. Cross-sectional study was conducted in Riga Maternity Hospital. 40 women in postpartum period were included in the study (age range 18-40 years old) and divided in two study groups: *primiparous* and *multiparous* women. Patients filled out a questionnaire and answers were analyzed using IBM SPSS Statistics 22. Risk was calculated using UR-CHOICE model (http://riskcalc.org/UR_CHOICE/).

Results. *Primiparous* women (n=25), mean age 28.28; SD=5.3 years, BMI M=22.27; SD=2.78 kg/m², have an average risk of 18% (IQR 15.50-25.00) for developing bothersome symptoms or getting treatment for POD in 20 years. Risk for pelvic organ prolapse: 5.0% (IQR: 4.0-6.0), urinary incontinence: 12.0% (IQR: 11.0-15.50), fecal incontinence: 2.0 (IQR: 1.50-2.50).

Multiparous women (n=15), mean age 34.53;SD=4.06 years, BMI 27.78; SD=4.0 kg/m² have an average risk of 56.13% (95% CI 44.87-67.40) for developing bothersome symptoms or getting treatment for POD in 12 years. Risk for pelvic organ prolapse: 23.93% (95% CI 18.32-29.55), urinary incontinence: 46.07% (95% CI 33.50-58.63), fecal incontinence: 9.27% (95%CI 6.97-11.56).

Urinary incontinence was present in two *primiparous* women and three in *multiparous* women. In *primiparous* group 48.2% (n=12) and in *multiparous* group 73.3% (n=11) women had urinary incontinence during pregnancy, p=0.117. In *primiparous* group 24.0% (n=6) and 20.0% (n=3) of *multiparous* group patients had positive family history of POD, p=0.769.

Conclusions. *Multiparous* group has a higher risk for developing bothersome symptoms or getting treatment for POD in 12 years, compared to *primiparous* group in which patients have a lower risk in 20 years. There was no significant difference between both groups in BMI, urinary incontinence before pregnancy or positive family history. During pregnancy, *multiparous* group had 1.5 times greater rate of urinary incontinence compared to *primiparous* group. These are preliminary results, further research will be continued.

Assessment of vital functions after neurosurgical interventions

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Background. Head and back traumas are a frequent cause of death and they take third place after cardiovascular diseases. Preliminary preventative measures, which help avoid complications, are important during the post-operative period. If patients are intubated for a longer time, disorders of the respiratory and vascular systems frequently occur. Post-operative hemorrhage rate accounts for about 1 %, the wound condition develop possible infection in neurosurgery.

Aim. To analyze changes in vital functions of neurosurgical patients during the post-operative period.

Methods. The research was performed in one of the Lithuanian hospitals for one year. The study involved 90 patients after neurosurgical operations. The following was used in the study: the analysis of medical records, the Roper, Logan and Tierney model of activities of living (according to 12 activities of living) monitoring protocol. Monitoring was carried out in two stages. Stage one was carried out in the intensive care unit on the first-second day; stage two - in the surgery unit on the third day. Questions about risk factors, breathing, arterial blood pressure (ABP) and temperature during the post-operative period were asked.

Results. During stage one it was established that 4 (4.4 %) research subjects had 4 vascular risk factors, 8 (8.9%) research subjects had one vascular risk factor and 37 (41.1%) research subjects had two vascular risk factors. A patient who lies on the back at 45° angle with several risk factors (intubated and with vascular and urinary catheters inserted) and who was operated for 2 - 4 hours, has 30.8 % of infection risk, the patient operated for 4 - 6 hours has 17.9 % of infection risk, and the patient operated for over 6 hours is subject to 20.5% of infection risk, ($p=0.5$). During stage two, temperature was assessed and a possible infection risk was monitored in 79.5% of the patients with subfebrile temperature and in 20.5% of patients with normal temperature, ($p=0.005$). When ABP increased, the wound condition of 2.6 % of the patients was normal, ($p=0.001$). To maintain the respiratory system, an oxygen catheter was used for 27 (30.0%) patients, dyspnoea was observed in 16 (17.8%) patients.

Conclusion. The respiratory and cardiovascular system disorders were observed in one third of the patients. They had an effect of the wound condition.

Preliminary preventative measures adopted during the post-operative period help avoid possible infection, disorders of the respiratory system and ABP.

Extragenital pathology among pregnant women with uterine myomas as a risk factor during the pregnancy, delivery and postpartum period.

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Background. Uterine myomas (UM) are the most common noncancerous growth of the uterus among women of the reproductive age. The combination of UM and pregnancy is 5-7%. The pregnancy with UM can be complicated with abortions in early terms, the progress of hemodynamic disfunction, leading to fetal hypoxia. During delivery period more often are the discoordination and uterine bleedings.

Aim. The aim of the current study was to analyze the influence of extragenital pathology in developing UM and study the influence of UM on pregnancy, delivery and postrartum period.

Methods. Altogether 60 patients were enrolled in the study. Devotion the women in 2 groups: 30- n1-main group women with UM, 30 -n2-control group (no UM). The data were analyzed by statistical program Biostat.exe and $p < 0,005$ as the level of significance.

Results. More frequent women at the age of 31-35 have UM ($p = 0,002$) and graviditas 1 in 30% ($n_1 = 9, n_2 = 0$). The first positive realization of reproductive function in 53,3% ($n_1 = 16$) and in 73,3% cases ($n_2 = 21$). In group n1 is more often extragenital pathology in 86,6% of cases ($n_1 = 26$), among them 10% ($n_1 = 3$) endocrinopathy, heart diseases 16% ($n_1 = 5$), digestive tract diseases 20% ($n_1 = 6$). Common in n2 group only 16,6% ($n_2 = 5$) with EGP. Authentically more often n1 group have obesity ($p = 0,001$). Missed abortions were in 30% ($n_1 = 9$) and 6% ($n_2 = 2$). Preeklampsia among 6% ($n_1 = 2$) and no in n2 group. Authentically more often SC in main group 60% ($n_1 = 16$) and in control group 16% ($n_2 = 5$). 6% of newborns ($n_1 = 2$) had the Apgar score 7, 6% ($n_1 = 2$) had a low weight because of chronic fetoplacental insufficiency.

Conclusion. Pregnancy with UM form a group of risk on having complications during the pregnancy, delivery and postpartum. Extragenital pathology in most of cases is in combination with UM. Pregnancy with myoma -high risk of preterm delivery and SC.

Hospitalization duration and treatment for hip fractures in Lithuanian hospitals in 2001–2010

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Background. Osteoporosis is a major contributing factor for fractures in elderly people. It is important to know most appropriate treatment options since these conditions have major impact for quality of life and subsequently mortal outcomes.

Aim. The aim of this study was to analyze duration of hospitalization for treatment of hip fractures in Lithuania during the period of 10 years (2001 – 2010).

Methods. A retrospective study of Lithuanian residents aged 40 and over, with primary hip fracture that occurred during the years of 2001 – 2010. Data was collected from 47 orthopedic–traumatology inpatient departments in Lithuania. Treatment was categorized to surgical treatment, arthroplasty and conservative treatment. The outcomes of the treatment were rehabilitation, long-term care hospital, discharge home and death. Pearson's correlation coefficient was used for assessment of numerical values, Spearman's correlation coefficient was used to assess categorical and numerical data.

Results. There were total of 23108 hip fractures registered in Lithuanian hospitals in 2001 – 2010. The female and male ratio was roughly 2:1. Mean age of the patient's population was 75 years. Mean hospitalization duration was 11.6 days. Most frequent duration of hospitalization was from 5 to 20 days. Strong positive statistically significant correlation between age and the duration of hospitalization has been found ($r = 0.997$; $p < 0.05$). During hospitalization, 73.3% ($n = 16929$) of patients were treated surgically. In 19.5% of cases ($n = 4507$) arthroplasty has been used as treatment method and conservative treatment had been used in 7.2% ($n = 1672$) of cases. The vast majority of the patients have been discharged home: in 79.2% of cases after surgical treatment, in 11.3% of cases after arthroplasty. In 47.7% of cases in-patient rehabilitation has been performed after surgical treatment and in 50.9% of cases after arthroplasty. After surgical treatment, 81.2% of patients were sent to the facility of out-patient rehabilitation. Strong positive statistically significant correlation between method of treatment and the duration of hospitalization has been found ($r = 0.981$; $p < 0.05$) suggesting that the more invasive and aggressive treatment is applied, the time of hospitalization is longer.

Conclusion. The time of hospitalization was mostly dependent on patients age and the treatment method applied. The most common treatment method was surgery, the vast majority of patients have been discharged home despite the treatment method applied.

Acknowledgements. There is no conflict of interests to declare.

Impact of chronic venous disease on quality of life: first results of patients undergoing different type of treatment of chronic venous disease

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Background. Chronic venous disease (CVD) is a disease that affects millions of people and which can negatively impact the quality of life (QoL). QoL can be defined as the functional effect of an illness and its consequent therapy upon patient, as perceived by the patient. CVD whose prognosis is poor limits patients lifestyle. The main goal of CVD's treatment is reducing symptoms and improving the patients QoL. The measurement of QoL provides a better understanding of the impact the disease has on the patient.

Aim. The aim of the current study was to assess: i) the QoL and to investigate whether the occurrence and intensity of leg pain is related to CEAP, ii) does postoperative leg pain depend on treatment method. The sample group consists of adult patients' diagnosed with CVD, who were interviewed before and one month after phlebectomy, endovenous laser ablation (EVLA) or VenaSeal closure system.

Methods. Altogether, 43 patients were enrolled in the study. Status of patients' symptoms was surveyed using Venous Clinical Severity Score questionnaire either during consultation or by phone call. The data was analysed using Microsoft Excel and IBM SPSS 22.0.

Results. The mean age was 50 years (SD 13.18, range 21–80 years). Patients were classified according to CEAP classification: 34.9% in C3, 32.6% in C4, 27.9% in C2, 4.7% in C6. The treatment was predominantly done with EVLA laser for 81.4% patients, phlebectomy for 11.6%, VenaSeal closure system for 7%. Before the treatment 27.9% of patients were complaining about mild occasional pain, 25.6% moderate, 23.3% severe pain. According to CEAP, 58.3% with C2 didn't have any pain, out of those with C3 – 66.6% had moderate to severe pain, and C4 – 78.6% had mild to moderate pain. One month after treatment 69.8% didn't assume any pain, 27.9% had mild pain, and 2.3% assumed to have moderate pain. 100% of all patients who underwent VenaSeal treatment, and 72.4% of those who had EVLA assumed to have no pain after operation, however, out of those who had phlebectomy 60% assumed to have mild pain.

Conclusion. The QoL is different among patients with mild and severe CVD. Individuals who underwent EVLA and VenaSeal treatment have shown better pain improvement than those who had phlebectomy. According to study, not only venous severity score but also method of treatment has an impact on patients QoL. A larger group of patients is needed for further research to generalize the results.

Leukocytosis and CRP in patients with Aneurysm of Abdominal Aorta treated with Endovascular Aneurysm Repair

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Background. Modern approach in treatment of Aneurysm of Abdominal Aorta (AAA) is Endovascular Aneurysm Repair (EVAR). Post-Implantation Syndrome (PIS) is benign systemic inflammatory response seen after EVAR as biochemical and clinical expression of inflammation without infection. Laboratory parameters are part of diagnostics. Differentiation from infection is fundamental. There is no consensus among vascular surgeons how to define PIS – febrile pyrexia is stable paradigm, but cut-off value of leukocytosis varies, thus influencing the incidence from 14% to 60%. Negative microbiological cultures strongly dominate early post-operative period in febrile leukocytotic patients.

Aim. The aim of the study was to observe the behaviour of leukocytes and CRP in AAA patients treated with EVAR during stationary recovery.

Methods. The operator issued surgical descriptions and laboratory results of the all 26 AAA patients treated with EVAR in Riga East Clinical University Hospital during 2017–2018 were systematically reviewed. Age, gender, size of AAA, leukocytes and CRP were analyzed retrospectively. Three patients were excluded from the study due to insufficient documentation. 23 patients were included in this retrospective study.

Results. Among patients were 3 females and 20 males aged from 52 to 88. Diameter of AAA was 5,0 – 10,1 cm, with mean 6,7 cm. Post-operatively during the first 24 hours leukocyte count varied from 5260/mm³ to 17450/mm³, median 9350/mm³, mean 9622/mm³, SD± 2659/mm³ and highest leukocyte counts occurred in 78,3% during this period. Leukocytosis > 9000/mm³ occurred in 56,5% during the first 24 hours and in 65,2% during the whole period of hospital stay with maximum leukocytosis being 17450/mm³. CRP increase follows the increase of leukocytes with a delay. 56,5% had their CRP peak value later than 24 hours. During the first 24 hours post-operatively only 21,7% had CRP > 40 mg/l and 13% had CRP > 60 mg/l, and nobody had CRP > 100 mg/l. CRP continued to increase after 24 hours post-operatively – 52,2% had CRP > 40 mg/l and 43,5% had CRP > 60 mg/l. More severe CRP was observed also after 24 hours post-operatively as 30,4% had CRP > 100 mg/l. During hospital stay the CRP maximum was 181,80 mg/l, median 49,70 mg/l, mean 67,28 mg/l and SD± 59,32 mg/l.

Conclusion. Leukocytosis and increased CRP occurred in majority of patients. PIS needs further studies in correlations of factors triggering it and more precise definition in the leukocyte cut-off point.

Acknowledgements. Authors have no conflict of interests.

The addition of common peroneal nerve block to femoral triangle block for postoperative analgesia in patients undergoing total knee arthroplasty

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Background. Postoperative pain remains an important problem in patients undergoing total knee arthroplasty (TKA) despite ubiquitous multimodal analgesia practice. Little information exists about the effectiveness of common peroneal nerve block in patients undergoing TKA, despite its major role in innervation of the anterolateral part of knee joint.

Aim. We hypothesized that adding a common peroneal nerve block to femoral triangle block for postoperative analgesia in patients undergoing TKA will provide better pain relief than femoral triangle block alone.

Methods. Twelve patients undergoing TKA were randomized to receive either common peroneal nerve and femoral triangle block (CPTF group, n = 6) or femoral triangle block alone (TF group, n = 6). Each patient received spinal anesthesia with 0.5% bupivacaine and multimodal analgesia. Pain was assessed on admission to postanesthesia care unit and after 2, 6, 12 and 24 hours using numerical rating scale. The primary outcome was the cumulative opioid consumption (parenteral morphine equivalent). The secondary outcome was the time to first opioid request.

Results. Median morphine consumption in group CPTF during the first 24 hours was 8.9 (SD 6.9) mg, which was not significantly different from TF group with the median morphine consumption 8.3 (SD 4.1) mg. The median time to first opioid request was 290 (SD 99) min in CPTF group compared to 265 (SD 135) min in TF group which also did not reach statistical significance.

Conclusion. According to the data we have, common peroneal nerve block provides no additional analgesia in patients undergoing TKA.

Acknowledgements. Nothing to declare.

Efficiency of rehabilitation for patients with miofascial syndrome

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Background. 85 people were evaluated using numerical analog scale and multidimensional pain assessment scales, that is the mainly used by the National Health Service.

There were two research groups made – experimental (I group) with 43 patients, where 29 were women and 14 were men and control (II group) with 42 patients, where 28 were women and 14 were men. The rehabilitation nonpharmacological technologies were applied only to the patients of the I group.

Numerical analog scale is 11 grade scale where pain intensity is displayed with numbers from 0 to 10. Pain is determined as intense or very strong, if the patient marks number 7 or higher, numbers 4-6 correspond to moderately strong pain and not very intense pain is marked by number 3 or lower. Multidimensional pain assessment scale that was used during the research showed not only the pain intensity but also its influence on functional capacity and life activity of the patients. The treatment complex including soft tissue techniques, exercises, amplipulse therapy (course 10 times) that refer to rehabilitation technologies was provided to selected group of participants.

Aim. To examine the effectiveness of nonpharmacological technology use for patients with myofascial pain syndrome.

Methods:

1. Surveying of patients with myofascial pain syndrome.
2. The comparative analysis of both groups before, during and after the research process.

Results. It was found that at the beginning of the research I group pain characteristics according NRS were more intense than those of the II group. The most significant difference according to Student criteria that shows the effectiveness of described rehabilitation technologies, is shown while comparing pain intensity in I group at the beginning and at the end of research. All the pain intensity indicators are lowered that obviously demonstrates the decrease of pain intensity. The pain intensity of the II group patients, where rehabilitation technologies were not applied, even increased in several positions at the end of the research. It proves the effectiveness and usefulness of the rehabilitation technologies.

Conclusion. Rehabilitation technologies used during the research showed statistically significant decrease of the pain syndrome in all the indicators of NRS pain intensity scale that proves the effectiveness of the rehabilitation method used.

Effect of Dexamethasone administration on the duration of analgesia using sciatic nerve block after lower leg and foot surgery

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Background. Sciatic nerve block is one of additional methods to minimise pain after lower leg surgery. Dexamethasone has been extensively studied as an adjuvant in peripheral nerve blocks, and it has shown significantly prolonged duration of analgesia. Despite many studies most efficient way of Dexamethasone administration is unclear.

Aim. Improvement of patients' quality of life by minimising pain after surgery. This can be achieved by determining if Dexamethasone prolongs duration of analgesia in sciatic nerve block and in which route of administration (intravenous or perineural) it prolongs analgesia most efficiently.

Methods. After obtaining approval from the Ethics Committee and obtaining written informed consent, 16 patients undergoing lower limb or foot surgery due to trauma were included. All surgeries were done under spinal anaesthesia. Patients were randomized into 3 groups. First group (control group) received Bupivacaine perineurally; second group received Bupivacaine perineurally and Dexamethasone intravenously; third group received Bupivacaine and Dexamethasone perineurally.

All patients received standardised multimodal analgesia and morphine as a rescue drug when NRS>4.

Injection was made up from the popliteal fossa. Point of injection was found with ultrasonography guidance and with nerve stimulation device. Injections contained Bupivacaine 0.25% 20–30mL or Bupivacaine together with Dexamethasone 8mg. Dose of Bupivacaine was dependent on patients BMI.

Times until first morphine dose and returning of sensory functions, total morphine consumption up to 72h after surgery, pain intensity in NRS on the day of surgery (D0), first (D1) and second (D2) postoperative days were measured

Data statistical analysis was performed using IBM SPSS Statistics 22.

Results. The duration of analgesia in the control group was 5h 32min±1h 56min and was significantly shorter than in other groups. Intravenous Dexamethasone group had a mean duration of analgesia 18h 56min±2h and perineural Dexamethasone group had mean duration of analgesia for 14h 17min ± 5h. Mean pain intensities according to groups were: control group – 3.71±0.05 (D0), 4.53±2.24 (D1) and 3.06±1.04 (D2); intravenous Dexamethasone group – 1.00±0 (D0), 1.66±0.57 (D1) and 0.34±0.58 (D2); perineural Dexamethasone group – 0.86±0.74 (D0), 2.16±0.52 (D1) and 1.91±0.62 (D2).

Conclusion. Duration of analgesia was significantly longer in groups where Dexamethasone was used comparing to control group. Using Dexamethasone as an adjuvant for sciatic nerve block prolongs analgesia in both of administration ways, but shows a tendency to prolong analgesia more effectively when used intravenously.

Acknowledgements. None.

A temporary bypass used in anastomosis of major vessels without stopping blood flow in the segment under repair

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Background. The problem of minimizing the time of ischemia when performing a vascular suture is still an important issue of surgery.

Purpose. Authors propose an original set of tools and a method of carrying out "end-to-end" anastomosis on major vessels, without stopping blood circulation in the vascular segment being repaired.

Methods. Proposed set of tools includes 10 silicone temporary vascular shunts with external diameters from 8 to 26 mm. The length of each tube is about 6 cm, and the wall thickness is 1.2 mm. A spiral notch with a step of 1.2 mm is made on the outer surface of the tubes, to a depth of 1 mm. The set of tools also includes a set of metal hollow half - cylinders having a through hole in the middle, designed to extract the shunt. At first, a shunt is selected, the outer diameter of which corresponds to the inner diameter of the damaged vessel. A stay-suture is laid in the center of tube, on its wall between two neighboring spiral notches. The ends of the temporary bypass, pre-filled with saline solution, are introduced into the distal and proximal ends of divided vessel and are firmly fixed with two elastic bands. After that, the blood flow is restored. The edges of the vessel are stitched to almost its entire circumference. The last additional suture is placed in the area of the stay-suture overlying the wall of the shunt and is not tightened. A half-cylinder is placed above the untightened vascular suture and the ends of stay-suture are stretched through its opening. Then, applying traction to the ends of stay-suture the mechanical destruction of the shunt along the line of spiral incision ensues. As a result, the tube is transformed into a double silicone rod, which is pulled through a through hole in the half-cylinder. After extraction, the anastomosis is completed by tying a knot on the provisional suture. To simulate proposed method, 10 operations were performed using a closed experimental circuit. The time of the operation and the reduction of the blood volume circulating in the experimental circuit, were evaluated.

Results. Experimental testing demonstrated effectiveness of the developed method. The average time of the operation was 10 minutes and the volume of blood loss did not exceed 4 ml.

Conclusions. The technique completely excludes the need for interrupting blood flow through the sutured vessel and minimizes the time of ischemia.

A topological classification of the superior mesenteric vein affluent branches

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Background. The problem is of outstanding importance since there is no unified classification of the superior mesenteric vein (SMV) affluent branches.

Purpose. A new classification of venous return from the right hemicolon based on the principles of topology and combinatorics is proposed.

Methods. The topographic study was performed on anatomical material (25 observations) by means of preparation in the right mesenteric sinus. After that, the construction and topological transformations of the volume figures reflecting the order of the SMV branches confluence were performed. To simplify the interpretation of obtained data, we didn't take into account branches of small intestine. Topological transformations make it possible to bring any SMV variant to a certain topological type. In almost all cases, approximately 6 permanent SMV's inflows were identified: middle colic vein, right gastro-omental vein, upper pancreatic-duodenal vein, anterior inferior pancreatic-duodenal vein, right colic vein and ileocolic vein. Between 6 constant branches there are 5 so-called topological nodes (TN) in which two basic states are theoretically possible: fusion and separation (*f/s*). In addition, at some distance from the node may form a connecting arcade (*a*). Since each node with the greatest probability represents only two states – *f/s*, the total number of all possible variants within a given topological type will be calculated according to the formula: $P=2^{(b-1)}$ (**P** – the number of t variations, **B** – the number of affluent branches). So, if there are 6 constant branches, the total number of possible variants will be $2^5=32$. If we take into account the probability of connecting arcades presence, then the number of variants will be $3^5=243$. If the adjacent branches merge into one trunk at the confluence into SMV, TN is assigned the value *f*, a separate confluence – the designation *s*, in the presence of arcades – *a*.

Results. The distribution of topological types identified in this study is following: **4ts** – 40%; **s3ts** – 32%; **5s** – 8%; **s2tst** – 4%; **s2t2s** – 4%; **2tsts** – 4%; **s4t** – 4%; **2s2ts** – 4%.

Conclusions. It was identified 8 variants of the SMV affluent branches confluence. The ileocolic vein most rarely merged with other branches and had a relatively constant place of confluence into SMV. It was found that the most common topological types are **4ts** and **s3ts** (10 and 8 observations out of 25). The topological variant **4ts** implies an increased risk of complications during surgery.

Insufficient physical activity as one of the risk factors for cardiovascular disease

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Background. Insufficient physical activity (IPA) is one of the main risk factors (RFs) for developing diseases of the cardiovascular system, accounting for 2/3 of the total mortality of the population of Ukraine.

Aim. To investigate the prevalence of insufficient physical activity among men living in the city aged 40–64.

Materials and methods of research. According to the results of a survey of a representative sample of men of urban population aged 40–64, an analysis of their physical activity was performed according to survey data, which was conducted using a unified questionnaire. Physical activity was considered insufficient if sitting time is 5 hours or more, and active leisure time in winter and summer, including time that they spent on the way to work and home is less than 10 hours a week.

Results. A total of 501 inquiries showed that four of the ten surveyed men lead a sedentary way of life. Most of them (75.6%) significantly increase motor activity in the spring–summer season of the year, however, only one third of men aged 40–49 (30.8%), one fifth in the age group of 50–59 (19.7 %) and every tenth (10.3%) compensate for the insufficient physical activity by regular physical activity (basketball, football, swimming) in the autumn–winter period. Among the men who lead a sedentary lifestyle, 3.5% of the insufficient physical activity is an isolated risk factor. As the age increases, the proportion of people in whom IPA is combined with other risk factors. The associativity of the IPA with one RF is noted at 11.1%, and with the two RFs – 44.9% of the surveyed. In 25.8% of the examined men, the IPA registers in conjunction with three or more RFs.

Conclusions. The received results, first of all, noted the significant association of the IPA with other RF, indicate that it is necessary to carry out preventive work aimed at increasing the physical activity of people who are in a sedentary way, in the future to carry out an explanatory work with them on the harmfulness of hypodynamia and the need engage in sports and other physical activities regularly to prevent the development of cardiovascular disease.

Remote medical service to improve quality medical care at the level of primary health care facility

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Background. The sixteenth task of the World Health Organization's International Health Strategy, "Health 21 - Health for All in the 21st Century," puts countries in the task of ensuring effective management of the quality health care and quality assurance health care. The strategy states that countries should introduce a new mechanism for quality management health care. The essence of it is to ensure constant improvement of the quality medical and sanitary care for the population, it is necessary to measure systematically the effectiveness indicators of the clinical care. Today the research and development of mHealth services and additions became one of the most important subjects in scientific community. Now mHealth is used for monitoring, prophylaxis and diagnostics of diseases. However, in Ukraine mobile and electronic devices are only beginning their development in medical sphere. We have no complete system of connection with dispensary patients viz. duo-channel system of DFM-patient communication to attend patient during their dispensary treatment.

Aim. Development of new methodological and Informational-communicative system for monitoring and analyzing the psycho-emotional and physical state patient's health at the first level of medical care.

Methods. Meta-analysis, systematical approach, informational-analytical systems' schemes projection, expositive modeling.

Results. For our aim realization, we created a new multifunctional informational-communicative system with service platform and screen form application. Also the aim of this program module using is active application of patients for self-control of all vital indexes, further healthy life and accurate following the doctor's prescription. Informational-communicative system is a complex of organization and technical methods for information storage, processing and sharing. The main steps of using are: users' registration and gathering of medical data, their processing, analytical processing, regulative decisions, feedback subsystem.

Created duo-channel system "doctor-patient" and "patient-doctor" will allow usual doctors of family medicine take the interactive dispensary cure and avoid uncontrolled illness progress. This system allows sending periodical or non-periodical messages-notifications about some recommendations and prescribing to health self-control to single patient or patients' group. These notifications are can be not answered on, but doctor can see whether patient had seen them or not. If necessary, patients have the opportunity to ask questions and consult their physician online.

Conclusions Duo-channel connection of informational-communicative system allows not only monitor health state of patient, react on it's changing, but also enlist patients for them can self-control their physical state, keeping healthy way of life and medical prescriptions. Developing of this program helps decrease the amount of work and optimize it for Family medicine doctors.

Scientific justification of need to change the population nutrition system in Ukraine

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Background. Population nutrition is closely related to the state socio-economic politic and affects the prevalence of alimentary-related diseases in the country.

Aim is to study Ukrainian population nutrition system in 1990–2018 and develop directions of it optimization.

Materials and methods. Annual data of food intake were obtained from the State Statistics and Cabinet of Ministers. Daily foods and nutrients intake were calculated per capita and compared with the world and national standards.

Results. Social and economic changes in Ukraine in 1990–2018 course significant transformations in the population nutrition: average intake of meat dropped by 25%, cereal products — by 24%, milk — by 44%, sugar — by 28.5%, and vegetables consumption fell by 28%, daily energy loss decreases by 860 kcal. Protein intake reduced from 105 g to 84g per capita. In 1995 - 2005, Ukrainians underwent significant critical shortage in the completed protein consumption. This coincided with growing the number of cardiovascular, neurological and oncological diseases, for which nutrition is an important risk factor. In 2005–2018 the consumption of completed protein has gradually reached the optimum. Intake of daily fat reduced from 146.1 g in 1990 to 92.0 g in 2018, and their share in the daily energy intake has meet norm. In the same time balance of omega-3 and omega-6 PUFAs ranged from 77: 1 to 91: 1, while the scientifically based value is 1: 1 - 5: 1. Daily intake of trans-fat is 3.4–14.1 g per person, their energy share in the daily energy intake reached 4.4 %, while recommended level up to 1%. Consumption of total carbohydrates has decreased from 439 g up to 372 g per day, but simple sugar intake is currently still high. Over the 28 years period the average consumption of fruits has not changed and is now 130 g/day, it is less than optimal value. The National Food Basket characterized by the same nutritional features.

Conclusion. The system of nutrition of the Ukrainian population is characterized by the excessively high level of simple carbohydrates consumption and by the significant imbalance of dietary fats. This create a threat to public health and dictate a need to change the state policy in the field of population nutrition in these directions.

Bladder Cancer Survival Trends in Latvia in 1990–2017

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Background. Bladder cancer is the tenth most common cancer in the world according to GLOBOCAN 2018 data and the sixth most common cancer in men. Bladder cancer is the thirteenth cause of deaths resulting from different types of cancer worldwide, while in Latvia it ranks seventh. It would be important to analyse survival trends in bladder cancer in Latvia, because previously there was not such epidemiological trend study.

Aim. The aim of the study was to evaluate bladder cancer survival trends in Latvia over the past 28 years.

Methods. Altogether 9191 patients with diagnosed bladder cancer between January 1990 and December 2017 and available follow-up data until 30 June 2018 were included in the retrospective study. Patients diagnosed with a bladder cancer at the time of death were excluded from the survival analysis. Data were taken from the Register of Latvian Centre for Disease Prevention and Control. The research data were analysed for the survival of bladder cancer, according to patients' gender and age. Data was analysed using Microsoft Excel 2017, SPSS version 22.

Results. The total number of included patients, who had available follow-up data and were selected for survival analyses, were 9191. The median overall survival rate of bladder cancer patients during the study period was 3.7 (95% CI 3.4; 3.9). Comparing overall survival of both genders, there were statistically significant difference between women 4.6 (95% CI 3.9; 5.2) and men 3.4 (95% CI 3.2; 3.7) ($p < 0.001$). Overall survival rates at 1, 5, 10, 15 and 20 years were 70.3%, 44.4%, 29.7%, 20.6% and 14.9%, respectively. Cancer-specific survival rates were the following for 1, 5, 10, 15 and 20 years were 74.4%, 56.2%, 48.0%, 42.7% and 40.1%. The 5-year overall survival rates were the lowest for cases of bladder cancer that were diagnosed at the beginning of the considered time period (from the year 1990 until 1994) – 41.7% (95% CI 39.0; 44.4) and then subsequently (from 2013 until 2017) increased to 46.8% (95% CI 43.9; 49.7). Comparing two periods mentioned above 5-year overall survival was significantly better in younger (<70 years) patients compared to older (>70 years) ($p < 0.001$).

Conclusion. Although the 5-year overall and cancer-specific survival rates improved over the reviewed period they still needed to get better.

Acknowledgements. Special thanks should be given to Latvian Centre for Disease Prevention and Control for provided data.

Evaluation of brucellosis incidence in Kazakhstan

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Background. Brucellosis is a global problem of medical health and veterinary well-being. Every year, almost 500,000 cases are recorded worldwide and more than 10 cases per 100,000 population in some countries. Brucellosis has been found to be the widespread trouble in many countries.

Aim. To study the spatiotemporal features of the brucellosis in Kazakhstan.

Methods. The material was the data of patients registered with brucellosis (ICD 10 – A23) reported by the Ministry of Health based on the consolidated reporting form № 1. Average values (P), average errors (m) and average annual growth/loss of equalized rates (T, %), 95% confidence intervals (95% CI) are calculated. A method based on the determination of the standard deviation (σ) from the mean (\bar{x}) is used for spatial evaluation.

Results. There were 17,694 registered cases of brucellosis in Kazakhstan for 2007–2016.

The average annual brucellosis incidence in the republic was 10.8 (95% CI=8.8–12.8) per 100,000 of the total population. In dynamics, the rate decreased from 14.8⁰/₀₀₀₀ (95% CI=14.2–15.4) in 2007 to 5.9⁰/₀₀₀₀ (95% CI=5.6–6.3) in 2016. The average annual of equalized rate decline was T = -10.4%, while the decrease is statistically significant (p<0.05).

Spatiotemporal evaluation of the incidence in different regions is one of the most important study aspects of diseases among people, because it identifies the inhabitants of places most affected by certain diseases and allows to analyze the processes of occurrence and spread of disease over time. The spatiotemporal evaluation (P±m, ⁰/₀₀₀₀ and T, %) revealed the following regions:

- In regions with low rates (up to 3.2⁰/₀₀₀₀) – Mangystau (0.2⁰/₀₀₀₀, T=+4.0%), North Kazakhstan (0.6⁰/₀₀₀₀, T=+13.1%), Kostanay (1.7⁰/₀₀₀₀, T=+40.1%), Karaganda (1.8⁰/₀₀₀₀, T=-12.3%), Pavlodar (2.7⁰/₀₀₀₀, T=+7.5%), Atyrau (2.9⁰/₀₀₀₀, T=+37.0%), Akmola (3.0⁰/₀₀₀₀, T=+6.1%) regions, also in Almaty (0.2⁰/₀₀₀₀, T=-5.1%) and Astana (1.0⁰/₀₀₀₀, T=-1.8%).
- Regions with average rates (from 3.4 to 13.4⁰/₀₀₀₀) – Aktobe (4.2⁰/₀₀₀₀, T=-1.9%), West Kazakhstan (7.4⁰/₀₀₀₀, T=+4.0%) and East Kazakhstan (12.7⁰/₀₀₀₀, T=-12.2%) regions.
- Regions with high rates (from 13.4⁰/₀₀₀₀ and above) – Kyzylorda (18.1⁰/₀₀₀₀, T=-18.4%), Almaty (19.9⁰/₀₀₀₀, T=-10.2%), South Kazakhstan (22.1⁰/₀₀₀₀, T=-14.6%) and Zhambyl (34.5⁰/₀₀₀₀, T=-10.8%) regions.

Conclusion. Thus, the evaluation of the brucellosis incidence among the entire population shows different zoonosis levels distribution within the republic and more clearly reflects their territorial distribution. The identified medico-geographical features of the brucellosis incidence are recommended to be used for reducing this pathology and further decreasing the rate in the dynamic regions of Kazakhstan.

Civil liability of a hospital. Insight into the scope of article 1782 of Latvian civil code.

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Background. Latvian court practice indicates that Article 1782 of the Civil Code is applied in civil disputes between hospitals and patients or their relatives on regular basis. A closer look opens up a scene where this section is used almost automatically – without sufficient evaluation. Taking into account that civil disputes in healthcare has a significant role, and earnest impact not only on individuals and hospitals, but also on public, there is necessity to analyze Article 1782 in – depth.

Aim. The aim of this research is to expand the understanding of Article 1782 by analyzing it from various points of view. Sufficient comprehension of its content, historical background, genesis, application in court practice and impact on procedural aspect of fair trial, will give the opportunity to improve rights to a fair trial and justice. Author has chosen to identify most debatable aspects of the application of Article 1782.

Methods. Author used grammatical, historical, systemic and teleological interpretation method of Latvian Civil Code. In addition author analyzed modern and historical Latvian court practice and legal literature on this topic from various periods.

Results. Research results are: 1) expanded understanding of article 1782 and its application; 2) more precisely illuminated preconditions to apply Article 1782 and denial of its application automatically; 3) wider view of hospitals civil liability; 4) some procedural observations in regard of the third party in the civil case.

Conclusion. Latvian Civil Code inherited historical regulation with meaning and importance in Latvian court practice today. It must be emphasized that article 1782 must be applied only when there are definitely found certain preconditions, but not automatically. There is important differences in certain preconditions and expressions of liability (e.g. culpa in eligendo, culpa in custodiendo). Latvian court practice basically do not separate responsible institutions and its workers in terms of qualification, peculiarities of profession etc.

Acknowledgements. Author pays respect and gratitude to the dean of Faculty of Medicine Prof. Valdis Folkmanis.

Central nervous system cancer in Kazakhstan: regional incidence trends

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Background. According to the International Agency for Research on Cancer, about 296,851 cases of central nervous system (CNS) cancer registered in the world and 52.6% of them corresponds to the Asia. The age-standardized incidence rate (ASR, World) of the CNS cancer in the world was $3.5^{0}/_{0000}$ and the high incidence established in Latvia ($10.1^{0}/_{0000}$), Macedonia ($9.2^{0}/_{0000}$) and Lithuania ($8.0^{0}/_{0000}$) to 2018.

Aim: To study the regional incidence trends of CNS cancer in Kazakhstan

Materials and methods. The material about CNS cancer (C70-72) was collected from all cancer institutions in the country (form 7). The data represents the incidence number of CNS cancer diagnosed for the first time among Kazakhstani population between 2007 and 2016. The least squares method were used to determine the incidence trends and to calculate the growth/decrease rates (T, %) of dynamic range was used the geometric mean that equal to the root of the degree n from the product of annual rate indicators. The age-standardized incidence rates of 10 years (2007–2016) were used to draw the graphical map of CNS cancer. The map was drawn by Igissinov's method (1974) which is based on indication of average quadrant decline (σ) from average (x).

Results. According to the obtained calculations, the map of CNS cancer incidence in administrative territorial zones of Republic was drawn with following defined groups:

1. Regions with low degrees ($<3.5^{0}/_{0000}$) – Atyrau (2.50, T=+3.9%), Northern Kazakhstan (3.0, T=-1.6%), Western Kazakhstan (3.0, T=-5.7%), Aktobe (3.2, T=+12.4%), Karagandy (3.4, T=-1.7%). Overall 5 regions.
2. Regions with average degrees ($3.5-4.7^{0}/_{0000}$) – Kostanay (3.5, T=+4.7%), Akmola (3.6, T=-4.8%), Pavlodar (4.0, T=+1.9%). Astana city (4.2, T=-1.5%), Almaty (4.2, T=+1.3%), Eastern Kazakhstan (4.2, T=-4.8%), Mangystau (4.2, T=+4.6%), Southern Kazakhstan (4.2, T=+3.9%). Overall 8 regions.
3. Regions with high degrees ($>4.7^{0}/_{0000}$) – Zhambyl (5.1, T=+9.2%), Almaty city (5.6, T=-0.6%) and Kyzylorda (7.5, T=-2.2%). Overall 3 regions.

Conclusion. These results can be serve as a basis for detailed study of the causes of CNS cancer in different regions of Kazakhstan with high and low levels of CNS cancer incidence. Determining and controlling important exogenous and endogenous risk factors may decrease its burden in the Kazakhstan.

Acknowledgements. The study supported by public association «Central Asian Cancer Institute». No conflict of interest.

Malignant tumors of eye and adnexa in Kazakhstan: epidemiological aspects

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Background. Malignant tumors of the eye and adnexa (MTEA) are relatively rare in the overall structure of cancer incidence. Scientific researches have particular relevance, aimed at finding the true causes of the development and growth of MTEA. The search and identification of possible risk factors in the development of tumors of this localization can contribute to effective prevention, and therefore reduce the incidence.

Purpose. The purpose of the study to define peculiar properties of MTEA incidence in Kazakhstan population.

Methods. The retrospective research is based on the official data of oncological institutions of Kazakhstan concerning new cases of MTEA (ICD 10 – C69) during 2007–2016. Age rate, crude rate (CR) and age-specific rate (world standard) of incidence on 100,000 ($^0/_{0000}$) in both sexes were calculated. Trends of incidence were determined by the Ordinary Least Squares, and calculated the rate of growth/loss (T, %).

Results. During the study, there was a total of 490 new cases of MTEA were registered in Kazakhstan, male– 227(46.3%) and female 263 (53.7%). A high proportion of patients were in patients younger than 30 years (33,7%). The average age of patients MTEA amounted to 42.4 ± 1.4 years. In dynamics, the average age of patients increased from 45.7 ± 4.3 years (2007) to 48.8 ± 3.8 years in 2016, and the average annual growth rate was $T = +0.7\%$.

Table. Incidence of MTEA in Kazakhstan

Age	Number (%)	Incidence, $^0/_{0000}$	
		P \pm m	T, %
<30	165 (33.7)	0.19 \pm 0.02	+2.8
30–39	22 (4.5)	0.09 \pm 0.02	–4.9
40–49	36 (7.3)	0.17 \pm 0.02	–18.1
50–59	102 (20.8)	0.59 \pm 0.07	+8.6
60–69	88 (18.0)	0.96 \pm 0.06	+3.3
70+	77 (15.7)	1.01 \pm 0.10	+4.2
Total	490(100.0)	0.30 \pm 0.10	+2.3

The average crude rate (CR) of MTEA was $0.30 \pm 0.01^0/_{0000}$. In dynamics CR incidence increased from $0.24 \pm 0.04^0/_{0000}$ (2007) up to $0.29 \pm 0.04^0/_{0000}$ in 2016 ($T = +2.3\%$). The average age-specific incidence of MTEA has maximum values in the age group 70 years and older are $1.01 \pm 0.10^0/_{0000}$ (table).

Conclusions. Some epidemiological features of the incidence of malignant tumors of the eye and the appendage apparatus in recent years in Kazakhstan, which are recommended for use in monitoring and evaluation of anti-cancer measures, have been established.

Acknowledgements. There is no conflict of interest. The study supported by public association «Central Asian Cancer Institute».

Limitations to safeguard the right to health care of children and adolescents suffering from emergency psychiatric conditions in the Riga region

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Background. Right to health care of children and adolescents is a priority of states and modern health care systems. Children having an emergency mental health condition should be entitled to available, accessible, acceptable, and quality (AAAQ) mental health care. Since 2009 the Ombudsman's Office has been identifying severe infringements of children rights law in all psychiatry units of Latvia. Since psychiatric emergencies are the most challenging, in respect to implementation of all the core elements, pitfalls have been studied, specifically covering the Riga region.

Aim. To identify the pitfalls of the treatment of children in emergency psychiatric conditions in one of the largest regions of Latvia and to make a proposal to improve the regional and national situation.

Methods. Data have been retrieved from reports of the State Emergency Medical Service, the Ombudsman's Office, the Centre for Disease Prevention and Control, and other health care institutions. Analysis of these data and corresponding legislative documents was performed.

Results. Number of emergency care situations for children with mental and behavioural disorders in Latvia is growing from 2559 cases in 2015 to 2989 in 2018.

In Riga region, psychiatric emergency care is provided by 3 hospitals. The Children's Clinical University Hospital (CCUH) admits patients under 16 and older nonaggressive patients. The Riga Centre of Psychiatry and Addiction Medicine (RPNC), admits a high number of nonaggressive and aggressive adolescents aged 16 and over. The Psychiatric Hospital "Gintermuiza" in Jelgava admits patients without restrictions, but it is at least 40 minutes' drive from Riga.

In RPNC there is a lack of appropriate accommodation, care, legitimacy of admission. Adolescents are placed with adults who are charged with crimes; are exposed to smoking, denied access to education and the presence of family members during the hospital stay. There is a lack of psycho therapeutic treatment and substantial differences in the duration of hospital treatment: in RPNC it is 23–24 days, whereas in CCUH 9–10 days.

Conclusion. The research reveals several shortcomings in emergency psychiatric care for children in Riga region. There are systematic insufficiencies in accessibility, availability, acceptability and quality of psychiatric emergency care.

Age- and sex- related peculiarities of the incidence of lung cancer in Kazakhstan

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Background. The incidence of lung cancer (LC) over the past 50 years has increased dramatically in many countries and more than 2 million new cases of LC are recorded every year, which is about 12% of all detected cancers, of which up to 60% are in developed countries. The average age of patients with LC is 62; men get sick much more often than women (9÷1). Numerous studies have identified the relationship of the incidence of LC with various exogenous and endogenous factors. The study of the epidemiology of LC has scientific and practical relevance, since it allows monitoring ongoing activities and assessing the impact of possible causal risk factors.

Aim. To study the incidence of LC 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 LC (form 7), as well as population data for 2007–2016, taking into account the age- and sex-related structure. A retrospective study using descriptive and analytical methods of epidemiology. The age-specific incidence rates (ASIR) is calculated at 100,000.

Results. In the Republic of Kazakhstan, 36,330 new cases of LC were recorded during this period: of these, 29,504 were men (81.2%) and 6,826 (18.8%) were women. The average annual incidence rate of LC was $37.0 \pm 0.5^0 /_{0000}$ for men and $8.0 \pm 0.2^0 /_{0000}$ for women, while the overall incidence ratio was 4.6÷1.0, and the largest difference in incidence by sex was set at the age of 60–69 (table).

Table. ASIR of LC in Kazakhstan, 2007–2016

Age	Both sex (T, %)	Male (T, %)	Female (T, %)	M÷F
<50	2.5±0.2 (–8.0)	3.6±0.4 (–9.7)	1.3±0.1 (–3.7)	2.8÷1.0
50–59	57.2±2.2 (–3.6)	107.5±5.0 (–4.5)	15.4±0.5 (–0.4)	7.0÷1.0
60–69	137.1±1.8 (+0.3)	284.0±3.4 (–0.2)	35.6±1.3 (+0.8)	8.0÷1.0
70+	141.0±2.3 (–0.3)	320.1±5.7 (–0.5)	50.8±1.6 (+0.9)	6.3÷1.0

ASIR of LC are characterized by unimodal growth with a peak in the older age group (70 and older) – $320.1^0 /_{0000}$ and $50.8^0 /_{0000}$, respectively for men and women, while incidence trends had different patterns (table).

Conclusions. Thus, the identified age- and sex-related epidemiological aspects of LC have to be used to conduct comprehensive and targeted interventions to strengthen prevention and reduce incidence.

Acknowledgements. The study is supported by public association “Central Asian Cancer Institute”.

Medical and geographical variability of incidence of melanoma skin in Kazakhstan

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Background. Medico-geographical map is a promising method for establishing the relationship between the factors of the geographical environment and the state of human health, the occurrence and dynamics of various diseases. Geographical variability of melanoma of the skin with the highest rates was observed among the white population living in countries with hot climates, namely in Australia ($33.6^0/_{0000}$), among the white population of the Hawaiian Islands, among white Americans, as well as among Swiss, Swedes, Danes, and Dutch. The identified regional features of the melanoma's spread of the skin made it possible to draw up a cartogram of the incidence, which indicate the regions of low, medium and high incidence rates.

Purpose. To study the medical-geographical variability of the incidence of melanoma of the skin among residents of Kazakhstan in different regions.

Materials and methods. This study contains a cartogram of the incidence of skin melanoma in Kazakhstan. Age-standardized rates (ASR) of incidence for 10 years (2007-2016) were used to compile cartograms. The cartogram compilation method used is based on the determination of the standard deviation (σ) from the mean (\bar{x}).

Results. At the beginning, incidence rates of skin melanoma were determined, which meet the following criteria: low – up to $1.38^0/_{0000}$, medium – from 1.38 to $2.26^0/_{0000}$, high – above $2.26^0/_{0000}$. On the basis of the above calculations, an incidence mapping chart has been compiled in various medico-geographical zones of the republic; the following groups of areas are defined:

1. Regions with low indicators (up to $1.38^0/_{0000}$) – Kyzylorda ($0.57^0/_{0000}$), Aktobe ($0.84^0/_{0000}$), West Kazakhstan ($0.88^0/_{0000}$), South Kazakhstan ($0.93^0/_{0000}$), Atyrau ($1.16^0/_{0000}$) and Zhambyl ($1.33^0/_{0000}$) area.
2. Regions with average indicators (from 1.38 to $2.26^0/_{0000}$) – Akmola region ($1.69^0/_{0000}$) and city of Astana ($2.00^0/_{0000}$).
3. Regions with high rates ($2.26^0/_{0000}$ and higher) – Karaganda ($2.26^0/_{0000}$), Pavlodar ($2.42^0/_{0000}$) North Kazakhstan ($2.51^0/_{0000}$), East Kazakhstan ($2.63^0/_{0000}$), Kostanay ($2.70^0/_{0000}$) and Almaty ($2.74^0/_{0000}$) region, as well as the city of Almaty ($3.48^0/_{0000}$).

Conclusion. Thus, the established epidemiological features of the incidence indicate geographic variability of skin melanoma 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 melanoma and its incidence, which should be used to monitor and evaluate anti-cancer measures.

Acknowledgements. The study supported by public association «Central Asian Cancer Institute».

Opportunities of kinesiological taping in the prevention of sports injury in athletes powerlifting

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Background. The problem of injury prevention in sports is very important. Today, the level of injuries in sports is quite high (2-5% of the total level of injuries). There is also a high level of chronic pathology of the musculoskeletal system, which can lead to acute and repeated injuries. It is necessary to look for new opportunities to identify latent chronic pathology of the musculoskeletal system and ways to prevent secondary injuries in athletes.

Aim. Assess the possibilities of kinesiological taping in the prevention of sports injury in athletes powerlifting.

Methods. Altogether 35 athletes powerlifting at the age of 20 to 35 years were enrolled in the study. High level of sportsmanship (as part of the Republican team). The clinical method and manual muscle testing were used to assess the biomechanics of the musculoskeletal system. Evaluation of pain syndrome was carried out on a visual analogue scale (VAS) and questioning. In addition, medical records were evaluated. Most of the athletes had a chronic pathology of the musculoskeletal system without clinical manifestations, but recorded in medical records. By manual testing of muscles in athletes, functional changes in the musculoskeletal system of varying severity were identified. On the basis of functional impairments at all stages of preparation for the main competitions, kinesiological taping (muscular-ligamentous, fascial, drainage and volumetric methods) was used.

Results. As a result of the study, none of the athletes had any acute injuries. The emergence of new pain syndromes was not registered either during the preparation for the competition or after. According to a study of sports results, it was found that all athletes improved their results.

Conclusion. The use of manual muscle testing reveals a "hidden" violation of the motor stereotype and kinesiological taping allows you to restore it, which in the future will reduce the likelihood of primary or repeated damage to the musculoskeletal system. This is the reason for the inclusion of these methods in the system of prevention of sports injuries.

Acknowledgements. No conflict of interest was declared.

Breast cancer in Kazakhstan: Changes in consequences of screening?

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Background. According to the IARC, in 2018 about 2,100 thousand cases of breast cancer (BC) were registered in the world, and this figure has doubled compared with 2008, which causes great concern and requires great effort in anti-cancer activities.

Aim: To study the changes in some indicators in BC in Kazakhstan.

Methods. Material of the research is based on a data of Health ministry of the republic of Kazakhstan – annual form 35, related to BC. A retrospective research (2007–2016) with descriptive and analytical methods of epidemiology was used as a main method. The periods before screening start (2007), the start of screening (2008) and the period of screening implementation as a part of the National Program of Oncological Aid Development in the Republic of Kazakhstan for 2012–2016 were analyzed.

Results. In 2016, it was registered 4,598 woman with the first ever diagnosis of BC and this number increased on 50.2 compared with 2007 (3,062 BC) (table).

Table. BC in Kazakhstan (data from №35)

Indicators	2007	2008	2012	2016
New cases	3062	3239	3924	4598
Morphological verification	2931 (95.7%)	3085 (95.2%)	3781 (96.4%)	4554 (99.0%)
I-II stage	2057 (67.2%)	2261 (69.8%)	2998 (76.4%)	3817 (83.0%)
III-IV stage	1004 (32.8%)	974 (30.1%)	916 (23.3%)	766 (16.7%)

In dynamic, the indicators of early diagnosis (the proportion of patients with stage I-II) increased from 67.2% (2007) to 83.0% in 2016. A reduction in the proportion of patients with stage III-IV BC was found from 32.8% in 2007 to 16.7% in 2016. The index of morphological verification of BC in 2007 was 95.7%, and in 2016 it was 99.0%.

Conclusions. Evaluating the obtained data, it can be noted that in Kazakhstan there is a global growth trend in patients with BC. At the same time, changes are observed in the indicators of the oncological service: the indicators of morphological verification and early diagnosis increase, the proportion of patients with stage III-IV decreases. Screening for BC in Kazakhstan was started in 2008 and it is certainly impossible to deny all the positive changes associated with this fact.

Acknowledgements. The study supported by public association “Central Asian Cancer Institute”.

The significance of hand hygiene training of medical staff in the formation of proper hand hygiene skills

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Background. An important factor in reducing the transmission of microbial contamination is the practical training of staff in hand hygiene skills for the prevention of hospital infections. The amount of microbial contamination on the staff's hands ranges from 3.9×10^4 to 4.6×10^6 CFU (colony forming unit). Poor hygiene of personnel hands is influenced by the nature of the procedure, lack of time, haste and lack of knowledge. Studies have shown that through unsafe procedures such as touching the skin of a patient, dressing up, staff can get hands on 100-1000 CFU *Klebsiella spp.* Studies also indicate that microbial contamination increases and intervention of the gram-negative sticks on the patient's skin and colonization during intervention procedures. The training encourages staff to become more familiar with the manual hygiene rules, visual hand-washing and antiseptic method materials. Knowledge of hand hygiene rules improves hand hygiene skills and reduces microbial contamination in the working environment.

Aim. The aim of the current study was to analyze hand hygiene errors made by medical staff and to evaluate the importance of training in the formation of proper hand hygiene skills.

Methods. The research was performed for three years in one of the Lithuanian hospitals. The monitoring method was chosen, medical staff was the focus group of the survey (n=272). Every employee was monitored 6 times in a year before the intervention procedure was performed. After the monitoring, once in a year (in total 2 times), hand hygiene training was performed. Staff hygiene skills were assessed before and after the training according to seven criteria: work clothing, hand jewellery, condition of hand skin, hand washing, drying, antiseptics, and compliance to hygiene rules.

Results. The most commonly observed hand hygiene mistakes of medical staff: hand jewellery (34.4%), work clothing (22.8%), non-compliance to the rules (21.0%), hand washing (19.3%). Every year the number of hand hygiene mistakes made by medical staff was decreasing (p=0.001). After the first hand hygiene training of the staff the number of mistakes decreased from 15.5% to 9.9%, after the second training – up to 7.6%.

Conclusion. Hand hygiene training of the medical staff had the considerable significance in the formation of practical hand hygiene skills – the number of hand hygiene mistakes has decreased twofold.

Evaluating of the common preanalytical blood sampling mistakes made by nursing staff in clinical laboratory

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Background. Biochemical, hematological and coagulation tests of venous blood often guide medical decisions, as changes in analyte concentrations can be observed without clinical signs of the disease. Because up to 60% of the testing process is centered around the preanalytical phase, preanalytical errors account for more than $\frac{2}{3}$ of all laboratory errors. Nurses play a major role at all stages of the preanalytical phase of blood tests.

Aim. The aim of this study was to analyse the most common mistakes made by nurses in the preanalytical phase of venous blood hematological, biochemical and coagulation tests.

Methods. Research is based on observation of 104 preanalytical phases of venous blood haematological, biochemical and coagulation tests. The study involved nurses who worked in four departments of the hospital in Vilnius. Observation data registered in the observation diary.

Results. 1. During blood sampling preparation 220 mistakes were made. Most common mistakes: not checking of expiry date of the equipment (100%), inadequate number of test-tubes (45.2%), ignoring of factors influencing study (25.9%), reuse of disposable gloves (25%) and holders (7.7%). More mistakes were made by older than 35 years nurses, who worked for more than 10 years, and nurses with higher non-university education ($p < 0,0001$). 2. During blood sample taking 971 mistakes were made. Most often mistakes: cleaning the puncture site in the wrong direction (91.3%), using of a small amount of tampons (88,5%), keeping of the filled tubes in the horizontal position (79.8%), venepuncture puncture before evaporation of antiseptic from the skin (77.9%), neglecting of hand preparation before puncture rules (51%), putting of the tampon used for disinfection on the puncture site (49%), failure to comply with order of the sampling tube (45.2%), puncture in the site of hematoma (40%), not mixing of the additive in the test-tube with blood (40%). More mistakes were made by nurses from 35 to 45 years who worked for more than 10 years, and nurses with higher non-university education ($p < 0,0001$). 3. Total number of mistakes are 1191 mistakes.

Conclusion. Correct blood collection technique is necessary to avoid false test results. Mistakes occur due to staff knowledge and lack of practical training, and the prevailing view that blood collection is a very simple procedure. In fact, the correct collection and delivery of blood samples to the laboratory requires a lot of knowledge, skills and experience, and only proper training and control can significantly reduce the likelihood of mistakes.

Motivation to provide first aid

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Background. Road traffic accidents are one of the most frequent causes of death, creating a burden on public health and development (Pathak, Jindal, Verma & Mahen, 2014). The number of deaths could be reduced if the first aid is given at the place of an accident before arrival of an emergency service since it may increase the likelihood to survive or get less severe injuries (Alinia, Khankeh, Maddah & Negarandeh, 2015). Motivation for taking an action can be affected by psychological aspects as a compassion or human instinct but also from logical action based on knowledge. The acquisition of knowledge gives the motivation a higher probability of achieving the goal.

Aim. The aim of the current study was to analyze how motivated people are to provide first aid and what are the factors affecting motivation. In particular, to determine in what occasions people are motivated to help others and what is the general perception of people.

Methods. Altogether 100 driving school students who attended first aid course in Riga area at age group from 18 to 45 years were enrolled in the study. Questionnaire with 15 multiple choice questions with one or several optional answers as well as a possibility to write own answer was developed which was tested in a pilot study beforehand.

Results. The data revealed that 68 respondents have had previous experience in situations when provision of first aid was needed. Majority of respondents (n=44) rated their motivation as "medium", 35 respondents noted that they have high motivation but only 3 marked that they do not have motivation to provide first aid. Data showed that respondents feel more motivated if the person in need is closely known (n=48). Questions about knowledge and other factors of motivation indicated that people have basic knowledge in provision of first aid, namely they know how to call emergency service (n=93), and 74 respondents believe that motivation would increase by gaining first aid knowledge.

Conclusion. This study confirmed the importance of first aid knowledge and how motivated people are to provide it. People have basic knowledge in first aid, however it should be advanced. Knowledge of first aid and first aid training while acquiring driving licence is essential and increases motivation for people to help others in life threatening situations.

Acknowledgements. No conflict of interest or funding occurred in this study

Aspects of Organ Donation in Latvia

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Background: The lack of donors can substantially delay development of transplantology. Transplantation as an industry has been little popularized. Media reflects a little information about organ transplantology and it is rarely with positive connotation.

A citizen of Latvia can express his consent or his ban on becoming an organ donor after his death by submitting an application to the Office of Citizenship and Migration Affairs (OCMA).

Aim: what aspects would encourage the people of Latvia to donate organs for transplantation.

Methods: Quantitative cross-sectional research method and the tool – a questionnaire which is based on the core values of theory of caring and bioethics.

The research was conducted on the Internet (www.visidati.lv) between adults in 2018.

Results: 113 questionnaires were filled out, of which 90.3% were filled by women, 68.1% of the respondents had children; mostly in reproductive age. 77% have a positive attitude towards organ and tissue donation. 48.7% of respondents got information on donations from the mass media, 24.8% of respondents have not come across such information at all. 80.5% have not applied to the OCMA. 70.8% would be willing to donate organs after their death. By agreeing to donate organs during their lifetime 20.4% would only donate to their children, 56.6% – only to relatives. 55.8% would not refuse to become organ recipients themselves. 61.9% of respondents believe organ donation during their lifetime can cause health problems to them. 72.6% believe that information campaigns on organ donation should be conducted and 60.2% think that positive information should be provided. 56.6% agree that any person could become an organ donor after death unless he or she has made a written prohibition.

Conclusions: The majority of respondents have a positive attitude towards organ donation in general; however, they have not applied to the OCMA as one of the reasons mentioning the lack of positive information campaign. Any person after death could automatically become a donor of organs or tissues if this person has not provided a written prohibition. Personal aspect is essential for organ donation during the lifetime; majority will not refuse to become organ recipients themselves. Respondents mention possible health problems as one of the reasons for refusing to donate organs during the lifetime. Religious belief is not an obstacle to organ donation.

The use of physician's personal experience and example in medical practice

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Background. The use of physician's personal experience in the process of treatment can have both positive and negative effects on patients. Only few studies have been found on positive and negative physician's influence on patients in their treatment process. A comprehensive analysis of this topic would allow to better understand the cause of patient's decision, motives, factors that may determine the course and outcome of the treatment.

Aim. The aim of this work is to ascertain how does the positive and negative physician's personal experience affect patients, how does their choice in their own treatment process depends on it.

Methods. 544 Lithuanian residents (246 men and 298 women) participated as respondents in an anonymous online survey. A retrospective statistical analysis of the data was performed using the software package of SPSS_22.0.

Results. The survey reflects that patients value the application of doctor's personal experience positively (N = 292; 53.7%). A doctor suggesting drugs because of his and his child's good personal experience can help to decide to start the treatment (N = 311, 57.2% and N = 279, 51.3% when P <0.05). A personal example can encourage to become a blood donor ("has a positive effect" chosen by N = 184, 33.8% when P <0.05). Patients appreciate physician's personal opinion on the conservative treatment ("has a positive effect" chosen by N = 304, 55.9% and N = 293, 53.9% when P <0.05). The operative experience has a statistically significantly positive effect on the choice of surgical treatment (N = 310, 57% and N = 325, 59.7% when P <0.05). Physician's recommendation not to vaccinate, not to become blood donors was evaluated neutrally. The patient, after hearing the physician's recommendation to avoid the selected drug, is most often guided by doctor's opinion (positive answer N = 270, 49.6% when P <0.05). A physician with harmful habits has a negative impact on the patient's choice (N = 360, 66.2%).

Conclusions. In conclusion, physician, giving information about positive experience of drug use, blood donation, conservative and operative treatment, has a greater influence, may faster determine / change patients' attitudes towards treatment. Harmful physician's habits, recommendation not to take the drug can negatively affect the choice.

Acknowledgements. None.

On prostate cancer incidence in Kazakhstan

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Background. Epidemiological studies demonstrate that prostate cancer (PC) rate is not same in different countries. According to estimated data of IARC were registered about 1,276 cases of prostate cancer in the world to 2018 and its age-standardized rate (ASR, World) is 29.3⁰/₀₀₀₀.

Aim. To study specific features of prostate cancer incidence in Kazakhstan.

Methods. As the material for this retrospective research of 10 years (2007–2016) was used data from all cancer institutions in our republic. According to the research was defined extensive, age-specific incidence rates (ASIR), CR, and ASR (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, 9,593 new cases of PC were registered in Kazakhstan. At the same time, high share of patients were at the age of 70 and older (47.7%) (Table).

Table. PC in Kazakhstan, 2007–2016

Age	Number (%)	M±m, ⁰ / ₀₀₀₀	95% CI, ⁰ / ₀₀₀₀	T, %
<50	104 (1.1)	0.16±0.03	0.10–0.22	–9.2
50–59	1,303 (13.6)	16.2±1.9	12.4–19.9	+9.9
60–69	3,610 (37.6)	92.5±12.3	68.5–116.5	+14.5
≥70	4,576 (47.7)	177.2±13.4	151.0–203.5	+7.9
Total	9,593 (100.0)	11.9±1.3	9.4–14.3	+11.4

Average age of patients with PC was 69.5 (95% CI=68.9–70.1). Over time, this indicator increased from 67.9 (2007) to 68.4 in 2016 (T=–0.1%).

Annual average ASIR showed unimodal growth with a peak at the age of 70 and older – 177.2⁰/₀₀₀₀ (table). At the same time, these differences in age-specific incidence rate were statistically significant (p<0.05). PC incidence trends were different: to reduction before the age of 50, and growth with the age of 50 and older (Table). Annual average CR of PC was 11.9⁰/₀₀₀₀ (95% CI=9.4–14.3⁰/₀₀₀₀); incidence rate grew (T=+11.4%). ASR (World) was 17.4⁰/₀₀₀₀ (95% CI=15.0–19.8⁰/₀₀₀₀). ASR also grew (T=+10.5%).

Conclusions. PC rate has grown in recent years in Kazakhstan. ASIR of PC was the highest with the age of 70 and older. Over time, ASIR before the age of 50 has reduced, and they have grown with the age of 50. ASR (World) of PC rate were significantly different from the CR, and growth has been noted over time.

Acknowledgements. The study supported by public association “Central Asian Cancer Institute”.

Public knowledge of possible weight loss methods

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Background. Adiposity is chronic disease that usually combines with other diseases and lowers quality of life. There are known three key approaches how to treat obesity: lifestyle change, weight loss medications and also weight loss surgery. Diet and physical activities are lifestyle components that can determine health condition, which in turn is closely related to obesity and its complications. Increased weight and obesity should be overviewed as a multifactorial outcome and there is no single specific factor predicting it.

Aim. The aim of the current study was to enucleate public awareness of various methods of combating overweight and adiposity.

Methods. Residents of Latvia via social networks were asked to fill anonymous electronic survey form. During the period of 2 weeks 189 unique survey records were received. Statistical analysis was done using SPSS 22 and MS Excel.

Results. The average age was 40 years, 97% of them were females. Average body mass index (BMI) was 31 kg/m² with interquartile dispersion 27–35 kg/m². Most of participants were overweight (BMI 25–29,99 kg/m²; 26,5%) or had obesity grade I (BMI 30–34,99 kg/m²; 23,3%). Both of groups admitted that during lifetime they have had even higher body weight and BMI than present (91,5 kg; BMI 32,6 kg/m² respectively). The most popular weight loss methods were diets and physical activities, but less often medications for weight loss, different meal replacements and weight management consultations. 60,3% of participants had at least one comorbidity like cardiovascular diseases, pulmonary diseases or endocrine system dysfunctions. More than 60% of participants agreed that their health condition would become better if they would succeed to reduce body weight. There was correlation in between physical activity and body weight – the more participants were doing sports, the less was weight and opposite. ¼ of participants noted the lack of willpower and need for support from families and friends to reduce weight. Median time amount that they spent for physical activities during week was 6 hours.

Conclusion. The public lacks sufficient and adequate information on how to gain and maintain a healthy body weight. It is important to set supporting groups also. Since only seldom participants choose specialist consultations, it is necessary to emphasize and broaden the knowledge of obesity for general public and also to explain the possible solutions for weight management including adequate physical activity.

Assessment of the quality criteria fulfillment of the rehabilitation process according to the patient satisfaction questionnaire data

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Background: Patient satisfaction with the provided health care is a significant component of quality assessment and healthcare outcomes. It is important to be able to identify weaknesses in systems and to aid improvement, thus resulting in better outcomes, both in terms of overall satisfaction with received care, and in terms of recovered health status. This may be done by utilizing the Patient Satisfaction Questionnaire Short Form (PSQ-18), a concise, validated tool that may be applied to various settings, as well as comparing interventions.

Aim: To assess the patient satisfaction with the provided health care in Pauls Stradiņš Clinical University Hospital, outpatient rehabilitation center.

Methods: The aim of the study is to assess and to describe patient satisfaction with the provided health care in Pauls Stradiņš Clinical University Hospital, outpatient rehabilitation center using (PSQ-18) questionnaire which consists out of 18 questions. The questionnaire was distributed to 174 patients who were treated in rehabilitation center during the time period from 16.07.18 until 21.12.18. and had to assess general satisfaction, technical quality, interpersonal manner, communication, financial aspect, time spent with doctor, accessibility and convenience. Each item is accompanied by five response categories (strongly agree, agree, uncertain, disagree, strongly disagree).

Results: Using descriptive statistics methods were analyzed the overall score distribution characteristics for the 7 subscales (general satisfaction, technical quality, interpersonal manner, communication, financial aspect, time spent with doctor, accessibility and convenience. Measured on a 5-point scale (1 = lowest satisfaction, 5 = greatest satisfaction).

The mean general satisfaction score was 4.25, satisfaction with technical quality was 4.28, for interpersonal manner was 4.58, for communication 4.28, for financial aspect 3.77, for time spent with doctor 4.26, for accessibility and convenience 3.67.

Conclusions: The results reveal patient dissatisfaction with the financial aspect of rehabilitation, as well as with the accessibility of rehabilitation concerning the time frame for the beginning of the rehabilitation. In general, one of the quality criteria of the provided rehabilitation service - patient satisfaction indicator, show good quality of rehabilitation services in Pauls Stradiņš Clinical University Hospital, Physical Medicine and Rehabilitation Center.

Study on the safety climate in Latvian Hospitals: the first evidences

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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 a safety culture and 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 hospitals' needs. Assessment of safety culture was recommended by international experts as an appropriate way to get the impression on patient safety situation.

Aim. The aim of the study was to assess the highest and the lowest characteristics of patient safety climate within staff of different hospitals in Latvia.

Methods. Twenty-four hospitals were enrolled into the study. Validated Safety Climate Survey was used to assess six safety domains: teamwork climate, safety climate, stress recognition, job satisfaction, perceptions of unit management, and perceptions of hospital management and work conditions. Assessment of each domain contained 42 questions expressed from 1 to 5. Reliability analysis and descriptive statistics was performed for each domain. In addition, descriptive statistics was performed for each question individually and for demographic variables of participants.

Results. Study sample included 744 participants, mostly women (92%) aged 40-65 and worked more than 10 years. Of them, 681 (91%) worked full time: (40%) in therapeutic and (22%) in surgery/operating theatre units. 146 (20%) participants were physicians, 321 (43%) were nurses, and 75 (10%) were from an administrative staff. 167 (22%) participants never attended a patient safety training. According to the Safety Climate Survey, the highest values were observed for job satisfaction and for stress recognition (3.63 and 3.73 of 5, respectively). The lowest values were observed for safety climate (3.43 of 5). For the individual questions the highest scores were observed for the next items: *I like my job* (4.40); *I know the names of the personnel I worked with during my last shift* (4.23). The lowest scores were observed for items: *The levels of staffing in my work area are sufficient to handle the number of patients* (2.55); *In my hospital is difficult to discuss errors* (2.88); and *In my work area is difficult to speak up if I perceive a problem with patient care* (3.01).

Conclusion. Learning from errors is limited when it is difficult to discuss them openly. Speak-up and communication gaps needs specific teamwork trainings.

The application of doctor's personal medical experience in treatment of children and adults

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Background. According to literature, the application of doctor's personal medical experience in the process of treatment has an influence on patients: adults and children. A doctor who often uses personal experience creates a close contact with patients more easily, gains their confidence and achieves better treatment outcomes. Analysis of doctor's personal experience application in clinical practice would allow not only to understand patient's decisions, but also to ascertain what type of experience a doctor should share with a patient.

Aim. Primary objective was to analyse the influence of doctor's personal experience and representative instances on children and adults. Secondary objective was to determine the influence of doctor's personal experience on different treatment methods, such as: operative, conservative (treatment of chronic diseases), preventive medicine (vaccination).

Methods. An anonymous survey based on articles about the influence of doctor's personal experience and examples of patients' options was created. 544 Lithuanian patients – 246 men and 298 women were selected randomly to be a part of the survey. A retrospective statistical analysis of the data was performed using the software package of SPSS_22.0.

Results. The results of the survey showed that patients value the application of doctor's personal experience positively (N=292; 53.7%, when $P < 0.05$). Doctor's negative personal experience after vaccination did not have an influence on patients' options (for adults N=234; 43% and children N=245; 45%, when $P < 0.05$). The results showed that a doctor who had an operation and used his positive experience, had a greater positive influence on the choice of operative treatment for children (N=325; 59.7%, when $P < 0.05$) than adults (N=310; 57%, when $P < 0.05$). It has been found, that when a doctor and a patient suffer from the same chronic disease, and the doctor shares his experience, this has a positive influence on adults (N=304; 55.9%, when $P < 0.05$). The provision of information about doctor's child's chronic disease has a positive influence (N=293; 53.9%, when $P < 0.05$). There has been a tendency to have a greater positive effect of doctor's personal experience on adults than children (55.9% vs. 53.9%, when $P < 0.05$) in treatment of chronic diseases.

Conclusion. The application of doctor's personal experience has a positive effect for operative and conservative treatment. Doctor's negative personal experience does not influence vaccination. In addition, doctor's personal experience has a greater positive effect on adults in treatment of chronic diseases, whereas, the application of experience in surgical treatment has a positive effect on children.

Acknowledgements. None.

The comparison of ankle injury rate in professional volleyball players and general population in Latvia

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Background. Ankle injury is the most frequent trauma among volleyball players. It includes ankle sprain, luxation, ligament damage and ankle bone fractures. Most frequent symptoms in case of ankle injury are stiffness, intense pain, inability to walk and swelling. Because of the heavy load on the legs during trainings and competitions, professional volleyball athletes are often prone to ankle injuries.

Aim. The aim of the current study was to compare the prevalence of ankle injury between professional volleyball players and general population in the age group 18 to 25 years old in Latvia. Despite both groups are similar age the physical activity is different. Figuring out particular physical activity, shows the biggest trauma rate.

Methods. Altogether 205 patients aged from 18 till 25 years old were enrolled in the study. To investigate this matter, questionnaire was made, in which both groups were asked about ankle trauma rate and type; how long professional volleyball players are doing professional sports; trauma preventive methods and others. To objectify professional volleyball players discomfort and pain level DABI index was used. That evaluates pain severity during running, jumping, landing and others. Data were processed using MS Excel 2010 and SPSS 20 programmes.

Results. Among 205 respondents, 101 are professional volleyball players, which included players from professional leagues and Latvia National team. 104 respondents do not play volleyball. Age ranged from 18 to 25 years. Average sporting time for professional players is 9 hours per week, but for population – 3 hours per week. From 101 professional volleyball players – 83 had ankle trauma. From 104 people who do not play volleyball – 52 had ankle trauma. This allows to hypothesize, that percentage of professional volleyball players that had ankle trauma (82.2%) is much higher, than percentage of people who do not play volleyball (50.0%).

Conclusion. Results show us that professional volleyball players are in higher risk group of having ankle trauma than other population.

The evaluation of keratoconus patients' quality of life

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Background. Modern medicine prolongs patients' lives with chronic diseases, therefore concept „quality of life” is essential. Keratoconus is a progressive corneal disease, which irreversibly reduces the quality of vision. Keratoconus patients have different apex positions – central and peripheral. Keratoconus starts at a very young age so it reduces the quality of life.

Aim. The aim of our study was to evaluate the impact of keratoconus apex on patients' quality of life.

Methods. Keratoconus subjects completed National Eye Institute Visual Functioning Questionnaire – 25 (VFQ-25) to understand their quality of life and there were measured visual acuity and contrast sensitivity too. The questionnaire consisted of three parts. At the first part, subject evaluated the general health and vision (four questions), at the second part, subject evaluated the difficulties to do everyday tasks (twelve questions), and at the third part, subject evaluated the created restrictions of vision in everyday tasks (nine questions). 39 questionnaires overall were completed, from them, nine subjects had the central keratoconus apex in both eyes, 18 subjects – the peripheral apex in both eyes, and 12 – the different location of keratoconus apex in both eyes.

Results. The most difficult tasks were in the near like reading or seeing names of the street for 88% of subjects with central keratoconus apex and 66% of all keratoconus subjects. Activities, like visiting other people or go to parties or restaurants, were difficult for one subjects in each group with central and peripheral apex, and with different apex positions. 56% of subjects with central apex, 44% with peripheral apex, and 58% with different apex positions didn't have the difficulties with activities like go to the cinema, playing games or other sports. Subjects (56% of subjects with central, 78% with peripheral, and 67% with different apex positions) didn't have the difficulties to go down the stairs or take a step in twilight or darkness.

Conclusion. The impact of the quality of vision on the quality of life could be explained by the finding differences of contrast vision sensitivity. Subjects with central keratoconus apex of our study have the reduced contrast vision by spatial frequency 7 cycle/degree; subjects with peripheral apex – by 11 cycle/degree, it could be the reason of difficulties to do everyday tasks where the subject need to get the information about the overall world and this information consists of the high spatial frequencies.

Acknowledgements. The authors have no conflicts of interest to disclose.

Trends of age-specific incidence rates of cancer of the corpus uteri in Kazakhstan

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Background. Age is a variable whose role should be considered in all epidemiological studies, since the state of health, perhaps more than other characteristics, is associated with age. Age, as is well known, is a universal factor and the most important determinant of the risk of developing malignant tumors, including cancer of the corpus uteri (CCU).

Aim. To study the trends of age-specific incidence rates of CCU in Kazakhstan.

Methods. The material of a retrospective study for 2007-2016 was the data of oncological institutions of the republic concerning CCU, 9,955 new cases for the studied period. Extensive, crude rate (CR) and age-standardized (ASR, World) incidence rates of CCU, 95% confidence interval (95% CI), average annual growth rates/decrease (T, %) are calculated.

Results. The average age of patients with CCU in Kazakhstan was 60.0 years (95% CI=59.4-60.5 years). The average annual CR incidence of CCU in Kazakhstan was 11.6⁰/₀₀₀₀ (95% CI=10.9-12.3⁰/₀₀₀₀). Age indicators for the studied periods had a unimodal growth with an incidence peak in the age group of 60-69 (Table).

Table. Changes of age-specific incidence rates of CCU in Kazakhstan

Age	2007	2012	2016	T, %
40-49	14.3±1.1	12.6±1.1	11.3±1.0	+0.4
50-59	31.3±1.9	32.5±1.8	36.6±1.9	+2.6
60-69	41.9±2.9	58.7±3.4	63.2±3.1	+3.9
70+	32.5±2.6	39.2±2.7	40.0±2.8	+1.7

Trends of incidence of CCU in different age groups make it possible to assess and characterize the general trend of growth or decrease in incidence rates. So, in the age groups up to 40 years high rates of incidence decrease are observed, especially up to 30 years (T=-5.2%). In other ages, an increase was determined, with the most pronounced in 60-69 years (T=+3.9%).

The ASR for CCU in Kazakhstan was 11.0⁰/₀₀₀₀ (95% CI=10.4-11.5⁰/₀₀₀₀). In dynamics, aligned ASR tended to increase, and the average annual growth rate was: T=+2.2%.

Conclusion. The results of the study show that the average age of patients has a slight tendency to aging. Analysis of age indicators indicates that the maximum incidence was found in 60-69 years, where high growth rates are also established. To sum up, the obtained results must be considered during monitoring and evaluating anticancer measures.

Acknowledgements. The study supported by public association "Central Asian Cancer Institute".

Years of life lost as a result of road traffic injuries in the Republic of Kazakhstan

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Background. Road traffic injuries are one of the most important medical and social problems not only in Kazakhstan, but in all over the world. The optimal tool for studying the overall picture of health and identifying the causes of its decline today is the global burden of disease, which contributes to the assessment of the overall picture of the health system, to evaluate the health loss associated with mortality and facilitates the comparison of indicators at country level.

Aim. Estimate the number of years of life lost (YLL) from road traffic injuries.

Methods. The materials of the study were data from the Statistics Agency of the Ministry of National Economy of the Republic of Kazakhstan on the number of deaths by sex and age structure for 1999–2016. In the calculations of the YLL index, the methodology was used according to the WHO international methodology.

Results. In 2016, total losses from road accidents amounted to 83,318 man-years of life (YLL), which was increased compared to 1999 (71,226 YLL) by 14.5% and decreased in comparison with 2007 (174,847 YLL) by 52%. The average age of those who died for the study period was $30,4 \pm 0,4$ years. Over the 18 year period, the peak of road traffic deaths is in 2007. The YLL at working age (15–49 years) in 2007 amounted to 140,402 YLL and decreased in 2016 to 60,306 YLL, or by 57%. Among women, YLL in 2007 was 39,815 years old, among men 120,684 years old.

In the dynamics of YLL per 100,000, the population from 1999 to 2007 grew from 476.3 0/0000 to 1135.60 / 0000, with a subsequent decrease in 2016 to 471.50 / 0000

Conclusion. The analysis showed that there is a high YLL index for both women and men. However, YLL is more pronounced in the male population. Particular attention is paid to the greatest number of lost years of life in the active working age as one of the factors affecting the demographic and economic growth of the country as a whole.

About the mortality of road traffic accidents in Kazakhstan

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Background. Road traffic accidents (RTA) are one of the most important public health problems and the leading cause of mortality worldwide. Traumatism leads to premature mortality and disability of the population, cause huge economic loss, reduces creativity and entails decrease of working capacity and reduced quality of life.

Purpose. Analysis of mortality from road traffic accidents in Kazakhstan.

Methods. The study materials were official reports of mortality rates of RTA from the Committee on Statistics of Ministry of National Economy of the Republic of Kazakhstan. Age-specific and standardized mortality rates per 100,000 ($^0/_{0000}$) were calculated. Trends of mortality were determined by the method of least squares and the rate of growth/loss (T, %) calculated.

Results. In Kazakhstan 55,758 people were died in a RTA during 1999–2016, including 41,257 (74.0%) of male and 14,501 (26.0%) of female. The average age of death was 37.3 years (both sexes), 36.7 years (male) and 38.9 (female). The age-standardized mortality rate of RTA was 19.4 for the whole population, 30.5 (male) and 9.7 (female). The standardized rates of the whole population from 1999 to 2007 increase from $13.8^0/_{0000}$ to $31.5^0/_{0000}$, with a subsequent decrease in 2016 to $15.3^0/_{0000}$. The average annual mortality rate increase in alignment amounted for 17 years for the whole population $T=+0.4\%$, $T=+0.3\%$ (male) and $T=+0.8\%$ (female).

The age-specific mortality rates had an increase in the age of 30–39 ($28.6^0/_{0000}$) and 40–49 years ($26.4^0/_{0000}$). The picture was similar for male and female.

Conclusion. The analysis has revealed that mortality of RTA has a tendency to decrease as since 2008. Undoubtedly, this is related with tightening of administrative measures (changes were introduced in 2008) for violation of traffic rules, which allowed to considerably reducing the number of RTA. Monitoring and evaluation of epidemiological indicators is a key tool to make decisions in the management of road safety in the country, to strengthen prevention in the field of Public Health.

Prescription opioids addiction: Peculiarities of consumption and demography

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Background: Opioids are widely used prescription medicines for acute and chronic pain relief and cough suppression. It is recommended to administer these drugs at the lowest possible dose for the shortest possible time. Permanent, higher dose abuse causes dependence and poses a risk of overdose and death.

Aim: To analyze patients treated for opioid dependence and to identify whether harmful habits might influence using higher doses of opioids.

Methods: We retrospectively evaluated 40 patients, who were diagnosed with opioid dependence to prescription opioids and had undergone opioid detoxification treatment at Vilnius University Emergency hospital from the year 2011 to 2018. Patients admitted for opioid overdose and those who had been using illegal drugs (heroin) were excluded from the study. Since patients had used different kinds of opioids, the doses were converted into morphine equivalent (ME). Data was processed by MS Excel and SPSS 22.0 software.

Results: 40 patients (18 women and 22 men), ages ranging from 29 to 87 years, were studied. Average duration of opioid consumption was 61.67 months, ranging from 2 months to 336 months. 6 patients were consuming more than 2 opioids at the same time, morphine was consumed by 20 patients, tramadol by 14, methadone by 3, oxycodone by 4, fentanyl by 4, tilidate by 1. 70% (n=28) patients were administering medicine orally and 30% (n=12) were using medicine intravenously. Average ME dose was 132.81 mg, ranging from 20 mg to 690 mg. Patients addicted to alcohol used statistically significantly higher ME dose than those not addicted to alcohol, $p=0,002$. Alcohol-addicted patients' ME average dose was 350 mg, not addicted to alcohol – 113.65 mg. Smoking patients used statistically significantly higher ME dose than non-smoking patients, $p=0.016$. Smoking patients' ME average dose was 249 mg, non-smoking – 109 mg.

Conclusion: Half of the patients had been using morphine. More than two-thirds were administering drugs orally. Smoking and alcohol use had a statistically significant impact on ME dose. Nevertheless, further investigations in the future should be done with larger samples and more changeable factors could be included.

Acknowledgements: None

Quality of life and lifestyle of medical students

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Background. Many factors that influence the quality of life can also affect university students. Academic, social and financial pressures lead to mental health problems, which have a negative impact on study success and consequently, the student's quality of life. In comparison with other university students, medical students have the lowest quality of life. Poorer physical health, due to mental exhaustion and unhealthy lifestyle, is only one aspect of low quality of life.

Aim. The purpose of our research was to study the level of quality of life and lifestyle of medical students at the Faculty of Medicine University of Maribor. Numerous aspects of students' life habits dimensions were examined: physical activity, diet, smoking and substance abuse, drinking and sleeping habits. The signs of mental health, presence of life purpose, social integration, as student's extracurricular activities were also taken into consideration.

Methods. The study was conducted in the 2017/18 academic year and included a total of 165 medical students enrolled in the 1st, 3rd and 5th year of study. Hypotheses were tested with The FANTASTIC Lifestyle Assessment Instrument Questionnaire to evaluate life habits. The questionnaire was supplemented by dimensions associated with mental well-being, life purpose, social inclusion and student activities. The data was statistically analysed with the SPSS software and plotted with descriptive statistical calculations.

Results. The main finding of the research was that the number of students, who eat an unhealthy diet, consume more alcoholic beverages, medications increases over the years of study. First and third year students statistically significantly ($p = 0.014 < 0.05$) have a more balanced and diverse diet than 5th year students. Furthermore, there is a surprisingly high level of occasional over-the-counter and illicit drug consumption among 3rd year students, who begin with clinical practice ($p = 0.003 < 0.01$). No deviations from the mean were found in the following lifestyle dimensions: mental state, life purpose, social inclusion and study activities.

Conclusion. Medical students are subjected to high expectations and demands regardless of their year of study. As a result of unhealthy life habits, medical students are not able to cope with study challenges. A noticeable turning point is the 3rd year of medical study, when students are confronted with stressful situations during clinical practice and high demands of their studies decrease their ability to relax, express themselves and their creativity.

Acknowledgements. All authors have no conflict of interest to report. The research received no funding.

The Association of Depression among Patients of Hepatitis C Virus Taking Direct Antiviral Agent

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Background. Hepatitis C virus (HCV) - induced decompensated liver cirrhosis is a life-threatening illness with an average 5-year survival rate of 50%. HCV is endemic in Pakistan and its burden is expected to increase in coming decades owing mainly to widespread use of unsafe medical procedures. A systematic review showed that HCV seroprevalence among the general adult Pakistani population is 6.8%, while active HCV infection was found in approximately 6% of the population.

Aim. The aim of the current study was to determine the association of depression among patients of hepatitis C virus taking direct antiviral agent.

Methods. It was a Cross sectional study conducted at Unit II, Department of Medicine, Jinnah Hospital, Lahore, Pakistan. The study was completed in Six months from September 2017 to March 2018. Total 110 Patients fulfilling the inclusion criteria were selected from OPD of Department of Medicine, Jinnah Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, duration of HCV and DAA treatment) was also obtained. Then patients were evaluated for depression by a senior psychiatrist having at least 4 years' residency experience with assistance of researcher. If HADS score >11, the depression was labeled (as per operational definition). Patients with depression were managed by standard hospital protocol along with HCV treatment. All this information was recorded on proforma (attached).

Results. The mean age of the patients was 45.82 ± 13.20 years the minimum age was 22 years and maximum was 69 years. There were 53(48.2%) males and 57(51.8%) females in our study. There were 36(32.7%) patients who were illiterate, 41(37.3%) were middle, 33 (30%) were having education as matric or higher. There were 45(40.9%) patients with depression and 65(59.1%) without depression who were taking direct antiviral agent. There was significant association between Depression and age groups as the p-value was significant. (p-value=0.000).

Conclusion. Study findings concluded that major depression is a frequent occurrence among patients with hepatitis type C taking antiviral therapy.

Acknowledgements. There were no conflicts of interest in our study and there was also no any source of funding it was a self-funded study

The impact of emotional intelligence on burnout syndrome among medical students and resident doctors in Latvia

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Background. Burnout syndrome is caused by chronic stress and is characterised by exhaustion, depersonalisation and reduced performance – symptoms that diminish quality of life and may lead to depression. Emotional intelligence (EI) is the ability to perform analysis based on emotions and to use emotional knowledge. Higher EI may be a protective factor against burnout. However, there is scarce data on Latvian students' and resident doctors' burnout and EI. Hence, it is crucial to evaluate data on mental health in future doctors.

Aim. The aim of the study was to determine burnout rates, EI score and to assess correlation between EI and burnout among medical students and resident doctors in Latvia.

Methods. By January 2019, 67 students and resident doctors have voluntarily and randomly participated in the cross-sectional study which is conducted at the University of Latvia and online. Participants were surveyed using the Maslach Burnout Inventory – General Survey consisting of 3 scales – Exhaustion, Professional Efficacy and Cynicism (MBI – GS, Maslach, Jackson & Leiter, 1996, adapted in Latvia by Daiga Caune, 2004) and The Self-Report Emotional Intelligence Test (SREIT, Shutte *et al.*, 1998, adapted by Viesturs Renģe, Jeļena Nižņika, 2012). SPSS Statistics 22 was used for the statistical analysis of the data. Statistical significance level was set at $p < 0.05$.

Results. Participants were 18 – 40 years old; half of individuals ($n=37$) were in the age group of 24 – 26 years. 88% were female. 60 participants (90%) were studying at the University of Latvia and 7 (10%) – at Riga Stradins University. 81% were students ($n=54$) and 19% were in residency ($n=13$). 58% of individuals worked, with 27% working two jobs ($n=18$). Most of the employed participants reported working for 21 – 30 hours a week.

Using Pearson correlation coefficient moderate, negative, statistically significant correlation was found between EI and Exhaustion ($r=-0.49$, $p < 0.001$), weak correlation between EI and Cynicism ($r=-0.28$, $p=0.02$), and a positive, moderate correlation between higher EI and higher Professional Efficacy ($r=0.56$, $p < 0.001$). Independent Samples t-Test showed no statistical significance between EI and burnout in working and non-working individuals (Exhaustion $p=0.4$, Cynicism $p=0.6$, Efficacy $p=0.054$). Spearman correlation coefficient analysis showed no correlation between age and burnout ($p=0.4$).

Conclusion. Statistically significant correlation was found between higher EI and lower burnout which coincides with world literature findings, suggesting that higher EI acts as a protective factor against burnout. It indicates a need for a broader research on the population to support these findings.

**SATELLITE SYMPOSIUM:
DNA INTEGRITY IN HEALTH AND PATHOLOGY
(JANUARY 29, 2019)**

Medicina (Kaunas) 2019;55(Supplement 1):211

**Inflammation and the chemical carcinogen benzo[a]pyrene:
Partners in crime**

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Background: Exposure to benzo[a]pyrene (B[a]P) is known to play a role in lung carcinogenesis and the underlying processes can be modified by the presence of inflammation. During the inflammatory process, mediators are released that create a microenvironment that is suitable for further stimulation of cancer development. For instance, inflammation creates an acidic microenvironment.

Aim: To investigate whether low pH changes the cellular response to the carcinogen benzo[a]pyrene (B[a]P),

Method: Human pulmonary epithelial cells (A549 and BEAS-2B) were incubated with nontoxic doses of B[a]P using culturing media of various pH's (extracellular pH (pHe) of 7.8, 7.0, 6.5, 6.0 and 5.5) for 6, 24 and 48 h. B[a]P metabolism was studied by HPLC-fluorescence detection. Cytochrome P450 (CYP1A1/CYP1B1) expression was studied by qPCR and its activity by ethoxyresorufin-O-deethylase activity. Finally, DNA damage and repair was assessed by ³²P-postlabeling, γ H2AX foci and comet assay.

Results: In most incubations, the pH in the medium returned to the physiological pH 7.8 after 48 h, but at the lowest pH (pHe < 6.0), this recovery was incomplete. Similar changes were observed for the intracellular pH. We observed that acidic conditions delayed B[a]P metabolism and at t = 48 h the concentration of unmetabolized extracellular B[a]P and B[a]P-7,8-diol was significantly higher in acidic samples than under normal physiological conditions (pHe 7.8) for both cell lines. CYP450 expression and activity was initially repressed at low pHe after 6 and 24 h, but increased at t = 48 h. In addition, DNA repair was ~80% inhibited for 6h at low pHe and concomitant exposure to B[a]P. However, at t = 48 h, the incision activity recovered to more than 100% of the initial activity observed at neutral pHe. After 48 h, higher B[a]P-DNA adduct levels and γ -H2AX foci were observed at low pH than at pHe 7.8.

Conclusion: Acidic pH delayed the metabolism of B[a]P and inhibited DNA repair, ultimately leading to increased B[a]P-induced DNA damage.

From the Exposome to Disease Platforms and Systems Medicine: The Big Picture is Now Complete

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The concept of the *exposome*, representing the totality of exposures from gestation onwards, has been introduced as a complement to genomic data in the study of disease etiology. The original purpose of such investigations was the discovery of key biomarkers of exposure, to be used in exploring hypotheses about sources of exposure, dose-response relationships, mechanisms of action, disease causality and public health interventions. On the other hands, the implementation of systems approaches in clinical practice, and the development of complex predictive models which – under the 4 P's perspective – include social, psychological, and life-style parameters in the therapeutic process, has determined the inclusion of epidemiologic knowledge into clinical studies. The possibility to model in the same playground the complexity of the exposome and the variety of real clinical practice will help to identify new ontologies and to improve disease recognition and treatment.

The role of genome instability in brain ageing

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Background: DNA repair systems such as base excision repair (BER) may become less effective with ageing resulting in accumulation of DNA lesions, genome instability and altered gene expression that contribute to cellular and tissue dysfunction and increase the risk of age-related degenerative diseases. The brain is particularly vulnerable to accumulation of oxidative DNA lesions and proper functioning of DNA repair mechanisms is thus important for neuronal survival. In addition, environmental and dietary factors can modulate DNA repair, especially when exposure occurs early in life. Although the mechanisms of age-related and exposure-related changes in DNA repair capacity are unknown, growing evidence suggests that epigenetic events, including aberrant DNA methylation, contribute to the ageing process and may be functionally important through dysregulated expression of DNA repair genes.

Aim. We hypothesized that life-style related factors can modulate DNA repair, specifically Base Excision Repair (BER), in the ageing brain and that epigenetic mechanisms are involved in mediating the effects.

Methods. Brains from C57/BL male mice were isolated to study base excision repair (BER) using a modified comet assay, DNA methylation using pyrosequencing and expression of selected BER-related genes (*Ogg1*, *Neil1*, *Mutyh* and *Xrcc1*). In a parallel study, we investigated the impact of maternal folate depletion during pregnancy and lactation, and high-fat feeding from weaning in the offspring.

Results. We observed significantly increased methylation of the promoter region of *Ogg1* with ageing, which correlated inversely with *Ogg1* expression. We also observed a significant inverse correlation between gene methylation and expression observed for *Neil1*. During ageing, there was a trend towards decreased expression of *Mutyh* and *Xrcc1*, in parallel to slightly higher gene methylation levels. The corresponding phenotype i.e. BER-related incision activity in brain was reduced significantly, which was associated with significantly increased 8-oxo-7,8-dihydro-2'-deoxyguanosine levels. These data indicate that *Ogg1* and *Neil1* expression can be epigenetically regulated and that this may play a role in the adverse effects of ageing on DNA repair in mammalian brain.

Whilst folate depletion increased BER activity in the offspring at weaning ($P=0.052$), in the long term in 6 month old offspring, the double insult i.e. maternal low folate supply and high-fat feeding from weaning decreased BER activity significantly in the cortex, cerebellum, hippocampus and subcortical regions ($P\leq 0.017$). This fall in BER activity was associated with small changes in methylation or expression of BER-related genes, and slightly increased oxidative DNA damage levels in subcortical regions of adult offspring, which may increase sensitivity to oxidative stress and predispose to neurological disorders.

Conclusion: The first study has provide evidence that through altered expression of BER genes, epigenetic mechanisms can reduce capacity for neuronal DNA repair during ageing. Data from the second study suggest that low folate supply during early-life may leave an epigenetic mark which can predispose the offspring to further dietary insults, causing adverse effects during adult life. This reduced capacity for DNA repair may contribute to the accumulation of oxidative DNA damage and mutations across the whole genome, causing genome instability and increasing the risk of age-related neurodegenerative diseases.

Acknowledgements. The Centre for Brain Ageing & Vitality is funded through the Lifelong Health and Wellbeing cross council initiative by the MRC, BBSRC, EPSRC and ESRC. This work was further supported by the Centre for Integrated Systems Biology of Ageing and Nutrition funded by the BBSRC and EPSRC. We thank Hoffmann-La Roche (Basel) for supplying Ro 19-8022. We also like to thank Adele Kitching, Satomi Miwa, Liz Nicolson and Julie Wallace for care of the animals and assistance with dissections.

The work has been published as Langie et al. FASEB J. 2013; and Langie et al. Genes 2017.

The use of buccal cells in human biomonitoring and early disease detection

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Background. Biomarkers used in human biomonitoring and disease detection usually involve sampling such as blood collection and can also require establishment of cell cultures to detect unrepaired or permanent DNA damage after the first cell division in which most of the DNA repair mechanisms were active. As both requirements are either invasive or time consuming, there is a need to have different type of sampling that would involve non-invasive cell collection that would be also informative as blood cells as biomarker and as DNA damage detection biomarker. Exfoliated buccal cells have demonstrated to be a good example of both requirements, as a non-invasive sampling source of cells and as a type of the cell that do not require cell culture, since DNA damage that has been made in these cells cannot be repaired after they start to differentiate from the basal buccal cells, and it was also demonstrated that the type of DNA damage detected in buccal cells can correlate in the type of damage detected in the circulating blood cells.

Aim. The aim of this literature overview was to show where buccal cells, mostly analysed by the micronucleus cytome assay and comet assay can be (potentially) used in human biomonitoring and early disease detection.

Methods. The Web of Science and PubMed database was analysed using key words such as buccal, oral epithelial, DNA damage, biomonitoring, disease, comet, micronucleus

Results. We have found 121 (buccal biomonitoring), 3173 (buccal disease), 489 (buccal DNA damage), 148 (buccal comet), 661 (buccal micronucleus), 84 (oral epithelial comet), 190 (oral epithelial micronucleus), 4861 (oral epithelial disease) articles and we have focused on the buccal cells as a biomarker of exposure and early disease detection not connected with metastases and oral tumours/cancers, etc. We will demonstrate just a small overview of the work in progress.

Conclusion. Buccal cells have demonstrated their usefulness in variety of exposure assessment, as an additional biomarker in early disease detection and as additional yet not fully explored biomarker in human biomonitoring studies, in which oral cavity and respiratory system can be a target system, but also, they showed their usefulness in other diseases and exposures.

Acknowledgements. The authors declare no conflict of interest

DNA integrity and expression of proteasomal genes in multiple sclerosis

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Background. Multiple sclerosis (MS) is both autoimmune and neurodegenerative disease of the central nervous system, which leads to neurological disabilities. Most patients are diagnosed with a relapsing-remitting MS (RRMS) which eventually transition to secondary progressive MS (SPMS). Reactive oxygen species (ROS) have been implicated as mediators of demyelination in MS and can cause DNA damage. Overproduction of nitric oxide in oligodendrocytes is considered to be a crucial step in the pathogenesis of MS. Accumulation of toxic protein aggregates is characteristic for MS patients and indicates dysfunction of ubiquitin-proteasome system (UPS), which is responsible for degradation of intracellular proteins and is one of the key factors in regulation of the immune system. Treatment with interferon β (IFN β) is the most common therapy for MS patients.

Aim. The aim of the current study was to investigate DNA integrity, NO production in blood of MS patients and controls, as well as proteasomal gene expression levels under conditions of different MS subtypes and IFN β treatment.

Methods. Groups of healthy subjects and MS patients were enrolled in the study. Single-stranded (ss-) DNA breaks were determined in whole blood and isolated peripheral blood mononuclear cell (PBMNC) samples of 28 patients and 15 controls by means of alkaline single cell gel electrophoresis (comet assay). NO level in blood of 22 MS patients and 22 controls was tested by applying electron paramagnetic resonance spectroscopy. Proteasomal gene expression levels were determined in blood of 127 MS patients and 17 controls by means of qPCR. The *PSMA6* (rs2277460 and rs1048990), *PSMC6* (rs2295826 and rs2294827) and *PSMA3* (rs2348071) proteasomal gene single nucleotide polymorphisms (SNPs) were genotyped on MS subtype- and treatment efficiency association in 280 cases /305 controls study.

Results. The level of ssDNA breaks was increased in whole blood and isolated PBMNC samples of MS patients compared to controls ($p < 0.05$). NO production was significantly elevated in the blood of MS patients ($p < 0.05$). There was no difference in *PSMA3*, *PSMA6* and *PSMC6* gene expression between RRMS and SPMS patients. IFN β therapy increased *PSMA3*, *PSMA6* and *PSMC6* gene expression in patients with common genotypes at *PSMA3* rs2348071 locus, *PSMA6* rs2277460 and rs1048990 loci, and *PSMC6* rs2295826 and rs2294827 loci compared to non-treated patients ($p < 0.05$).

Conclusion. Results suggest that onset of MS increases the level of ssDNA breaks and NO production in blood. Treatment with IFN β , but not the MS subtypes, affects proteasomal gene expression in MS patients.

Acknowledgements. The study was funded from the UL research project ERAF SAM No. 1.1.1.1/16/A/016 project "Determination of proteasome-related genetic, epigenetic and clinical markers for multiple sclerosis".

Use of saliva in exposure assessment

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Background. Peripheral blood lymphocytes (PBLs) are widely used in human biomonitoring studies for the assessment of exposure to occupational and/or environmental genotoxic xenobiotics. However, the standard method for obtaining PBLs is invasive (the median cubital vein and median antebrachial veins are usually considered for blood withdrawal) and the procedure could be not accepted by some subjects (e.g. children). Buccal cells (BCs) are becoming increasingly popular in human biomonitoring studies, particularly because they can be obtained non-invasively, and have been used in several approaches to assess DNA damage by the comet assay. However, BCs samples contain a mixed population of cells, mainly epithelial cells and leukocytes (but also erythrocytes and fibroblasts), with yields and proportions of cell types strongly depending on the isolation procedure and the physiological state of donors. Very few studies have applied the comet assay on isolated buccal leukocytes/lymphocytes.

Aim. It has been suggested that buccal lymphocytes (BLs) might be potential substitute for PBLs in the comet assay. We have evaluated the procedure proposed for the comet assay on BLs.

Methods. Volunteers stimulated and rinsed their mouths with normal saline (0.9% NaCl); mouthwashes were collected into sterile 50 ml conical centrifuge tubes and centrifuged for 15 min (4°C). The supernatant was carefully removed, and the cell pellets re-suspended in 10 ml of PBS. The samples were centrifuged again, the supernatants discarded, and cell pellets re-suspended in 6 ml of MEM. BLs (more correctly, buccal mononuclear cells) were isolated from the cell suspension by density gradient centrifugation using Lympholyte®. BLs were then examined for viability, and cell diameter. BLs were finally re-suspended in 0.7% low-melting point agarose for the comet assay.

Results. We have obtained a total BLs number that ranged from 1.2×10^5 to 2.0×10^6 (mean value 0.8×10^6). The viability was always high, with an average value of about 90%. The average diameter of the cells was 10.9 μm (9.6–13.4 μm), demonstrating that we were actually dealing with lymphocytes. Slight differences in the extent of DNA damage were observed among the volunteers.

Conclusions. This method is totally non-invasive, quick, cheap, reproducible and suitable for all ages. Moreover, it apparently affects neither the cell viability nor the DNA integrity, itself. We supposed that the observed differences in the extent of DNA damage could be related to inter-individual variability (age, tobacco use, physical activity/inactivity, diet, xenobiotic exposure).

Acknowledgements. The authors declare no conflict of interest