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**UNIVERSITĀTE**

ANNO 1919

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**75<sup>th</sup> Conference  
of the University of Latvia**

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**Book of Abstracts**

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# 75<sup>th</sup> Scientific Conference of the University of Latvia INTERNATIONAL MEDICAL SECTION

24<sup>th</sup> of February, 2017

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# 75<sup>th</sup> ANNUAL CONFERENCE MEDICAL SECTION

UNIVERSITY | FACULTY OF | 24.02  
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## 75<sup>th</sup> Scientific Conference of the University of Latvia INTERNATIONAL MEDICAL SECTION

24<sup>th</sup> of February, 2017

*University of Latvia, Academic Centre for Natural Sciences  
Jelgavas iela 1, Riga, Latvia*

### PROGRAMME

1 <sup>st</sup> floor	8:15-9:00	<b>REGISTRATION</b>
Room 223	9:00-9:50	<b>OPENING CEREMONY</b>
		<p>Welcome address (10 min.)</p> <p>Prof. <b>Indriķis Muižnieks</b>, Rector of the University of Latvia</p> <p>Prof. <b>Mārcis Leja</b>, Conference Chair, Faculty of Medicine, University of Latvia</p> <p>Prof. <b>Kārlis Ketners</b>, State Secretary of the Ministry of Health</p> <p>Prof. <b>Inguna Ebela</b>, Faculty of Medicine, LU 20 years since the restoration of the University of Latvia Faculty of Medicine</p> <p>Prof. <b>Gustavs Latkovskis</b>, Vice Dean, Faculty of Medicine, LU LU Faculty of Medicine in the 21<sup>st</sup> century – goals and challenges (10 min.)</p> <p>Address by the AYUSH Ministry, India, Joint Secretary Mr. P. N. <b>Ranjit Kumar</b> (10 min.)</p>
Room 223	9:45-10:30	<b>PLENARY SESSION</b>
		<p><b>Session chairs:</b> prof. Valdis Folkmanis, prof. Mārcis Leja, prof. Gustavs Latkovskis</p>
		<p><b>Rauls Vēliņš</b> (<i>State-of-Art</i>) The Future of Education in Medicine (15 min.)</p> <p>Prof. <b>Edgaras Stankevicius</b> (<i>State-of-Art</i>) The Role of the Endothelium in Vascular Relaxation (20 min.)</p>
		<b>COFFEE BREAK (OPTIONAL)</b>



319	10:30-12:00	<b>BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY &amp; REGENERATIVE MEDICINE, Part I</b> (session in Latvian)
702	10:45-14:00	<b>INTEGRATIVE MEDICINE, Part I</b> (session in English)
320a	10:50-12:00	<b>PEDIATRICS</b> (session in Latvian)
223	12:30-14:00	<b>INTERNAL MEDICINE, Part I: CARDIOVASCULAR MEDICINE</b> (session in English)
401	12:30-14:00	<b>GASTROENTEROLOGY, HEPATOLOGY &amp; GASTROINTESTINAL ONCOLOGY, Part I</b> (session in English)
601	12:30-14:30	<b>BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY &amp; REGENERATIVE MEDICINE Part II</b> (session in Latvian)
320a	12:00-14:00	<b>PUBLIC HEALTH AND HEALTHCARE ORGANIZATION</b> (session in Latvian)
	14.00-15.00	<b>LUNCH BREAK</b>
223	15:00-16:30	<b>INTERNAL MEDICINE, Part II: INTERNAL MEDICINE &amp; INFECTIOUS DISEASE</b> (session in English)
401	15:00-16:30	<b>GASTROENTEROLOGY, HEPATOLOGY &amp; GASTROINTESTINAL ONCOLOGY Part II</b> (session in English)
405	15:00-16:20	<b>SURGERY, ANESTHESIOLOGY, GYNECOLOGY, ONCOLOGY</b> (in Latvian & in English)
702	15:00-16:40	<b>INTEGRATIVE MEDICINE, Part II</b> (session in English)
702	17.00-19.00	<b>INTEGRATIVE MEDICINE, Part III</b> (session in English)
2 <sup>nd</sup> floor	10:30-16:30	<b>POSTER SESSIONS</b> (session in Latvian & English)

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**10:50-12:00 PEDIATRICS** (session in Latvian)

Room 320a **Session chairs:** prof. Ingrida Rumba-Rozenfelde,  
assoc. prof. Ilva Daugule

1. PREVALENCE OF PATHOGENIC *ESCHERICHIA COLI* IN STOOLS OF HEALTHY CHILDREN AND ASSOCIATION WITH PREVIOUS ANTIBACTERIAL THERAPY (7+3 min.) **Ilva Daugule**, *Silvija Remberga, Daiga Karklina, Dmitrijs Perminovs, Mikus Gavars, Ingrida Rumba-Rozenfelde*
2. EVALUATION OF COUGH CAUSES, DIAGNOSTIC METHODS AND SUGGESTED THERAPY AMONG 2–10 YEARS OLD CHILDREN (7+3 min.) **Jelena Danilova**, *Silvija Remberga*
3. CORRELATION BETWEEN GHRELIN AND INSULIN-LIKE GROWTH FACTOR AMONG CHILDREN WITH OVERWEIGHT AND OBESITY (7+3 min.) **Ieva Štrauhmane**, *Irēna Rinkuža, Ināra Kirillova, Līva Grīviņa, Ingrida Rumba-Rozenfelde, Dace Rudzīte, Ilva Daugule*
4. STUDY ON CHILD HEALTHCARE AND DEVELOPMENT ISSUES WITHIN THE 2<sup>ND</sup> CHILDREN'S REPORT OF LATVIA TO THE UNITED NATIONS (7+3 min.) **Inguna Ebela**, *Danute Ražuka-Ebela, Kristīne Varte, Sandra Gabrena, Mārtiņš Ražuks-Ebels*
5. RECOMMENDATIONS. CHILDREN WITH AUTISM SPECTRUM DISORDERS (7+3 min.) **Aleksandrs Vasiļonoks**, *Valdis Folkmanis*
6. TRENDS OF LATE FETAL DEATH IN LATVIA, 2001–2014 (7+3 min.) **Irisa Zīle**, *Inguna Ebela, Valdis Folkmanis, Ingrida Rumba-Rozenfelde*
7. REVIEW OF CLINICAL MANIFESTATIONS, DIAGNOSIS AND TREATMENT OF VEIN OF GALEN MALFORMATION IN LATVIA (7+3 min.) **Zane Saleniece**, *Kārlis Kupčs, Jānis Šavlovskis*

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**12:10-14:00 PUBLIC HEALTH AND HEALTHCARE ORGANIZATION**

Room 320a (session in Latvian and in English)

**Session chairs:** assoc. prof. Juris Bārzdīņš, asst. prof. Kārlis Purmalis

**Romualds Ražuks** (*State-of-Art*) CAN STATE OBLIGATORY HEALTH INSURANCE SAVE HEALTHCARE IN LATVIA? (20 min.) Chairman of the Public Health Subcommittee of the Social and Employment Matters Committee, *Parliament of the Republic of Latvia*

1. SOCIO-TECHNICAL CHALLENGES IN INTRODUCTION OF PUBLIC MONITORING FOR HEALTHCARE QUALITY AND EFFICIENCY (7+3 min.) **Juris Bārzdīņš**
2. GASTRIC CANCER SCREENING COST EFFICIENCY ANALYSES USING BIOMARKERS (7+3 min.) **Kārlis Purmalis**, *J. Priede, Daiga Santare, Ilona Kojalo, Mārcis Leja*
3. HUMAN FACTORS. TRAINING AND LEARNING FROM INCIDENTS AS AN APPROACH TO INCREASE INVOLVEMENT OF CLINICIANS IN REPORTING AND PATIENT SAFETY IMPROVEMENTS (7+3 min.) **Evija Palčeja**

4. PRENATAL EXPOSURE TO MATERNAL ANXIETY-DEPRESSIVE SYMPTOMS AND ITS INFLUENCES ON INFANT DEVELOPMENT AND BEHAVIOUR (7+3 min.) **Nikita Sakels**, *Nina Sakele, Jūlija Meščerjakova, Margarita Pukite, Inta Barengo*
5. ASSESSMENT OF MANAGEMENT PROCESS IMPROVEMENT IN CLINICS OF THE CHILDREN'S UNIVERSITY HOSPITAL (7+3 min.) **Ieva Lejniece**
6. NON-INVASIVE FETAL RHESUS FACTOR GENOTYPING ASSAY DEVELOPMENT AND VALIDATION (7+3 min.) **Natālija Novikova**, *Dmitrijs Perminovs, Ludmila Voložonoka, Liene Korņejeva, Violeta Fodina*
7. SURVEY OF LATVIAN PHARMACISTS ABOUT IMPLEMENTATION OF ADDITIONAL PHARMACEUTICAL CARE SERVICES (7+3 min.) **Zane Rumbiņa**, *Jānis Kurlovics, Ruta Muceniece*
8. SURVEY ABOUT ANAEMIA, ANTI-ANAEMIC MEDICINES AND ANALYSIS OF BLOOD TESTS (7+3 min.) **Liene Bundziņa**, *Kristīne Saleniece*
9. MEDICAL STUDENTS WITH MENTAL HEALTH CONDITIONS: LEGAL, ETHICAL AND POLICY CHALLENGES (7+3 min.) **Solvita Olsena**, *Signe Mežinska*

## 12:30-14:00 INTERNAL MEDICINE, CARDIOLOGY AND

Room 223 **INFECTIOUS DISEASE**

**Part I. CARDIOVASCULAR MEDICINE** (session in English)

**Session chairs:** prof. Andrejs Ērglis, prof. Edgaras Stankevičius, prof. Gustavs Latkovskis

**Andrejs Ērglis (State-of-Art)** THERAPEUTIC HORIZONS FOR INTERVENTIONAL TREATMENT OF HEART FAILURE (20 min.)

1. DIURETIC USE IS ASSOCIATED WITH HIGHER PLASMA TRIMETHYLAMINE-N-OXIDE LEVELS (7+3 min.) *Gustavs Latkovskis, Mairita Mažule, Līga Bondare, Anastasija Račicka, Elīna Makarova, Dace Hartmane, Ieva Strēle, Andrejs Ērglis, Maija Dambrova*
2. BIOCHEMICAL DIAGNOSTIC METHODS FOR EARLY DETECTION OF CHEMOTHERAPY INDUCED MYOCARDIAL INJURY (7+3 min.) **Alla Chapule**, *Marina Berzina, Gustavs Latkovskis*
3. ECHOCARDIOGRAPHIC DIAGNOSTIC METHODS FOR EARLY DIAGNOSIS OF CHEMOTHERAPY INDUCED MYOCARDIAL INJURY (7+3 min.) **Alla Chapule**, *Marina Berzina, Gustavs Latkovskis*
4. CHARACTERISTICS OF PROBANDS AND RELATIVES INCLUDED IN THE LATVIAN REGISTRY OF FAMILIAL HYPERCHOLESTEROLEMIA (7+3 min.) **Vita Saripo**, *Gustavs Latkovskis, Arta Upena-Roze, Dainus Gilis, Andrejs Ērglis*
5. EFFECTS OF ROSUVASTATIN ON PULSE WAVE VELOCITY AT ONE MONTH OF TREATMENT (7+3 min.) **Emma Sokolova**, *Vitālijs Grebjonkins, Andrejs Ērglis, Gustavs Latkovskis*
6. EVALUATION OF DIETARY HABITS OF PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN LATVIA ACCORDING TO PREDIMED SCORE (7+3 min.) **Dainus Gilis**, *Gustavs Latkovskis, Vita Saripo, Arta Upena-Roze, Andrejs Ērglis*

7. *KCNE1* VARIATIONS RS1805127 AND 1892593 ASSOCIATION WITH A RISK OF DEVELOPMENT OF ATRIAL FIBRILLATION (7+3 min.) **Irina Rudaka**, *Dmitrijs Rots, Arturs Uzars, Lubova Grinevica, Jelena Strelca, Ludmila Strelca, Linda Piekuse, Oskars Kalejs*
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**15:00-16:30**      **INTERNAL MEDICINE, CARDIOLOGY AND INFECTIOUS DISEASE**  
Room 223

**Part II. INTERNAL MEDICINE & INFECTIOUS DISEASE**

(session in English)

**Session chairs:** prof. Uga Dumpis, Dr. Kristien Van Acker,  
Dr. Jeļizaveta Sokolovska

**Kristien Van Acker (State-of-Art)** THE DIABETIC FOOT AS CINDERELLA, BUT A MIRROR OF A LOT OF CO-MORBIDITIES (20 min.)

1. SIGNIFICANT ASSOCIATION OF FOUR SNPS WITH LOWER AGE AT DIAGNOSIS IN PATIENTS WITH GROWTH HORMONE SECRETING PITUITARY ADENOMA (7+3 min.) **Raitis Pečulis**, *Inga Balcere, Andra Valtere, Ilze Konrāde, Olivija Caune, Valdis Pīrāgs, Jānis Kloviņš*
2. HEPATITIS C PREVALENCE IN MEDICAL PERSONNEL AT INTENSIVE CARE UNITS IN LATVIA (7+3 min.) **Edīte Fridrihsone**, *Ieva Tolmane, Jelena Storozenko, Lilija Lapke, Baiba Rozentale*
3. THE VALUE OF AN INVENTORY IN TRANSFER OF KNOWLEDGE AND ORGANIZATION BETWEEN SWEDEN AND THE BALTIC REGION REGARDING FOOT COMPLICATIONS IN PATIENTS WITH DIABETES MELLITUS (15 min.) **Kurt Andersson**, *Börje Åkerlund, Paul Lundgren, Jonas Malmstedt, Valdis Pirags, Natalija Fokina, Andre Trudnikov, Veronika Palmiste-Kallion, Rasa Verkauskiene, Ieva Garbauskaitė*
4. BASELINE DATA OF DIABETIC FOOT AMPUTATIONS IN LITHUANIA (7+3 min.) **Ieva Baikstiene**, *Egle Kreivaitiene, Jonas Ceponis, Evalda Danyte, Rasa Verkauskiene*
5. PSORIATIC ARTHRITIS SUBCLINICAL DETECTION IN PATIENTS WITH PSORIATIC NAIL DISEASE (7+3 min.) **Tatjana Sidorcika**, *Viktors Linovs, Maija Radzina, Andris Rubins, Silvestrs Rubins, Nora Valdmāne*
6. ASSESSMENT OF QUALITY OF LIFE IN PATIENTS WITH SENSITIVE SKIN (7+3 min.) **Lana Kasparane**, *Jana Janovska*
7. COMPARISON BETWEEN UNILATERAL AND BILATERAL OBSTRUCTION OF LACRIMAL DRAINAGE SYSTEM AND THE RISK FACTORS IN PATIENTS WITH EPIPHORA (7+3 min.) **Dace Reinholde**, *Sarmīte Dzelzīte*

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**12:30-14:00 GASTROENTEROLOGY AND  
Room 401 GASTROINTESTINAL ONCOLOGY PART I**  
(session in English)  
**endorsed by the European Society  
of Digestive Oncology – ESDO**



**Session chairs:** prof. Mārcis Leja, asst. prof. Aiga Stāka

**Mārcis Leja (State-of-Art)** GISTAR – MULTICENTRIC RANDOMIZED STUDY OF *H. PYLORI* ERADICATION AND PEPSINOGEN TESTING FOR PREVENTION OF GASTRIC CANCER MORTALITY – DESIGN AND PRELIMINARY RESULTS (20 min.)

1. ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER – CASE REPORT (7+3 min.) **Ivars Tolmanis**, *Inta Liepniece-Karele, Mārcis Leja, Ilze Kikuste, Aigars Vanags, Evgeny Fedorov*
2. COMPARISON OF OVERALL TEST POSITIVITY AND GENDER DIFFERENCES OF FAECAL IMMUNOCHEMICAL TEST RESULTS (7+3 min.) **Daiga Šantare**, *Ilona Kojalo, Mārcis Leja*
3. THE PREVALENCE OF ANTI-PARIETAL CELL AND ANTI-INTRINSIC FACTOR ANTIBODIES, PEPSINOGENS, GASTRIN-17 AND *H.PYLORI* INFECTION IN CORPUS-RESTRICTED GASTRITIS PATIENTS (7+3 min.) **Petra Kriķe**, *Zakera Shums, Dace Rudzīte, Inese Polaka, Sergejs Isajevs, Gary L. Norman, Mārcis Leja*
4. THE PREVALENCE OF ANTI-PARIETAL CELL AND INTRINSIC FACTOR ANTIBODIES IN PATIENTS WITH GASTRIC ADENOCARCINOMA (7+3 min.) **Anete Urķe**, *Petra Kriķe, Zakera Shums, Dace Rudzīte, Inese Polaka, Armands Sīviņš, Ivans Jelovskis, Sergejs Isajevs, Inga Bogdanova, Viesturs Boka, Uldis Vikmanis, Gary L. Norman, Mārcis Leja*
5. COLORECTAL CANCER SCREENING PROGRAMME EVALUATION – EARLY INDICATORS IN THE CANCER REGISTRY (7+3 min.) **Una Kojalo**, *Ilona Kojalo, Santa Pildava, Daiga Šantare*
6. ANTIMICROBIAL RESISTANCE IN *HELICOBACTER PYLORI* ISOLATED FROM GASTRIC BIOPSIES IN ADULT POPULATION IN LATVIA (7+3 min.) *Dace Rudzīte, Katrīna Leja, Ilze Kikuste, Aiga Rūdule, Reinis Vangravs, Daiga Šantare, Ģirts Šķenders, Mārcis Leja*
7. IS PEPSINOGEN SCREENING IN GENERAL CAUCASIAN POPULATION JUSTIFIED? RESULTS FROM A CROSS-SECTIONAL POPULATION STUDY IN LATVIA (7+3 min.) **Jelizaveta Pavlova**, *Olga Sjomina, Pavel Janovic, Ilze Kikuste, Aigars Vanags, Ivars Tolmanis, Dace Rudzīte, Inese Polaka, Ilona Kojalo, Inta Liepniece-Karele, Sergejs Isajevs, Daiga Santare, Valdis Pirags, Jelena Pahomova, Vilnis Dzerve, Andrejs Erglis, Marcis Leja*

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**15:00-16:30 GASTROENTEROLOGY AND GASTROINTESTINAL ONCOLOGY PART II**

Room 401

(session in English)

**endorsed by the European Society of Digestive Oncology – ESDO**



**Session chairs:** Dr. Ilze Kikuste, Dr. Ivars Tolmanis

**Ilze Kikuste (State-of-Art) QUALITY ASSURANCE IN COLONOSCOPY (20 min.)**

1. GASTRIC CANCER SCREENING QUESTIONNAIRE, FINAL RESULTS (7+3 min.)  
*Mārcis Leja, Evita Gašenko, Inese Polaka, Raul Murillo, Dmitry Bordin, Alexander Link, Liliانا Garkalne, Peter Malfetheriner, Rolando Herrero, Hossam Haick*
2. ROLE OF DIETARY HABITS IN *HELICOBACTER PYLORI* INFECTION IN THE LATVIAN POPULATION (7+3 min.) **Danute Ražuka-Ebela, Ieva Grinberga-Dērica, Inga Škendere, Ilva Daugule, Aiga Rūdule, Dace Rudzīte, Daiga Šantare, Inese Polaka, Inguna Ebela, Raul Murillo, Jin Young Park, Rolando Herrero, Mārcis Leja**
3. THE ROLE OF *PNPLA3, RNF7, MERTK* AND *PCSK7* GENE POLYMORPHISMS WITH LIVER FIBROSIS AND CIRRHOSIS (7+3 min.) **Irena Valantiene, Juozas Kupcinskas, Greta Varkalaitė, Ruta Steponaitiene, Jurgita Skieceviciene, Jolanta Sumskiene, Vitalija Petrenkiene, Jurate Kondrackiene, Gediminas Kiudelis, Frank Lammert, Limas Kupcinskas**
4. TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN TREATMENT OF PORTAL HYPERTENSION – EXPERIENCE OF ONE CENTRE (7+3 min.)  
**Sigita Gelman, Imantė Lasytė, Agnė Kacinskaitė, Andrius Pranculis, Limas Kupcinskas**
5. UPPER GASTROINTESTINAL ENDOSCOPY FINDINGS AND INCIDENCE OF GASTRIC PRECANCEROUS CONDITIONS IN AMBULATORY PATIENTS (7+3 min.) **Zane Dzērve, Ilze Kikuste, Ivars Tolmanis, Aigars Vanags, Dans Stirna, Mārcis Leja**
6. ASSOCIATION OF INTRATUMORAL INFILTRATING LYMPHOCYTES WITH THE DEGREE OF DIFFERENTIATION AND GROWTH PATTERN OF GASTRIC CARCINOMA (7+3 min.) **Māra Melnalksne, Juliana Gabriella Mohova, Margarita Tatičeka, Arina Tupīte, Sergejs Isajevs, Mārcis Leja, Aija Linē**

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**10:30-12:00 BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY AND REGENERATIVE MEDICINE PART I (session in Latvian)**

Room 319

**Session chairs:** prof. Nikolajs Sjakste, assoc. prof. Una Riekstiņa

**Una Riekstiņa (State-of-Art) EKSTRACELLULAR VESICLES: TOOL FOR INTERCELLULAR COMMUNICATION IN TUMOR MICROENVIRONMENT (20 min.)**

1. DNA LESIONS IN HEALTHY SUBJECTS: A LITERATURE REVIEW (7+3 min.)  
**Elīna Ļeonova, Nikolajs Sjakste**
2. PSMA6 GENE POLY(dA:dT) TRACT GENETIC VARIATIONS ARE ASSOCIATED WITH AUTOIMMUNITY RELATED PATHOLOGIES IN LATVIANS (7+3 min.)  
**Natalia Paramonova, Tatjana Sjakste, Ilva Trapina, Nikolajs Sjakste**

3. STUDY OF ANTIOXIDANT PROPERTIES AND INTERACTIONS WITH DNA OF 1,4-DIHYDROPYRIDINE DERIVATIVES USING SPECTROSCOPIC METHODS (7+3 min.) **Edgars Smelovs**, *Elīna Ļeonova, Nikolajs Sjakste*
4. THE INTRACELLULAR INTERACTION OF AV-153-NA (7+3 min.) **Anna Švacka**, *Evita Rostoka, Kaspars Jēkabsons, Tūrs Selga, Nikolajs Sjakste*
5. NITRATE CONCENTRATION CHANGES IN TYPE 1 DIABETES IN THE PATIENT'S BLOOD AND URINE (7+3 min.) **Laura Celma**, *Evita Rostoka, Jeļizaveta Sokolovska, Nikolajs Sjakste*
6. S-PHENYLPYRACETAM BINDS TO DOPAMINE TRANSPORTER AND REDUCES BODY WEIGHT GAIN IN OBESE ZUCKER RATS AND HIGH FAT DIET-FED MICE (7+3 min.) **Baiba Zvejniece**, *Līga Zvejniece, Baiba Svalbe, Edijs Vavers, Maija Dambrova*
7. OPTIMIZATION AND VALIDATION OF *IN VITRO* MONOCYTE-MACROPHAGE DIFFERENTIATION MODEL (7+3 min.) **Ineta Popēna**, *Kārlis Pleiko, Una Čonka, Una Riekstiņa*

**12:30-14:30 BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY AND REGENERATIVE MEDICINE PART II** (session in Latvian)  
Room 601

**Session chairs:** prof. Vija Kluša, prof. Baiba Jansone

1. SELECTION OF ssDNA APTAMERS TARGETING METASTATIC RENAL CELL CARCINOMA USING CELL-SELEX TECHNOLOGY (7+3 min.) **Kārlis Pleiko**, *Līga Saulīte, Una Riekstiņa*
2. QUANTUM DOT TRANSFER FROM MESENCHYMAL STEM CELLS TO BREAST CANCER CELLS IN 3D CO-CULTURE MODEL (7+3 min.) **Līga Saulīte**, *Dominyka Dapkute, Sabīne Plūduma, Ričardas Rotomskis, Una Riekstiņa*
3. IZOLĒTU (*Nicotiana tabacum L.*) HLOROPLASTU IZMANTOŠANAS IESPĒJAS CILVĒKU ŠŪNU KULTIVĒŠANĀ *IN VITRO* (7+3 min.) **Tūrs Selga**, *Gatis Melkus*
4. SEARCH FOR STRUCTURES OF HYPOXIA-INDUCED EXOSOMAL PROTEINS IN DATA BASIS (7+3 min.) **Ilva Nakurte**, *Kaspars Jēkabsons, Una Riekstiņa, Aija Line, Elina Zandberga, Arturs Abols, Ruta Muceniece*
5. COMPOSITION PROFILES OF VARIOUS CONIFER POLYPRENOLS (7+3 min.) **Ilona Vanaga**, *Ilva Nakurte, Ausma Marija Korica, Ojārs Polis, Ruta Muceniece, Baiba Jansone*
6. DEVELOPMENT OF POLYPRENOL PROLIPOSOMES (7+3 min.) **Ilona Vanaga**, *Uģis Klētnieks, Laila Plakane, Līga Plakane, Ruta Muceniece, Baiba Jansone*
7. IDENTIFICATION AND MEASUREMENT OF DOLICHOL LEVELS IN RAT ORGANS (7+3 min.) **Marta Raituma**, *Reinis Rembergs, Ilva Nakurte, Kaspars Jēkabsons, Jana Namniece, Ruta Muceniece*
8. QUANTIFICATION OF GLYCOALKALOID LEVELS IN EXTRACTS OF PEELED POTATO SKIN (7+3 min.) **Jana Namniece**, *Ilva Nakurte, Silva Priede, Kaspars Jēkabsons, Ruta Muceniece*
9. MECHANISMS OF NEUROPROTECTIVE ACTION OF MUSCIMOL (7+3 min.) **Karina Narbutė**, *Vladimirs Pilipenko, Ulrika Beitnere, Baiba Jansone, Vija Klusa*

10. BACLOFEN, A GABA-B RECEPTOR AGONIST, SHOWS MEMORY IMPROVING AND ANTI-INFLAMMATORY ACTIVITY, AND INCREASES CHOLINERGIC ACTIVITY IN ALZHEIMER'S DISEASE MODEL-RATS (7+3 min.) **Vladimirs Pilipenko**, *Ulrika Beitnere, Karina Narbutė, Juris Rumaks, Jolanta Pupure, Baiba Jansone, Vija Klusa*
11. AN IMPROVED METHODOLOGY FOR LONG-TERM CONTINUOUS INTRACEREBRAL INFUSION OF EXPERIMENTAL SUBSTANCES BY ALZET MICROSMOTIC PUMPS (7+3 min.) **Jolanta Upīte**, *Adam Sike, Vladimirs Pilipenko, Ulrika Beitnere, Markus Krohn, Henrik Biverstal, Vija Klusa, Jens Pahnke, Baiba Jansone*
12. THE EVALUATION OF ACUTE TOXICITY OF PENICILLIUM VIRIDE LANSO-AMP DEAMINASE FOLLOWED BY IV ADMINISTRATION IN MICE (7+3 min.) **Ērika Orliņa**, *Juris Rumaks, Mārtiņš Boroduškis, Anna Ramata-Stunda, Ilze Blake, Vizma Nikolajeva, Baiba Jansone*

**10:45-14:00 INTEGRATIVE MEDICINE PART I** (session in English)

Room 702 **Session chairs:** prof. Valdis Pīrāgs, Dr. Madan Thangavelu

1. OPENING OF THE LATVIAN TRANSLATION OF THE BOOK "ASHTANGA HRIDAYA" (15+5 min.) **Valdis Pīrāgs, Vijai Kumar, Sintija Sauša, Somit Kumar**
2. INTEGRATIVE HEALTHCARE IN INDIA (20 min.) **Ranjit Kumar**, *Joint secretary AYUSH Ministry, Government of India*
3. THE SIGNS AND SCIENCE OF WELLNESS: LESSONS FROM INDIA'S ANCIENT SYSTEMS OF HEALTH AND WELLNESS INFORMING FUTURE GLOBAL HEALTHCARE SYSTEMS (15+5 min.) **Madan Thangavelu**, *Cambridge, UK*
4. CONTRASTING STRATEGIES OF TREATMENT OF CHRONIC DISEASE IN MODERN AND TRADITIONAL MEDICINE (15+5 min.) **Alex Hankey**, *S-VYASA University, Bangalore, India*
5. YOGA & NATUROPATHY: STRATEGIES FOR HUMAN ADAPTATION AND WELLNESS (15+5 min.) **B. Raghavendra Samy**, *Molecular Biosciences Laboratory, S-VYASA University, Bangalore, India*
6. THE EVIDENCE BASED AYURVEDA IN MODERN GASTROENTEROLOGY (15+5 min.) **Goda Denapiene**, *University of Vilnius, Lithuania*
7. REVERSE PHARMACOLOGICAL APPROACH TO UNDERSTAND AYURVEDIC FORMULATION IN MANAGEMENT OF CHRONIC DIABETIC FOOT ULCER (15+5 min.) **Somit Kumar, Sintija Sauša, Arya Vaidya Chikitsalayam and Research Institute, Coimbatore, India; University of Latvia**
8. THE FIRST *IN VITRO* STUDY ON AYURVEDIC FORMULATION IN EUROPE (10+5 min.) **Tatjana Tračevska, Somit Kumar, Baiba Zandersone, Iveta Līduma, Sintija Sauša, Ilona Mandriķa, Sabine Šturme, Agnese Zvaigzne, Paul Dinil, Arnolds Jezupovs, Valdis Pīrāgs, University of Latvia**
9. ANTI-INFLAMMATORY EFFECTS OF JATYADI THAILAM PLANT EXTRACTS *IN VITRO* (10+5 min.) **Ilona Mandriķa, Ramona Petrovska, Somit Kumar, Valdis Pīrāgs, Tatjana Tračevska, University of Latvia**



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**15:00-16:40 INTEGRATIVE MEDICINE PART II** (session in English)

Room 702 **Session chairs:** Dr. Sintija Sauša, Dr. Elmar Stapelfeldt

1. STRENGTHS AND WEAKNESSES OF INTEGRATION (15+5 min.) **Nikolajs Nikolajevs**, *Latvian Association for Holistic Medicine & Naturopathy*
2. CAN WE USE EXPANDED CATEGORIES BASED ON INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH (ICF) FOR QUICK UNDERSTANDING OF TRADITIONAL CHINESE MEDICINE? (10+5 min.) **Inese Kokare**, *University of Latvia, Qi, Qi, Department of Integrative Oncology, Fudan University, Shanghai, China*
3. IMAGE MEDICINE AS A PART OF QIGONG THERAPY AND TRADITIONAL CHINESE MEDICINE (10+5 min.) **Edgars Vasilevskis**, *Rīga Stradiņš University, Riga, Latvia*
4. PANCHABHAUTIK APPROACH IN AYURVEDIC DIAGNOSIS (15+5 min.) **Priyanka Chorge**, *Pune, India*
5. INTEGRATING AYURVEDA MEDICINE AT THE CHARITÉ MEDICAL UNIVERSITY BERLIN (15+5 min.) **Elmar Stapelfeldt**, *Charité University, Berlin, Germany*
6. MANAGING AN AUTHENTIC AYURVEDA CLINIC AND TREATING 25.000 PATIENTS WITH PANCHAKARMA AT THE MAHARISHI AYURVEDA HEALTH CENTER IN BAD EMS (15+5 min.) **Lothar Pirc**, *Maharishi AyurVeda Health Centre Bad Ems, Germany, the International Maharishi AyurVeda Foundation*

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**17:00-19:00 INTEGRATIVE MEDICINE PART III** (session in English)

Room 621 **Chairs:** Kerstin Rosenberg, Mark Rosenberg

1. VASTU SHASTRA – THE AYURVEDA FOR LIVING AND WORKING SPACES (40+5 min.) **Mark Rosenberg**, *European Academy for Ayurveda, Birstein, Germany*
2. AYURVEDIC DIET: FOOD AS FOOD – FOOD AS MEDICINE (40+5 min.) **Kerstin Rosenberg**, *European Academy for Ayurveda, Birstein, Germany*
3. MY PERSONAL EXPERIENCE IN INCORPORATING THE USE OF AYURVEDA METHODS IN LATVIA (10+5 min.) **Ilona Ābele-Šrenka**, *Aparmita, Rīga, Latvia*
4. INTEGRATIVE MEDICINE AT THE REHABILITATION CENTER “JAUNĶEMERI” (10+5 min.) **Rita Pedāne**, *Jūrmala, Latvia*
5. AYURVEDA PALACE (10+5 min.) **Aleksejs Kovaļevskis**, *Jūrmala, Latvia*

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**15:00-17:00 SURGERY, GYNECOLOGY, ANESTHESIOLOGY, ONCOLOGY**

Room 601 (session in Latvian and in English)

**Session chairs:** assoc. prof. Jānis Eglītis, asst.prof. Armands Siviņš,  
asst. prof. Igors Ivanovs

1. EVALUATION OF POST OPERATIVE ANALGESIA METHODS FOR TOTAL SHOULDER REPLACEMENT SURGERY (7+3 min.) **Rūdolfs Jānis Viksne**, *Māra Klibus, Aleksejs Miščuks, Iveta Golubovska, Aigars Vugulis, Mārcis Radziņš, Sergejs Zadorožnijs (in English)*
2. EFFICIENCY OF THE TRUST PERIOPERATIVE BLOOD TRANSFUSION PREDICTING SCALE IN PATIENTS UNDERGOING OPEN HEART SURGERY (7+3 min.) **Leonids Solovjovs**, *Agnese Ozolina, Agnese Zdanovska, Tatjana Mikijanska, Eva Strike (in English)*
3. FEATURES OF THE PATHOGENESIS AND DEVELOPMENT OF LOCOREGIONAL RECURRENCE OF BASAL CELL CARCINOMA IN THE CERVICAL – FACIAL REGION (7+3 min.) **Jelena Moisejenko-Golubovica**, *Valeria Groma, Anna Ivanova, Raimond Karl (in English)*
4. THE PATTERN OF TIBIAL ARTERY RUN-OFF IN PATIENTS WITH LONG SEGMENT POPLITEAL ARTERY STENTING (7+3 min.) **Aina Kratovska**, *Sanita Ponomarjova, Andrejs Bernšteins, Patrīcija Ivanova*
5. URETHRAL PRESSURE PROFILOMETRY DATA CORRELATION IN WOMEN WITH DIFFERENT TYPES OF URINARY INCONTINENCE (7+3 min.) **Zane Pilsetniece**, *Kuralay Sharipova, Egils Vjaters*
6. NEUROLOGICAL OUTCOMES IN PATIENTS WITH OUT-OF-HOSPITAL CARDIAC ARREST ACHIEVING RETURN OF SPONTANEOUS CIRCULATION (7+3 min.) **Agnese Zdanovska**, *Leonids Solovjovs, Anita Kalēja, Roberts Stašinskis, Indulis Vanags*
7. TREATMENT OF BENIGN SKIN TUMORS USING THE PLASMA GENERATING DEVICE PLEXR® (7+3 min.) **Ingrīda Rītiņa**, *Silvestrs Rubins, Andris Rubins*
8. LAPAROSCOPIC TRANSABDOMINAL PRE-PERITONEAL (TAPP) REPAIR OF INGUINAL HERNIA USING SELF-GRIPPING MESHES (7+3 min.) **Arturs Trischenkovs**, *Igors Ivanovs*

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**10:30-16:30 POSTER PRESENTATIONS** (session in Latvian and English)

2<sup>nd</sup> floor hall

**BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY AND REGENERATIVE MEDICINE**

1. PROGNOSTIC SIGNIFICANCE OF SELECTED MORPHOLOGICAL AND CLINICAL CHARACTERISTICS IN GLIAL TUMOURS **Selga Slaidiņa**, *Viktorija Grabovņicka, Sarmīte Boka, Sergejs Isajevs*
2. INFLUENCE OF METABOLIC PROCESSES ON TUMOR PROLIFERATION IN VITRO **Laura Martinkute**, *Baltramiejus Jakstys, Saulius Šatkauskas, Edgaras Stankevicius*

3. ULTRASOUND AND MECHANICAL SHOCK INDUCED VASCULAR RELAXATION **Silvijus Abramavičius**, Vytautas Ostaševičius, Vytautas Jūrėna, Edgaras Stankevičius
4. INFLUENCE OF CYCLOSPORINE AND EVEROLIMUS ON THE MAIN MYCOPHENOLATE MOFETIL PHARMACOKINETIC PARAMETERS. CROSS SECTIONAL STUDY **Aurelija Noreikaitė**, Franck Saint-Marcoux, Pierre Marquet, Edmundas Kaduševičius, Edgaras Stankevičius
5. CORRELATION STUDY BETWEEN LIFESTYLE, HABITS AND SALIVARY NITRITE LEVEL IN THE LATVIAN POPULATION **Anna Beikule**, Evita Rostoka, Nikolajs Sjakste
6. THE ROLE OF OXYGEN AVAILABILITY IN EMBRYONIC SKIN DEVELOPMENT **Jurijs Markovs**, Gundega Knipse, Dzanna Krumina, **Agate Galuza**
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# ABSTRACTS

## PEDIATRICS

### 1. PREVALENCE OF PATHOGENIC *ESCHERICHIA COLI* IN STOOLS OF HEALTHY CHILDREN AND ASSOCIATION WITH PREVIOUS ANTIBACTERIAL THERAPY

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**Background.** Although *Escherichia coli* (*E.coli*) is a part of normal gastrointestinal microflora, pathogenic variants could cause diarrheal and extraintestinal diseases. However, data about asymptomatic carriage of pathogenic *E.coli* appear in children.

The aim of the study was to identify the presence of different pathogenic *E.coli* in stool samples of asymptomatic children and analyze a possible association between previous treatment with antibiotics and presence of pathogenic *E.coli*.

**Methods.** Faecal samples were gathered from 53 children without gastrointestinal symptoms (median of age – 5.5 years, boys 45%). Parents of children completed a questionnaire about treatment with antibiotics received during the previous month or the previous year.

DNA was extracted from stool samples and analysed for the presence of pathogenic *E.coli* – enterotoxigenic (ETEC), enteroaggregative (EAEC), enteropathogenic (EPEC) and enterohemorrhagic (EHEC) – by PCR.

**Results.** Among children without gastrointestinal symptoms 15% (8/53) of isolates were positive for pathogenic *E.coli*: 13% (7/53) were positive for EPEC; one sample was positive for ETEC, one – for EHEC, one – for EAEC. One child carried simultaneously three types of pathogenic *E.coli* – EPEC, EHEC, ETEC; another child carried two types of pathogenic *E.coli* – EPEC and EHEC. Children carrying pathogenic *E.coli* had not received antibacterial therapy more often compared to children without pathogenic *E.coli*.

**Conclusions.** Data from the studied patient sample indicate that healthy children in Latvia may carry potentially pathogenic *E.coli* (predominantly EPEC). Clinical significance and factors promoting colonization with pathogenic *E.coli* should be studied further.

**Acknowledgements/Funding** *The study was supported by the grant from Latvia State Research Programme “Biomedicine”.*

## 2. EVALUATION OF COUGH CAUSES, DIAGNOSTIC METHODS AND SUGGESTED THERAPY AMONG 2–10 YEARS OLD CHILDREN

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**Background.** Cough among children is one of the main causes why parents seek medical help. Cough is widespread among pre-school age children and mostly is caused by upper airway viral infections. Respiratory diseases are among the leading death causes of children under 5 years, which highlights the necessity to precisely evaluate the symptoms, to find the underlying condition and to prescribe the appropriate treatment.

**Purpose.** To analyze and evaluate cough causes, used diagnostic methods and suggested therapy for 2–10 years old children.

**Materials and methods.** A questionnaire for children's primary caregivers and a protocol for child's medical history were used to gather information about demographic data, clinical diagnosis, provided diagnostic services and set treatment. Data were analysed using mathematical statistics.

**Results.** This study was carried out from 1.02.2016. to 1.05.2016. During this period, 46 participants were included in research, mostly those were 4–6 years old children (47.8%). 93.5% of children had acute cough and the most common causes of it were acute pneumonia (34.8%), acute bronchitis (23.9%) and acute pharyngitis (8.7%). There were no statistically significant risk factors directly associated with the conditions. Several algorithms for patients' evaluation are used in Rēzekne regional hospital. Each patient was checked for respiratory sounds and almost everyone (97%) had undergone blood tests and 69.6% had lung X-ray. Less than a half (41.3%) were checked for infections. The most common prescribed drugs were antipyretics (95.7%) and mucolytics (91.3%), every patient received symptomatic treatment, as well. Some patients received unreasonable antibiotic therapy.

**Conclusions.** The most common causes of cough among children who received treatment in Rēzekne regional hospital were acute pneumonia, acute bronchitis and acute pharyngitis. Provided diagnostic tools and services were appropriate in most cases and were selected according to the set algorithms. Several cases of unreasonable antibiotic therapy use were discovered.



### 3. CORRELATION BETWEEN GHRELIN AND INSULIN-LIKE GROWTH FACTOR AMONG CHILDREN WITH OVERWEIGHT AND OBESITY

*Ieva Štrauhmane<sup>1</sup>, Irēna Rinkuža<sup>2</sup>, Ināra Kirillova<sup>2</sup>, Līva Grīviņa<sup>1</sup>, Ingrīda Rumba-Rozenfelde<sup>1</sup>, Dace Rudzīte<sup>3</sup>, Ilva Daugule<sup>1</sup>*

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**Background.** Obesity is an increasing problem in industrialised countries. One of the hormones responsible for regulation of food intake is ghrelin. Ghrelin reduces glucose-stimulated insulin secretion, thus increasing blood glucose level. On the other hand, insulin resistance and increased glucose levels could cause decline in the release of ghrelin. In addition, ghrelin production disturbances could also affect insulin-like growth factor-1 (IGF-1) metabolism.

**Purpose.** To analyze correlation of plasma ghrelin levels with IGF-1 among adolescents with overweight and obesity.

**Methods.** Fasting blood samples were taken from consecutive adolescents coming to endocrinologist consultation due to weight increase. The patient group included 75 adolescents (median age 12 years), mean BMI 26,5kg/m<sup>2</sup> (95,7 percentiles, 95%CI:94,2-97,1). All patients had weight increase, two patients had Prader Willi syndrome, three patients – hypothyroidism and one patient had decreased height. The level of total and acylated ghrelin was detected by ELISA method.

Statistical methods: Spearman's rank correlation.

**Results.** The median level of total ghrelin and acylated ghrelin was 295,5 pg/ml (95%CI:264,3-342,3) and 192,3 pg/ml (95%CI:156,930-247,974), respectively. Level of IGF-1 negatively correlated with total (correlation coefficient (-0,3), p=0.01) and acylated ghrelin (correlation coefficient (-0,4); p=0.002), respectively. A significant correlation was observed also between ghrelin and height (p=0.02) and age (0.001).

**Conclusions.** Among children with overweight and obesity the levels of ghrelin negatively correlated with the levels of IGF-1, thus suggesting an association between ghrelin and IGF-1 production. The exact interaction and possible clinical significance should be studied further.

**Acknowledgements/Funding** *The study was supported by the grant from Latvia State Research Programme "Biomedicine".*

#### 4. STUDY ON CHILD HEALTHCARE AND DEVELOPMENT ISSUES WITHIN THE 2<sup>ND</sup> CHILDREN'S REPORT OF LATVIA TO THE UNITED NATIONS

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**Background.** The UN Convention on the Rights of the Child (CRC) requires that a non-governmental report be submitted after the state report on the situation of the implementation of the UNCRC. Non-governmental reporting has brought substantial benefit to children in member states, in the form of UN recommendations on necessary changes, implementation thereof mandatory to the government. The Children's Report, as an adjunct to the nongovernmental report, provides valuable insight into the situation from the perspective of children themselves.

**Purpose.** Assess the opinion of children/adolescents on violations of their rights concerning healthcare and development. Report to UN Child Rights Committee the information necessary for drafting of recommendations to Latvia.

**Materials and methods.** 350 randomly selected students aged 18–20 (underage during the period studied) were surveyed at the University of Latvia in 2013–2015 on healthcare, social relations and inclusion, education, and sexual orientation, and were asked for suggestions to the governing structures of Latvia and EU. Survey results were complemented by analysis of case reports submitted by the students and were compared to the results of the first Children's Report to the UN in 2005.

**Results.** Regional distribution of residence was representative of Latvia. Participants indicated that during 2003–2014 they knew children, who: lacked necessary medication (46%), access to a doctor (48%), enough to eat (23%); suffered from alcohol use in the family (76%); had to work to survive (47%); sometimes lacked electricity/heating (41%), household items (63%); lacked the possibility of participating in events (76%), suffered from parents being employed abroad (91%), unemployed (88%), cruelty in the family (46%), feeling lonely and depressed (82%); have contemplated suicide (25%); have to sell sex (8%); were discriminated against due to being different (66%), of different sexual orientation (15%), disabled (46%), or addicts (67%). 12% knew of cases, where help was refused to children with addiction issues.

This study was included in the Children's Report to the UN, according to which UNCRC Committee drafted and submitted UN Recommendations 2015 to Latvia on necessary changes that must be implemented, resulting in the drafting of an action plan in the Cabinet of Ministers.

**Conclusions.** Immediate systemic changes are necessary concerning child healthcare accessibility, school and family environment, learning difficulties, attitude towards underprivileged children and those of different sexual orientation, underage prostitution. Non-governmental reporting is valuable for ensuring real feedback between the needs of children, the government and parliament through the UN as a moderator and counsellor. This practice must be continued, with the third Children's Report due in 2020.

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## 5. RECOMMENDATIONS. CHILDREN WITH AUTISM SPECTRUM DISORDERS

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**Background.** Topicality is dictated by the increasing number of children who are diagnosed with AST. Children's psychomotor development dynamics evaluation indicates a high efficiency multi-sensory therapy applications.<sup>1</sup>

**Purpose.** To develop optimal treatment algorithm AST to treat the manifestations of psychomotor retardation and correction possibility of dynamics.

**Materials and methods.** During the period of 2013–2015, the Children's Clinical University Hospital and the University of Latvian Social Pediatric Center conducted a prospective study of the effectiveness of treatment for children with AST. 100 children (incl. 28 without autism diagnoses) aged 2 to 5 years were grouped according to their psychomotor capacity to enable the evaluation by questionnaire derived from the development of scales and Munich Denver functional test, in the following five categories: 1. Children with hearing perception disorders; 2. Children with visual perceptual disorders; 3. Children with language development disorders; 4. Children with fine motor disabilities; 5. Children with large motor development and daily operations.

**Results.** The study yielded the following results: the greatest efficiency, evaluating children's psychomotor development momentum was achieved through special classes with teachers – 74%, classes at the Montessori method showed improvement in 72% of children. Based on the results obtained, treatment plans were created and implemented according to the specific needs of child development: 1) Children's overall development. 2) Children's physical development and motor function improvement. 3) Promotion of child's socialization. 4) Child's general perception of development. 5) Improvement of child's information collecting and analyzing capacity.

### **Conclusions.**

1. The use of multi-sensory therapy improved the child's psychomotor development of the criteria and proved to be effective in working with AST patients.
2. Most rational multisensor therapies, combined with the general development of the algorithm, which greatly accelerates the child's psychomotor development, optimize the treatment options and eliminate the risk of recourse.
3. Early appropriate treatment resulted in positive AST patients' psychomotor development dynamics or lack of negative dynamics.

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<sup>1</sup> Василёнок А., Фолкманис В., Артаева Т., Шена И. Возможности развивающей терапии в лечении детей с нарушениями аутистического спектра // РМЖ. 2016. №6. С. 376-378.

## 6. TRENDS OF LATE FETAL DEATH IN LATVIA, 2001–2014

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**Background.** European Perinatal Health Monitoring data (PERISTAT) analysis shows that the average reduction of stillbirths in 2010 compared to 2004 was about 19% (variations among countries to 38%). Latvian statistics data shows that late fetal death rate ( $\geq 28$  GW) decreased from 5.2/1000 in 2001 to 3.3/1000 in 2015. Late fetal death rates are used for international comparisons because of large stillbirth rate variations between countries.

**Purpose.** To examine trends in late fetal death by multiple births, birth weight, maternal age and causes of death in the two time periods.

**Materials and methods.** Data from Medical Birth Register were used. Design – retrospective cohort study. Late fetal deaths were defined as stillbirths occurring after 28 completed weeks of gestation and weighing at least 500 g. In total, the data on 1,340 stillbirths were analysed from 2001 to 2014, divided 2 periods of 7 years (2001–2007 and 2008–2014). Averages (maternal age, fetal birth weight and gestational week) as shown in the median, indicating the 25<sup>th</sup> and 75<sup>th</sup> percentile. Late fetal death rates were calculated per 1000 total births in each time period. Time trends were analysed by calculating rate ratios (RR), with 95% confidence intervals (CI), comparing rates in 2001–2007 with those for 2008–2014.

**Results.** There were 74% late fetal death from all stillbirth during 2001–2014. The median of maternal age in the surveyed population was 28 years (23–33), birth weight – 2380 g (1620–3100) and gestational week – 36 (32–39). 79.2% ( $n=1,061$ ) of cases (95% CI 77.7–82.0) were ante partum stillbirth. The overall late fetal death rate showed slight statistically significant reduction ( $p<0.001$ ) by 18% between 2001–2007 and 2008–2014. Late fetal death rate decreased to 4.2/1000 (95% CI 3.9–4.5) in 2008–2014 from 5.0/1000 (95% CI 4.6–5.3) in 2001–2007, RR is 0.8/1000 (95% CI 0.2–1.9). There was a slight increase in the mortality rate from multiple pregnancies 10.2/1000 (95% CI 7.1–14.1) to 11.3/1000 (95% CI 8.2–15.3) in the period (2008–2014), RR is 1.1/1000 (95% CI 0.6–1.9). There were no big differences in the late fetal death rate by maternal age during these time periods. RR is 1.0/1000 (95% CI 0.3–2.4) in the age group  $\leq 19$  years, respectively mortality rate is 4.7/1000 (95% CI 3.7–6.0) to 4.5/1000 (95% CI 3.2–6.1); RR is 0.9/1000 (95% CI 0.2–2.0) ( $p<0.01$ ) in the age group 20–34 years and mortality rates from 4.4/1000 (95% CI 4.0–4.8) to 3.9/1000 (95% CI 3.5–4.0); more substantial reduction was observed in the age group  $\geq 35$  years with RR 0.6/1000 (95% CI 0.2–1.2) ( $p<0.001$ ) and mortality rate reduction from 9.2/1000 (95% CI 7.8–10.8) to 5.8/1000 (95% CI 4.9–6.9) in 2008–2014.

Describing antenatal care factors which may be associated with adverse pregnancy outcomes, 29.0% ( $n=389$ ) were registered late for antenatal care (after 12 GW). However, in those time periods a decrease was observed by 13 percentage points (from 34.9% to 21.9%) ( $\chi^2=27.5$ ;  $p<0.01$ ).

Analyzing the structure of death causes, the most common are different perinatal period conditions (*ICD-10; P00–P96*) – 92.6% (95% *CI* 91.1–93.9), congenital anomalies (*ICD-10; Q00–Q99*) is 6.0% (95% *CI* 6.9–7.4). In two time periods changes are not observed due to congenital anomalies as death cause, respectively RR is 0.9/1000 (95% *CI* 0.2–1.9) and 0.7/1000 (95% *CI* 0.2–1.0). Late fetal death due to perinatal period conditions declined statistically significant ( $p < 0.01$ ) – from 4.6/1000 (95% *CI* 4.2–4.9) to 3.9/1000 (95% *CI* 3.6–4.2) in the period from 2008 to 2014.

**Conclusions.** The overall late fetal death rate showed slight statistically significant reduction ( $p < 0.001$ ) over the study periods (2001–2007 and 2008–2014). Late fetal deaths due to perinatal period condition also declined significantly ( $p < 0.01$ ), as well as in the two maternal age groups (20–34 years and  $\geq 35$  years) ( $p < 0.01$  and  $p < 0.001$ ). Further investigation of the detailed late fetal death causes is needed.

## 7. REVIEW OF CLINICAL MANIFESTATIONS, DIAGNOSIS AND TREATMENT OF VEIN OF GALEN MALFORMATION IN LATVIA

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**Background.** The vein of Galen, also known as the great cerebral vein, is located under the cerebral hemispheres. It drains the anterior and central regions of the brain into venous sinuses of the posterior cerebral fossa. The vein of Galen malformation is rare, but, at the same time, the most common congenital vascular malformation affecting neonates and young children. Unfortunately, this malformation carries a high mortality rate amongst neonates. Typical clinical manifestations of this condition are congestive high-output heart failure, development delay, hydrocephalus and seizures. In most cases, the vein of Galen malformation is treated performing endovascular embolization.

**Purpose.** The vein of Galen malformation is not widely studied in Latvia before. This condition can cause severe and irreversible damage to the brain and other organ systems. Early diagnosis and most effective option of treatment are extremely important to provide better quality of life and normal mental development in neonates and children with this vascular malformation.

**Materials and methods.** We retrospectively reviewed the radiology imaging studies, hospital clinical charts and notes of six children diagnosed and treated for vein of Galen malformation at the Children's Clinical University Hospital. Clinical manifestation, diagnostic methods, treatment strategies and outcome were documented for each patient.

**Results.** Between August 2006 and April 2015, six children (five boys, one girl) were diagnosed with vein of Galen malformation. There were two infants and three children one to five years old amongst the affected patients. Five of six patients had signs of heart disease – one of them had hypertrophic cardiomyopathy, two patients had patent *ductus arteriosus* and two other patients had intraventricular conduction disorders presenting in electrocardiography. Hydrocephalus was discovered in three of six children. For one patient, ventriculoperitoneal shunt was performed because of hydrocephalus. Three of six patients had neurological symptoms. Four of six children were treated by endovascular embolization, and complete occlusion of malformation was reached in all those patients. One child had intraventricular haemorrhage before embolization. One patient had spontaneous intracranial haemorrhage after embolization. Both patients were treated successfully.

**Conclusions.** The vein of Galen malformation can affect children of different ages, and it can be combined with other congenital abnormalities. This malformation can be easily diagnosed performing digital subtraction angiography and effectively treated by endovascular embolization methods.

**Acknowledgements/Funding.** We are grateful to neurosurgeon Dāvis Ozoliņš for his responsiveness and help with providing access to clinical charts and notes about patients from archive of Children's Clinical University Hospital for this study.

# PUBLIC HEALTH AND HEALTHCARE ORGANIZATION

## 1. SOCIO-TECHNICAL CHALLENGES IN INTRODUCTION OF PUBLIC MONITORING FOR HEALTHCARE QUALITY AND EFFICIENCY

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**Background.** Transparency has become a widespread doctrine for many governments and organizations to improve public services. The value of public monitoring has rarely been questioned today. Also in the field of healthcare in many countries, the transparent providers' performance data has been increasingly used to improve the quality and efficiency of care. Latvia, in contrast, yet has made limited progress in this direction despite the growing availability of data that could be publicly reported.

**Purpose.** The aim of this research is to explore both social and technical elements of introduction of public monitoring for quality and efficiency in healthcare.

**Materials and methods.** The paper is based on an extensive study of various health care transparency initiatives documented in professional medical and health management literature and organizational research performed on locally initiated activities towards health transparency.

### **Results.**

1. At the national level, the construction and the implementation of indicator-based monitoring system should be based on data stored in such governmental organizations as National Health Service (NHS) (database of individualized reimbursement claims from care providers), Centre for Disease Prevention and Control (CDPC) (national registries for selected diseases and database of death certificates) and State Emergency Medical Service (SEMS) (data representing individuals' interaction with this service). However, these organizations have no routine practices established for data exchange.
2. To ensure substantive changes in both organizational performance and professional behaviour of individuals providing care, publicly reported indicators should represent all aspects – structure, process and outcome. For the identification of such indicators, the individual patient level data should be used. However, there are no locally adapted practices for patient data anonymization and it prevents the analytical usage of stored data.
3. Existing initiatives towards healthcare data transparency highlights the need to address such technical issues as patient data safety, data consistency and quality as well as effective data visualisation issues. The most prominent social challenge in the development of transparency approach is the motivation and engagement of health professionals to take an active role in defining quality and efficiency indicators reliable for further improvement through peer review process.

**Conclusions.** The autonomy of healthcare organizations guaranteed by purchaser-provider split and autonomy of individual clinicians within those organisations guaranteed by professional autonomy of medical profession limits the usage of traditional managerial approaches in healthcare settings. Transparency has potential to shape public and professional behaviour of care providers towards further improvement of quality and efficiency without increased direct legislative and managerial control of clinical process.

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## 2. GASTRIC CANCER SCREENING COST EFFICIENCY ANALYSES USING BIOMARKERS

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**Background and purpose.** Gastric cancer is the third leading cause of cancer death worldwide, with the highest rates reported in East Asia, South America and Eastern Europe. Although early-detection screening is routine in areas with high disease rates, no major organization recommends general population screening for gastric cancer. The aim of the research was to analyze cost efficiency of gastric cancer through organized and selected screenings of the population in Latvia.

**Methods.** During the research, the gastric cancer treatment costs were calculated through disease stages of the patients in Latvia. According to the objective of the research, the loss was calculated for the national economy caused by gastric cancer without any prevention activities taking into account the cost of treatment and value of lost years of life. Calculations of cost efficiency were made for 25-year projection of gastric cancer screening for age group 40–69. Distribution of patients in different stages of disease used in calculations: I stage – 14,5%, II stage – 19,7%, III stage – 22,1%, IV stage – 43,7%. Population forecast data by *Eurostat* were used in calculations. Biomarkers Overall accuracy of biomarkers: 76,1639; sensitivity: 91,0448; specificity: 71,2159 parameters were used.

**Results.** Gastric cancer treatment costs are: I stage – 1895 EUR, II stage – 1915 EUR, III stage – 2108 EUR, IV stage – 941 EUR and reflect significant information for the further detailed analysis of the issue.

Loss for the national economy caused by gastric cancer is 30 million EUR annually without any prevention activities. With organized screening costs are over 150 million EUR annually with trend to increase by increasing participation rate. If voluntarily screening takes place, there are no loss for national economy and gain for the national economy exceeds 1 million EUR in 7 years period. These results lead to significant conclusions for the policy makers.

**Conclusions.** Organized screening using sample biomarkers for gastric screening is not cost efficient in Latvia, but selective screening is. Explanation for that is relatively low prevalence of disease and high diagnostic cost.

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### 3. HUMAN FACTORS. TRAINING AND LEARNING FROM INCIDENTS AS AN APPROACH TO INCREASE INVOLVEMENT OF CLINICIANS IN REPORTING AND PATIENT SAFETY IMPROVEMENTS

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**Background.** There is evidence on human factors (HF) and non-technical skills (NTS) such as situation awareness, decision making, communication, team work, leadership, stress, and fatigue management as the main causes of adverse events in high risk industries, however there is lack of research how to implement HF based approach in hospitals. This problem is of outstanding importance since hospitals implement risk reductions strategies to improve patient safety, including blame free incident's reporting and learning system. Children's University Hospital (CUH) launched incident reporting on March 2013. Number of reports increased from 78 in 2013 to 194 in 2015; however, openness about errors was still low.

**Purpose.** The objective of the current study was to develop, realize and assess how targeted HF training and learning from incidents improves patient safety culture and involvement of the clinicians.

#### **Materials and methods.**

1. Developed HF training seminar: 5 academic hours including interactive case study and human factors analysis. Altogether 42 CUH professionals participated in 4 seminars: 11 physicians, 20 nursing leaders, 11 administrative specialists (human resources, customer, relationships, labour specialists, lawyer).
2. Twelve lectures (30–45 min.) for physicians and nurses, including HF feedback from CUH case studies.
3. Incorporated HF in Root Cause Analysis (RCA).
4. Team approach to sentinel events' RCA, involving clinicians – 5 sentinel events analyzed, improvement actions identified.

Study was performed during the year 2016 (12 months).

**Results.** Applied approach showed improvement in 4 directions:

1. Reporting activity increased 2,3 times. Number of reports increased by 123 reports (63%) reaching 317 compared to an increase of 41 reports (27%) during the year 2015;
2. Increased number of reports in often underreported category: Clinical process/ Procedure – 2,6 times (subcategory Diagnosis/Assessment – 2,4 times; Procedure / Treatment/Intervention – 2,7 times);
3. Clinicians reporting activity increased from 34% in 2015 till 47% in 2016.
4. HF approach resulted in clinicians' initiative to organize national Patient Safety conference, which took place in October 2016 with more than 500 attendees.

**Conclusions.** Reporting benefits detection of system weaknesses. Patient safety can be improved by better understanding of human-system interface, which is important to produce better-designed systems and processes instead of blaming the individuals. This study shows the way, how to involve professionals in patient safety improvements and could be implemented in hospitals setting. HF training should be part of medical education and healthcare managers as well. HF approach should be implemented in Healthcare Inspectorate investigation. Study should be continued in the future.

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## 4. PRENATAL EXPOSURE TO MATERNAL ANXIETY-DEPRESSIVE SYMPTOMS AND ITS INFLUENCES ON INFANT DEVELOPMENT AND BEHAVIOUR

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**Background.** Depression is one of the most common mental disorders worldwide. Women are more at risk of anxiety and depression disorders while they are pregnant, and during the first months of postpartum period. Latest researches report that about 12–20% of pregnant women suffer from depression, which might influence the children's development during pregnancy as well as it can have a serious negative affect as delay in child postnatal development. Children born to mothers who are depressed are in risk of adjustment and behavioral disorders, attention deficit hyperactivity disorder, autism spectrum disorders, total mental retardation, anxiety and depressive disorders, endocrine and immune system development pathologies.

### Objectives

1. To establish the correlation between episodes of depression before, during and after pregnancy.
2. To find out all types of damage to the fetus, if the mother is in depression.
3. To figure out the percentage of anxiety and depression symptoms among the pregnant in Latvia.

**Materials and methods.** Pregnant women undergoing antenatal care in Latvia, Riga were interviewed using PHQ-9 and GAD-7 scales, the obtained data from the scale's results were analyzed and summarized in an analytic cross-sectional study. Also, we analyzed literature in literature systematic review.

**Results.** From analysis of the scientific literature, we observe a high correlation ( $r = 0,8$ ) between the depressive episodes before pregnancy, depressive symptoms during pregnancy and postpartum depression, as well as it can have a serious negative effects in child postnatal development. Using PHQ-9 (Patient Health Questionnaire) and GAD-7 (Generalised Anxiety Disorder Assessment) screening scales, an inquiry was set up among 150 pregnant women in Riga, Latvia (2016). It was determined that depressive symptoms (PHQ-9) are observed in 45% of pregnant women. 36% of pregnant women have mild depression symptoms, 3% moderate symptoms, 5% moderately severe symptoms and 1% – severe depression symptoms ( $P < 0,05$ ). Anxiety disorder (GAD-7) screening results, in turn, are the following: 35% of pregnant women have mild anxiety symptoms, 9% moderate anxiety symptoms; 3% severe anxiety symptoms ( $P < 0,05$ ). In total, the anxiety disorder symptoms are noted by 47% of pregnant women. 36% of respondents note both depression symptoms and anxiety disorder symptoms. Therefore, we can see that anxiety and depression has a direct connection.

### Conclusion

1. PHQ-9 and GAD-7 scales are informative, quick and easy for patients to complete.
2. Children development and behavior has a strong association with maternal depressive state during pregnancy.
3. There is a high level of depression symptoms among pregnant women in Latvia.

## 5. ASSESSMENT OF MANAGEMENT PROCESS IMPROVEMENT IN CLINICS OF THE CHILDREN'S UNIVERSITY HOSPITAL

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**Background.** Children's Hospital experiences a shortage of doctors, but the average age of the current doctors gradually increases. Simultaneously, the best and the most talented doctors are being promoted to manage clinics, where they occasionally lack the required management skills and experience, and even less time is available for the core function – treatment of patients.

**Purpose.** The objective of the study was to research and analyse the possibilities to increase medical treatment services and to enhance medical process management functions in the clinics of Children's Hospital, and to prepare proposals for process improvements in an environment of limited resources.

### **Materials and methods:**

1. 65 sources were used in the process of research
2. Semi-structured interviews with 10 heads of clinics that allowed to promptly obtain information on their daily duties
3. A survey that allowed to gather empirical data on the workload and split of the workload for 10 heads of clinics
4. Semi-structured interviews with 12 industry experts that allowed to promptly gather expert opinions and new solutions

### **Results:**

1. Evaluation of activities' performance of Children's Hospital
2. Identification of medical staff duties not connected with patient treatment
3. Identification of the amount of duties not connected with patient treatment in the management of clinics
4. Identification of necessary competencies and conditions for attraction of administrative managers
5. Development of a job description for a clinical administrative manager
6. Development of a plan for attracting additional resource for clinics of Children's Hospital

**Conclusions.** It is possible to delegate part of administrative functions to a manager without medical background in Children's Hospital. The additional time that could be devoted to patient care if the administrative tasks would be delegated to administrative managers employed for that purpose, amounts to 29% in average for all 10 heads of clinics. At the moment, 10 clinics would require 3 to 4 full time administrative managers, assuming administrative managers and heads of clinics spend the same amount of time on executing the relevant functions.

## 6. NON-INVASIVE FETAL RHESUS FACTOR GENOTYPING ASSAY DEVELOPMENT AND VALIDATION

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**Background.** Prenatal foetal Rh factor testing in RhD negative women helps to identify risk of D-alloimmunization, which may cause haemolytic disease of the foetus and newborn, and is necessary for initiation of early management. Non-invasive foetal rhesus genotyping is complicated due to several factors – RHD gene similarity with RHCE gene, low cell-free foetal DNA (cffDNA) fraction in plasma and cffDNA extraction methodology, especially from the frozen samples. The use of commercial kits is limited due to high costs and limited availability in Latvian market.

**Purpose.** Develop non-invasive RHD genotyping assay for effective and robust prenatal foetal RhD determination, validate the assay typing samples of known genotype. Provide recommendations for effective assay application.

**Materials and methods.** CffDNA was extracted from 71 plasma sample genotyped before (47 Rh-positive and 24 Rh-negative samples), the average GA was 20.8±2.4 weeks. 59 DNA samples (83%) were extracted using *QIAamp Ultrasens Virus Kit* and 12 samples (17%) using *Analytik Jena free-circulating DNA Extraction Kit*.

Designed primers and probes targeted RHD exons 5, 7 and 10, and GAPDH gene as internal control, probes were labelled with FAM, HEX, ROX and Cy5 fluorophores, respectively. Primers for each locus were tested separately using SybrGreen technology. Further cffDNA were analyzed in multiplex (TaqMan), reaction conditions were approved and optimised using gDNA.

**Results.** Validation results were divided into four groups: “complete match” – all four loci were consistent to previously determined genotype (40 samples, 58%); 15 samples (21%) showed “partial match” – at least two loci matched, including IC; 2 samples (3%) showed the opposite genotype. 14 samples (20%) were invalid and therefore excluded from analysis. Sensitivity of the assay is 94,6%, specificity – 99%. CffDNA samples extracted with *Analytik Jena free-circulating DNA Extraction Kit* matched in 83% of cases, but those extracted with *QIAamp Ultrasens Virus Kit* in 76%.

**Conclusions.** RHD primers were designed, genotyping reagents were accordingly selected and assay conditions were optimized for robust assay usage. Validation of RHD genotyping assay proceeded successfully, sensitivity and specificity of the assay is enough for further its application in a diagnostic laboratory. According to the results, 20% of the samples were invalid, therefore following recommendations were formulated: use blood vacutainers with cffDNA stabilizer, genotype foetal RHD after GA 20 weeks, thaw frozen plasma gradually at 4-8°C, optimal plasma volume for the cffDNA extraction is 600 µL.

**Acknowledgements.** Authors are grateful to “IVF Riga” reproductive genetics clinic for the support and complete funding of the study.

## 7. SURVEY OF LATVIAN PHARMACISTS ABOUT IMPLEMENTATION OF ADDITIONAL PHARMACEUTICAL CARE SERVICES

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**Background.** Pharmacist's role in health care system is changing. Previously, the preparation of extemporal formulations was the main duty of a pharmacist working in community pharmacies. Nowadays, in many EU countries pharmacist gives consultations to customers and thus helps to improve the overall health care system. Contemporary pharmaceutical care includes various other services that pharmacies are offering to their customers in addition to the basic consultation about medical products and dispensing them. The reason to offer additional services is to attract more clients, to promote relationships between pharmacist and its client and to ensure the utmost quality when fulfilling customers' needs.

**Purpose.** The objective of the current study was to survey Latvian pharmacists about the possibility to implement 10 additional services similar to that which are offered in pharmacies of Ireland and to identify barriers for implementing additional pharmaceutical services in Latvian community pharmacies.

**Materials and methods.** The questionnaires were distributed to pharmaceutical specialists in Latvia – pharmacists, pharmacist assistants and persons with scientific degree in pharmacy working in pharmaceutical industry. 107 filled respondents' questionnaires were used for data analysis.

**Results.** Latvian pharmacists' opinions about additional pharmaceutical services differ greatly: 42% of responders support implementation of services similar to Ireland in community pharmacies in Latvia, but 58% of respondents are against it. The employees of Latvian pharmacy are the most interested in an in-depth patient consultation about new medications (57%), and they support programs for weight loss (48%) and smoking cessation (47%). The most negative attitude of responders was expressed regarding the idea to provide vaccination (67%) and first aid for small injuries and wounds (66%) in pharmacies. The reasons mentioned by respondents against implementation of additional pharmaceutical care services are the following:

- Differences in the Irish and Latvian community pharmacy space planning requirements – Latvian pharmacy does not necessarily need to have a private space for counselling;
- A lack of standards of additional pharmaceutical care services;
- Long working hours and shortages of experienced, trained staff at the pharmacy.

**Conclusions.** Implementation of additional pharmaceutical care services in Latvian community pharmacies would be difficult, mainly because of negative attitude from pharmacists. In order to facilitate the implementation of such services the professional organizations should carry out the explanation work and facilitate the improvements in legislation aspects.

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## 8. SURVEY ABOUT ANAEMIA, ANTI-ANAEMIC MEDICINES AND ANALYSIS OF BLOOD TESTS

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**Background.** Anaemia is the most common blood disorder in the world, which affects almost 25% of population, mostly women.

**Purpose.** The objective of the current study was to evaluate prevalence of anaemia. Tasks: 1) To find out frequently dispensed anti-anaemic medicines in the pharmacy and analyse usage of anti-anaemic medicines and nutritional supplements. 2) To survey medical staff about prevalence of patients with anaemia. 3) To analyse results of blood tests collected by *E. Gulbis Laboratory Ltd.* in the period from 01.01.2015. to 30.04.2016.

**Materials and methods.** 1. The data basis of pharmacy “Medinfo”; 2. Questionnaires for population (altogether 460 respondents – including students and visitors of pharmacy) and 162 specialists of health care (pharmacists, gynaecologists, family doctors, staff of medical emergency) via internet platform “visidatilv” and dispensing hand-completed paper forms. 3. 1 303 932 blood tests from the data basis of *E. Gulbis Laboratory Ltd.* analysed by *Microsoft Office Excel 2016.*

### **Results.**

1. 64.4% (n=29) women was prescribed medicine, which contains iron (III)-hydroxide polymaltose complex, but 62.5% (n=5) men – iron (II) sulfate. The most sold of non-prescription medicines was iron (II) fumarate containing medicine.
2. 45.5% (n=209) of respondents was diagnosed anaemia, from which 90.4% (n=189) were women. 83.7% (n=175) had iron deficiency anaemia. 74.1% (n=341) have ever used anti-anaemic medicines mostly to avoid anaemia.
3. 98.1% (n=152) of health care specialists have patients with anaemia, 53.7% (n=87) thinks that anaemia mostly affects adults.
4. Decreased haemoglobin had 5.37% (n=37388) women and 16.44% (n=57853) men in 2015, but 6.81% (n=17365) women and 6.77% (n=8512) men in analysed period of 2016. Reduced red blood cell count was found in 14.65% (n=102 106) women's blood tests and 15.26% (n=53711) men's in 2015 and accordingly 5.29% (n=3490) and 3.18% (n=3994) in period of 2016.

**Conclusions.** 74.1% of respondents use anti-anaemic medicines to treat or prevent anaemia. Anaemia is diagnosed in 45.5% respondents, mostly women and cause of their anaemia is iron deficiency. Anaemia is often diagnosed illness – 98.1% of health care specialists have these patients. Blood tests show that the frequently diagnosed type of anaemia is iron deficiency anaemia in women.

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## 9. MEDICAL STUDENTS WITH MENTAL HEALTH CONDITIONS: LEGAL, ETHICAL AND POLICY CHALLENGES

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**Background.** According to public health data, 15–25% of the general population have experienced a mild to moderate mental health conditions, like stress, depression, and anxiety disorders. Research data proves, that medical students may have more instances of mental health conditions, e.g. depression and anxiety are more prevalent amongst medical students than among peers of a similar age (Hope & Henderson, 2014).

**Purpose.** To stimulate development of a legal and ethical framework for support and protection of medical students with mental health conditions in Latvia.

**Material and methods.** Analysis of published research data and policies developed and implemented by different medical schools.

**Results.** There is no data on persistence of mental health issues in medical students in Latvia or data allowing to explore to what extent medical students have perceived a need for or have used mental health services. There are no policies developed and implemented to tackle the problem at medical faculties in Latvia. Any medical school ought to promote good health and wellbeing of students, and should stand for equality among students without discrimination of those with mental health issues. Therefore universities in general and medical faculties in particular should develop policies and practices securing legally and ethically justified support for students with mental health conditions, including support services, occupational health consultations, accessible information and training for faculty members.

**Conclusions.** There is a need for empirical research on medical student mental health in Latvia, as well as a necessity to develop and implement a policy for support of medical students with mental health conditions, e.g. interventions to promote mental health at the university, to improve access to mental health providers, to ensure confidentiality, to reduce stigma and other barriers to mental health treatment, and to encourage a help seeking behaviour in medical student population.



# INTERNAL MEDICINE, CARDIOLOGY AND INFECTIOUS DISEASE

## PART I: CARDIOVASCULAR MEDICINE

### 1. DIURETIC USE IS ASSOCIATED WITH HIGHER PLASMA TRIMETHYLAMINE-N-OXIDE LEVELS

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**Background.** Increased blood level of trimethylamine-N-oxide (TMAO) is a novel cardiovascular risk marker. We have previously reported association of diabetes, age and body mass index with increased TMAO levels. Effect of cardiovascular drugs on TMAO levels is not known with the exception of meldonium that lowers TMAO levels.

**Purpose.** We aimed to evaluate a potential effect of cardiovascular drugs on plasma levels of TMAO.

**Materials and methods.** In a cross-sectional study patients with increased cardiovascular risk undergoing coronary angiography at the Latvian Center of Cardiology were included. Patients on anti-diabetic drugs were excluded. Information on cardiovascular medications, doses and duration of use was recorded, and TMAO plasma levels were measured in fasting state. All patients were requested to abstain from any intake of fish, fish products and omega-3 supplements one day before and on the day of sampling. For the purpose of data normalization TMAO values were logarithmically transformed.

**Results.** Three hundred patients were included in the study. Mean logarithmically transformed values of TMAO levels (log-TMAO) were significantly higher in diuretic users (n=81) compared to non-users (n=219):  $0.409 \pm 0.306$  vs.  $0.324 \pm 0.263$ , respectively (p=0.017). Patients using loop diuretics (n=15,  $0.517 \pm 0.332$ ) but not those on thiazides/thiazide-like diuretics (n=62,  $0.378 \pm 0.305$ ) had significantly higher log-TMAO values compared to non-users (p=0.007 and p=0.164, respectively). Association with loop diuretics remained significant after adjustment for multiple comparisons (p=0.025 for loop diuretics, p=0.354 for thiazides). Four patients were taking both groups of diuretics and were excluded from subanalysis. No significant difference was observed between use of indapamide (n=41) and hydrochlorthiazide (n=21):  $0.395 \pm 0.332$  and  $0.345 \pm 0.246$ , respectively (p=0.546). Spironolacton users (n=28) had higher log-TMAO than non-users (n=272):  $0.482 \pm 0.293$  and  $0.333 \pm 0.273$ , respectively (p=0.007). Additive effect of loop diuretics and spironolacton was observed. After exclusion of 43 patients with detectable meldonium levels, the absolute values of TMAO in subgroups did not change significantly. No other analyzed cardiovascular drugs (statins, antiplatelets and antihypertensives) were associated with TMAO levels in this sample.

**Conclusions.** Our observational data suggest that use of loop-diuretics and spironolactone is associated with increased plasma TMAO levels.

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## 2. BIOCHEMICAL DIAGNOSTIC METHODS FOR EARLY DETECTION OF CHEMOTHERAPY INDUCED MYOCARDIAL INJURY

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**Background.** Laboratory testing such as troponin I (TnI), creatine kinase MB (CK-MB), B- type natriuretic peptide (BNP), galectin-3 (Gal-3) blood concentrations, may detect chemotherapy-induced myocardial damage. Rise of biochemical indicators may help identify patients at risk of developing heart failure.

**Purpose.** To detect biochemical changes suggestive of early myocardial damage in patients receiving anthracycline-based chemotherapy to predict and timely diagnose heart failure development.

**Materials and methods.** First-time oncological patients with indications to anthracycline based chemotherapy, at least 3 courses were enrolled. Before and day after each anthracycline containing chemotherapy course, three weeks, three and six months after the end of chemotherapy we measured: TnI with *ADVIA Centaur XP TnI-Ultra* (99<sup>th</sup> percentile 40 ng/l) or *ARCHITECT Stat High Sensitive Troponin-I* test (99<sup>th</sup> percentile for women 15.6 ng/l), CK-MB with *ADVIA Centaur XP CK-MB* (normal range till 5 ng/ml) or CK-MB with *ARCHITECT Stat* (normal range for women till 3.4 ng/ml), BNP with *ARCHITECT BNP* test (normal range till 100 pg/ml), Gal-3 with *ARCHITECT Galectin-3* test (normal range till 17.8 ng/ml). TnI test results were standardized to 99<sup>th</sup> percentile, CK-MB to the upper normal range.

**Results.** 38 patients enrolled (23 completed chemotherapy, 13 continue, 2 excluded after the second course because of chemotherapy change). Included patients were 35–74 years old, women 97.4%. Before the second chemotherapy course statistically significant increase of TnI blood concentrations was found compared to baseline (standardized value  $0.21 \pm 0.15$  vs.  $0.15 \pm 0.10$ ,  $p=0.007$ ), which remained significantly elevated before the third, fifth, sixth course, three weeks, three months after the end of chemotherapy ( $p<0.05$ ). CK-MB blood concentration statistically significantly increased only three weeks after the end of chemotherapy (standardized value  $0.30 \pm 0.27$  vs.  $0.22 \pm 0.17$ ,  $p=0.033$ ). BNP blood concentrations statistically significantly increased the day after the first course [80.95 (IQR 66.43-108.30) vs. 21.35 (IQR 9.0-45.1) pg/ml,  $p<0.001$ ] and were significantly increased the day after each course, three weeks after the end of chemotherapy ( $p<0.05$ ). No significant Gal-3 changes were found. Patients over 65 years, compared with the youngest, had significantly higher TnI, BNP, Gal-3 blood concentrations before the second chemotherapy course [4.4 (IQR 3.7-7.0) vs. 1.9 (IQR 1.4-2.6) ng/l,  $p=0.001$ ; 69.5 (IQR 40.6-87.2) vs. 20.7 (IQR 11.8-36.7) pg/ml,  $p=0.001$ ; 18.6 (IQR 11.3-14.8) vs. 13.8 (IQR 13.0-21.2) ng/ml,  $p=0.016$ , respectively].

**Conclusions.** TnI, CK-MB, BNP, but not Gal-3 concentrations rise early, already before the second anthracycline containing chemotherapy course. It is necessary to clarify predictive role of the findings for the long-term prognosis.

### 3. ECHOCARDIOGRAPHIC DIAGNOSTIC METHODS FOR EARLY DIAGNOSIS OF CHEMOTHERAPY INDUCED MYOCARDIAL INJURY

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**Background.** As a result of chemotherapy induced myocardial damage heart failure may develop, echocardiographic monitoring is important before the start of chemotherapy, during and after completion.

**Purpose.** To detect early echocardiographic changes, suggestive of myocardial damage in patients receiving anthracycline based chemotherapy to predict and timely prevent development of heart failure.

**Materials and methods.** First-time oncological patients with indications to anthracycline based chemotherapy, at least 3 courses, and no initial echocardiographic abnormalities were enrolled. Transthoracic echocardiography using supplemented standard protocol performed before the start of chemotherapy, after the first and fourth courses, three weeks, three and six months after the end of chemotherapy. Global longitudinal myocardial deformation of the left ventricle (LV) was analysed using PHILIPS QLAB software (global longitudinal strain- GLS) and mitral valve (MV) ring plane systolic excursion (MAPSE).

**Results.** 38 patients enrolled (23 completed chemotherapy, 13 continue, 2 excluded after the second course because of chemotherapy change). Compared with baseline, heart chamber dimensions statistically significantly enlarged after the first course of chemotherapy: left atrial volume index (LAVI),  $20.86 \pm 5.98$  vs.  $22.63 \pm 6.07$  ml/m<sup>2</sup> ( $p < 0.001$ ); right atrial area 11.0 (IQR 10.0-13.0) vs. 12.0 (IQR 11.0-13.3) cm<sup>2</sup> ( $p < 0.001$ ); end diastolic diameter of LV 42.0 (IQR 39.5-48.0) vs. 44.0 (IQR 42.0-48.3) mm ( $p < 0.001$ ); basal diameter of right ventricle (RV) 29.0 (IQR 27.0-31.0) vs. 30.0 (IQR 28.8-32.0) mm ( $p = 0.001$ ). Global longitudinal deformation of LV, measured by both methods, significantly decreased after the first chemotherapy dose administration [ $23.0$  (IQR 21.5-25.0) vs.  $22.0$  (IQR 21.0-24.0)%,  $p < 0.001$ ;  $22.81 \pm 2.03$  vs.  $21.97 \pm 1.93$ %,  $p = 0.002$ ] and remained decreased on every subsequent visit ( $p < 0.05$ ). The MV ring peak systolic velocity ( $s'$ ) and tricuspid valve (TV) ring plane systolic excursion (TAPSE) statistically significantly decreased only three months after the end of chemotherapy ( $10.26 \pm 1.55$  vs.  $9.15 \pm 1.92$  cm/s,  $p = 0.028$ ;  $25.0$  (IQR 20.5-30.0) vs.  $20.0$  (IQR 18.75-26.25) mm,  $p = 0.036$ ). RV systolic pressure (RVSP) considerably increased after the first course of chemotherapy [ $25.0$  (IQR 20.0-30.0) vs.  $30.0$  (IQR 20.0-30.0) mmHg,  $p = 0.004$ ] and remained statistically significantly higher three months after the end of chemotherapy. Patients receiving anthracycline dose  $> 300$  mg/m<sup>2</sup>, after the fourth course of chemotherapy showed significantly lower LV ejection fraction [ $63.5$  (IQR 57.7-66.8) vs.  $68.5$  (IQR 64.3-69.8)%,  $p = 0.048$ ] and significantly extended the LV isovolumetric relaxation time [ $95.0$  (IQR 86.8-104.3) vs.  $68.5$  (IQR 48.5-89.3) ms,  $p = 0.026$ ].

**Conclusions.** Early echocardiographic changes are detected after the first anthracycline containing chemotherapy course. LV myocardial deformation analysis, determining GLS or using MAPSE, is essential for early myocardial injury diagnosis.

#### 4. CHARACTERISTICS OF PROBANDS AND RELATIVES INCLUDED IN THE LATVIAN REGISTRY OF FAMILIAL HYPERCHOLESTEROLEMIA

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**Background.** Familial hypercholesterolemia (FH) is an autosomal dominant disorder with a prevalence of 1:250, and it leads to 20-fold increased risk of premature cardiovascular disease.

**Purpose.** To overview characteristics of individuals included in the Latvian Registry of Familial Hypercholesterolemia (LRFH), that was founded in February 2015.

**Materials and methods.** In patients referred from physicians and self-referred individuals diagnosis of FH was evaluated according to Dutch Lipid Clinic Network (DLCN) criteria. Cascade screening of the 1st degree relatives using age and gender specific percentiles of LDL-C was performed in cases of definite and probable FH. Presence of atherosclerosis was evaluated using MS CT or invasive coronary angiography and ultrasound of brachiocephalic arteries.

**Results.** Two hundred and eight adult patients were included in LRFH by January 2017. Majority (n=165, 79%) were index cases, of whom 40 (24%) had definite, 33 (20%) probable and 66 (40%) possible FH. In cascade screening of eligible relatives LDL-C above 95<sup>th</sup> percentile was found in 26 of 43 relatives (60%). Thus, altogether 99 patients were diagnosed with clinical FH (mean age 54.9±10.8 years in probands and 41.2±18.5 in first-degree relatives).

Mean (SD) highest-ever LDL-C was 7.3±1.6 mmol/l and 6.1±1.2 mmol/l in index cases and relatives, respectively. At the time of inclusion mean LDL-C was 5.3±2.2 mmol/l and 5.8±1.3 mmol/l in index cases and relatives, respectively. Only 50 probands (69%, mean LDL-C at inclusion 4.5±1.9 mmol/l) and 5 relatives (18%, mean LDL-C at inclusion 6.3±1.1 mmol/l) were on lipid lowering therapy, and treatment goal was reached in 7 (10%) probands and none of relatives at inclusion.

Forty seven of 73 (64%) FH probands and 8 of 26 (31%) relatives had known premature atherosclerotic disease: 19 (40%) cases of coronary artery disease, 14 (30%) of brachiocephalic artery disease and 14 (30%) had both localisations in probands, and 3 (37%), 4 (50%) and 1 (13%), respectively, in relatives.

**Conclusions.** During the first two years approximately 1.3% of estimated 8000 FH patients in Latvia have been identified at the LRFH. At the time of inclusion most patients were diagnosed belatedly, many had premature CVD and had not been managed appropriately. There is a major need to further develop LRFH.

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## 5. EFFECTS OF ROSUVASTATIN ON PULSE WAVE VELOCITY AT ONE MONTH OF TREATMENT

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**Background.** Arterial stiffness and pulse wave velocity (PWV) is an independent non-invasive indicator of cardiovascular morbidity and mortality. Statins are lipid-lowering agents with described other pleiotropic effects. Limited data are available on association between arterial stiffness and statin treatment.

**Purpose.** To evaluate changes in pulse-wave velocity and central blood pressure parameters in high-risk patients with hypercholesterolemia treated with rosuvastatin.

**Materials and methods.** This is an ongoing open-label, one-center prospective study. Non-hypertensive patients with hypercholesterolemia matching high or very high cardiovascular risk criteria were included in the study. Any blood-pressure lowering agent was an exclusion criterion. All patients are scheduled to receive daily treatment with rosuvastatin 40 mg for 12 months. Here we report the interim analysis of the follow-up at 1 week (V2) and 1 month (V3). Serological markers, central and peripheral arterial pulse velocity were measured and PWV levels assessed at baseline and following. Measurements of PWV and pulse wave analysis were performed with Mobil-O-Graph monitor.

**Results.** Fifteen patients had completed the study per protocol up to one month. Respective PWV at V2 and V3 was 8.160 m/s and 8.157, compared to 8.203 at baseline (p values 0.439 and 0.857, respectively). No significant changes in cSBP (central systolic blood pressure) (from 110.93±7.50 to 108.73±5.43, mmHg, p=0.407), cDBP (central diastolic blood pressure) (from 81.13±6.81 to 79.47±4.84, mmHg, p=0.406), augmentation pressure (p=0.650), total vascular resistance (p=0.526) were observed during one month. Total cholesterol levels (p<0.001) and low-density lipoprotein cholesterol levels (p<0.001) decreased significantly, but no other parameters changed on biochemistry or full blood count.

**Conclusions.** The interim analysis found no significant reduction of arterial stiffness, cSBP or cDBP with rosuvastatin early after onset of treatment up to one month, although an absolute reduction in the three parameters was observed. The study should be continued with a longer follow up, up to 12 months in a larger group of patients.

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## 6. EVALUATION OF DIETARY HABITS OF PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN LATVIA ACCORDING TO PREDIMED SCORE

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**Background.** The most acknowledged diet to reduce cardiovascular risk is Mediterranean diet as shown in PREDIMED (*Prevención con Dieta Mediterránea*) study. Until now dietary habits of FH patients in Latvia have not been studied.

**Purpose.** To evaluate dietary habits of FH patients of the Latvian Registry of Familial Hypercholesterolemia (LRFH) founded in January 2015.

**Materials and methods.** Patients with FH (66 index cases and 24 first degree relatives) from LRFH were interviewed according to PREDIMED questionnaire (score range 0 to 14) at inclusion in the registry.

**Results.** The mean PREDIMED score was 5.8±2.6 points (6.0±2.6 in probands and 5.4±2.4 in relatives). The most compliant was the age group of 31-50 years with the mean PREDIMED score 6.4±3.1 points, in comparison to age group of 18-30 with 4.8±2.1 points and age group over 50 years with 5.7±2.4 points (Table).

Table. PREDIMED score in age groups

Age group	PREDIMED 0–5 (poor compliance)	PREDIMED 5–10 (medium compliance)	PREDIMED 11–14 (high compliance)
18-30 years	81% (n=9)	19% (n=2)	0
31-50 years	33% (n=10)	57% (n=17)	10% (n=3)
≥ 51 years	48% (n=28)	52% (n=30)	0

The most observed principle of Mediterranean diet in the age group from 18 to 30 was usage of olive oil as the main fat source and restriction of fatty dairy products (observed by 36% of this group). The least followed principles were sufficient consumption of fruits, nuts and fish (9%, 9% and 0%, respectively).

In the age group from 31 to 50, the most common healthy habits were fruit consumption and restriction of sweets and sugary drinks (47%), followed by optimal fish consumption (27%). Legume consumption was the least frequent of all habits (10%). Patients over 50 showed the best results in preferable choice of meat (fowl over pork) and optimal consumption of fruit, vegetables and olive oil (66%, 52%, 40% and 40%, respectively).

**Conclusion.** The results reveal poor dietary habits of FH patients, especially in younger age. The findings emphasize need for more focused dietary advice in these high-risk patients, especially in younger generation, as the lifestyle is an important part of primary cardiovascular prevention.

## 7. *KCNE1* VARIATIONS RS1805127 AND 1892593 ASSOCIATION WITH A RISK OF DEVELOPMENT OF ATRIAL FIBRILLATION

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**Background.** Atrial fibrillation (AFib) is the most common type of arrhythmia. It is known that ion channels (electrical remodelling) and left atrial volume (structural remodelling) play an important role in the development of AFib, but the etiopathogenesis of AFib is still an open issue. *KCNE1* gene encodes potassium ion channel. *KCNE1* gene allelic variants rs1892593 and rs1805127 were selected for the study.

**Purpose.** The aim of this study was to investigate the association between *KCNE1* allelic variants and the risk of a development of AFib.

**Materials and methods.** There were 72 patients with the persistent non-valvular AFib included in the case-control study. Patients with pulmonary, thyroid, systemic inflammatory and coronary artery diseases, cardiomyopathy and diabetes were excluded from the study. Data about 503 control subjects of European origin were obtained from The 1000 genome project. The age of onset of AFib and left atrial volume index (LAVI) were available for the analysis. DNA isolation was performed by the phenol-chloroform method from the venous blood. Genotyping for rs1892593 and rs1805127 was performed by the PCR-RFLP assay. SPSSv22 software was used for statistical analysis.

**Results.** Genotypes AA and GA for variant rs1805127 are associated with decreased risk of developing AFib but the association did not reach level of statistical significance (OR=0.6, 95%CI=0.376-1,014; p=0.055). Genotype frequencies for rs1892593 did not differ between case and control groups. Further analysis was performed only for rs1805127. The age of onset of AFib did not differ between rs1805127 genotypes (GG vs. GA vs. AA = 56.7±12.6 vs. 60.9±11.2 vs. 58.9±7.9 years, p=0.449). LAVI value varied between different genotypes – GG=40.2±10 ml/m<sup>2</sup>, GA=41.4±6.8 ml/m<sup>2</sup>, AA=27.9±8.1 ml/m<sup>2</sup>, but statistically significant result was found only in dominant model of inheritance (GG+GA vs. AA = 40.8±1.5 ml/m<sup>2</sup> vs. 27.9±4.7 ml/m<sup>2</sup>, p=0.022).

### Conclusions

1. *KCNE1* gene variant rs1805127 is associated with risk of AFib development.
2. Association of *KCNE1* variant rs1892593 and risk of AFib was not observed in our study.
3. Genotypes GG and GA at rs1805127 are associated with greater LAVI.
4. Further studies with a control group of Latvian origin are necessary to assess the influence of the *KCNE1* gene variants on AFib in the Latvian population.

# INTERNAL MEDICINE, CARDIOLOGY AND INFECTIOUS DISEASE

## PART II: INTERNAL MEDICINE AND INFECTIOUS DISEASE

### 1. SIGNIFICANT ASSOCIATION OF FOUR SNPS WITH LOWER AGE AT DIAGNOSIS IN PATIENTS WITH GROWTH HORMONE SECRETING PITUITARY ADENOMA

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**Introduction.** Pituitary adenoma (PA) is the most common type of human intracranial neoplasms. Although mostly benign, these tumors significantly increase mortality and morbidity for the patients. Approximately one person out of 1000 has clinically significant PA during lifetime. The third most common type of PA is somatotropinomas (~13% of all clinically significant PA). Several genetic and epigenetic factors that influence development and characteristics of PAs have been described in the literature.

**Purpose.** Our main objective was to investigate the involvement of genes in the development and characteristics of PAs in a patient group from Latvia.

**Materials and methods.** 66 patients diagnosed with somatotroph adenoma were included in the study. Their blood samples were collected, leucocyte derived DNA extracted via phenol-chloroform extraction method and 96 tagging single nucleotide polymorphisms (SNP) from seven genes (AIP, DRD2, GNAS, MEN1, PRKAR1A, SSTR2 and SSTR5) genotyped using Illumina BeadXpress GoldenGate system. Data analysis was performed, using Illumina Genome Studio v2010.3 for genotype calling and quality control. Plink v1.07 was used for linear regression analysis.

**Results.** Four SNPs in three genes showed significant association with younger age at somatotroph PA diagnosis (Table 1).

Table 1. Significant SNP associations with age at PA diagnosis

CHR	GENE	SNP ID	BETA	P
11	MEN1	rs607969	-19,1	0,007
16	SSTR5	rs34037914	-9,2	0,009
11	MEN1	rs624975	-9,1	0,009
11	DRD2	rs1800497	-8,6	0,013

The most pronounced effect was shown by rare variant rs607969 in MEN1 gene, whose carriers were diagnosed with somatotroph PA 19 years earlier on average than individuals homozygous for wild type allele. The three other associated SNPs displayed similar effect on age at diagnosis decreasing it by about 9 years per allele on average. The influence



of these risk alleles seems to be cumulative – the correlation coefficient between age at diagnosis and number of risk alleles carried by individual is -0,61. Implying that carriers of more risk alleles are younger at the time of somatotroph PA diagnosis.

**Conclusions.** Four SNPs at three genes showed marked and statistically significant influence on younger age at diagnosis for somatotroph PA patients. It remains to be discovered whether this correlation is due to earlier development of somatotroph PA, earlier onset of clinically significant symptoms or due to combination of these and/or other factors.

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## 2. HEPATITIS C PREVALENCE IN MEDICAL PERSONNEL AT INTENSIVE CARE UNITS IN LATVIA

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**Background.** In Europe Latvia is considered as one of the countries with high hepatitis C (HCV) prevalence with one of the highest number of newly diagnosed cases in Europe. In the population study in Latvia the prevalence of HCV antibodies (anti-HCV) was 2.4%, the prevalence of HCV ribonucleic acid (HCV-RNA) was 1.7%. Medical professionals are considered a risk group for C hepatitis infection. The prevalence of anti-HCV and HCV-RNS among medical personnel in Latvia has never been studied before.

**Purpose.** The objective of the study was to calculate HCV prevalence in medical personnel at Intensive Care Units in Latvia and compare that with population data.

**Materials and methods.** In total, 777 health care workers at 26 Latvian hospitals with 35 intensive care units were tested for anti-HCV with 4<sup>th</sup> generation ELISA test. Anti-HCV positive results were tested for HCV-RNA by real time polymerase chain reaction. The research participants also filled in a questionnaire that included questions about accidents at work, performed post-exposure preventive measures and previous C hepatitis testing. The results acquired were summarised and statistical data processing was performed.

**Results.** Out of the 777 subjects tested, 18 were positive for anti-HCV (2.3%; 95% CI 1.3 to 3.4%), HCV-RNA test were positive in 9 subjects (1.2%; 95% CI 0.4 to 1.9%). 464 of 777 (59.7%) research participants indicated accidents at work with potential exposure to hepatitis C. 313 out of 464 (67.5%) participants applied local preventive techniques as the only measure for C hepatitis infection prevention; 76 (16.4%) of the research participants performed wound washing, tested both the source of exposure and the injured employee for hepatitis C. 471 out of 777 (60.6%) research participants had previously been tested for anti-HCV, 254 (32.7%) had not been tested.

**Conclusions.** The anti-HCV prevalence among medical personnel at intensive care units in Latvia is similar to that in the population and corresponds to high prevalence. The prevalence of HCV-RNS among health care workers is slightly lower than observed in the population and may contribute to the post-exposure procedures and the treatment of hepatitis C infection. Post-exposure interventions are limited with local preventive techniques for the majority of participants and only small portion carry out all necessary post-exposure measures. Approximately one third of medical personnel included in study have never been tested for hepatitis C, despite high risk for exposure at work.

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### 3. THE VALUE OF AN INVENTORY IN TRANSFER OF KNOWLEDGE AND ORGANIZATION BETWEEN SWEDEN AND THE BALTIC REGION REGARDING FOOT COMPLICATIONS IN PATIENTS WITH DIABETES MELLITUS

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**Background.** A request from the Baltic countries to Diabetic Foot Center Karolinska, DFCK was made in order to establish a Center of Excellence for multidisciplinary diabetic foot care.

**Purpose.** To evaluate the importance of an Inventory was evaluated in the transfer of organization and best clinical practice for patients with diabetes mellitus and foot complications.

**Material and methods.** An Inventory, based on an inventory list and an inventory session, of the current structural capital and requirements for a successful implementation was accomplished by the project partners. The inventory list covered the organizational and technical facilities at respective future centre. With the use of a representative diabetic foot case the different roles of the Swedish multidisciplinary team specialists was exemplified and further discussed with the local audience. The aim of this discussion was to create a positive atmosphere that would encourage and stimulate multidisciplinary organizational work and in the patient situation clearly indicate how valuable the improved interaction between the team members of a multidisciplinary team could become if the communication pathways are shortened. Any suboptimal competence of the participating specialists, i.e. diabetological, vascular surgical, orthopedic surgical and in infectious disease aspects as well as the orthopedic engineering and podiatry/chiropodist resources in the three countries could then be estimated. The Inventory also includes evaluation of possible quality control markers.

**Results.** In summary, we find the Inventory is an essential instrument to evaluate need of sufficient technical facilities and medical competence together with organizational structure. We found sufficient technical facilities and adequate competence but suboptimal organizational structure in all three Baltic countries.

A general deficiency in quality control markers for evaluation of the management and organizational change was observed.

**Conclusions.** We find that the Inventory is essential for any implementation of organization and best clinical practice management of patient with diabetes mellitus and foot complication.

The Inventory should then be followed by an implantation phase including, primary, the establishment of a Center of excellence in each country, secondly, assisting in the spread of the management to local hospitals and to the primary care and to the patient. The implementation also includes establishment of a quality register and initiation of a Health Economical analysis.

## 4. BASELINE DATA OF DIABETIC FOOT AMPUTATIONS IN LITHUANIA

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**Background.** Diabetes mellitus is the leading cause of all non-traumatic amputations. Proximal amputations reduce life-quality and are a substantial cost for the society.

**Purpose.** The objective of the study was to analyze the data on diabetic foot amputations in Kaunas county during the period 2012–2013.

**Materials and methods.** The retrospective study performed. The data on amputations of lower extremities was collected from records of operating theatres and pathology departments of hospitals in Kaunas county. The diagnosis of diabetes was based on ICD-10 code of E1\_.\_ and the presence of hypoglycaemic medications in medical documentation. The amputations were divided into proximal (above the ankle) and distal (part of the foot). Reamputation in the same year was considered as one case. If reamputation was performed in the following year, it was considered as a new case. The amputation of the opposite leg was treated as separate case.

**Results.** 533 amputations were performed. Almost two thirds of amputations were performed on males – 327 (61.35%) vs. 206 (38.65%) females. The distribution of proximal diabetic amputations by gender: 60 males (55.05%), 49 females (44.95%). Mean age at all amputations – 69.41±14.89 years. Mean age at proximal diabetic amputation – 67.71±12.05 years. More than one third of amputations – 195 (36.59%) were performed for persons at age <65 years vs. 338 (63.41%) ≥65 years. Distribution by age in proximal diabetic amputations: 42 (38.53%) at <65 years and 67 (61.47%) and at ≥65 years.

Table 1. Distribution by type of amputations

	2012 year		2013 year		Total
	Proximal	Distal	Proximal	Distal	
Non diabetic amputations	149	42	152	31	374
Diabetic amputations	59	26	50	24	159
Total	208	68	202	55	533

**Conclusions.** Every fourth proximal amputation was performed on a diabetic patient. High rate of proximal amputations against distal amputations could be related to abandoned personal health issues in minor stages or lack of relevance of data of distal amputations. Relevance of data related to distal amputations should be reconfirmed.

**Acknowledgements.** We are grateful for hospitals of Kaunas county for cooperation in this study.

## 5. PSORIATIC ARTHRITIS SUBCLINICAL DETECTION IN PATIENTS WITH PSORIATIC NAIL DISEASE

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**Background.** It has already been proved that inflammation of the enthesis ("enthesis organ") is the primary lesion of psoriatic arthritis. In clinical practice, nail psoriasis is more frequently found in psoriatic arthritis than psoriatic involvement of the skin and is an independent predictor of the onset of this chronic inflammatory rheumatism without any clinical or laboratory findings. Over the last ten years, ultrasonography has become an important imaging modality in rheumatology and dermatology in peripheral psoriatic arthritis early detection, because of its ability to reveal subclinical enthesitis, long before the appearance of radiographic anomalies and patient complaints.

**Purpose.** To find correlation between psoriatic onychopathy and psoriatic arthritis subclinical manifestations.

**Materials and methods.** The pilot prospective study included 32 patients: 7 patients with nail psoriasis (clinically and laboratory confirmed) with no history of previous rheumatology disease, 15 patients with psoriasis without onychopathy with no history of previous rheumatology disease and 10 control (healthy) persons. Sonographic Evaluation of Plantar aponeurosis, Achilles tendon, proximal and distal patellar ligament, quadriceps tendon, triceps tendon entheses on both extremities was performed. Twelve entheses were scored according to the Madrid Sonographic Enthesis Index (MASEI) in both groups using ultrasound. Laboratory rheumatology tests involved: CRO, RF, HLA-B27. Clinically, all patients were evaluated using psoriatic arthritis assessment survey.

**Results.** Median age of patients was 32 years (Range=18, IQR=6). Two entesites were diagnosed in two patients in psoriatic onychopathy group, both in the Achilles tendon with hypoechoic and thickened enthesis. Fisher's exact test show correlation between psoriatic onychopathy and enthesitis ( $p<0,05$ ), although there is no correlation between psoriasis and enthesitis ( $p=1$ ). No correlation between laboratory tests and enthesitis, as well as between clinical evaluation and enthesitis was observed ( $p>0,05$ ).

**Conclusion.** Ultrasound could be valuable diagnostic tool for subclinical detecton of enthesitis in patients with psoriatic onychopathy, which is proved to be predisposing factor of psoriatic arthritis.

## 6. ASSESSMENT OF QUALITY OF LIFE IN PATIENTS WITH SENSITIVE SKIN

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**Background.** Sensitive skin is a clinical condition that is observed in all industrialized countries, with almost the same spread in America and Eurasia – 68 and 64% [Farage & Maibach; 2010] and is mainly manifested with different intensity of subjective indications, such as burning and soreness, as a response to triggers like wind, heat, dryness, air condition, psycho-emotional stress, hormonal disbalance, as well as too frequent and/or improper skin care, which do not cause anything under normal circumstances.

Pathophysiological mechanism unfortunately is still not completely known in the scientific field. Skin barrier function changes and neurogenic inflammation is most frequent described and investigated field.

**Purpose.** To evaluate how sensitive skin effect quality of life of the patient.

**Materials and methods.** The prospective study was implemented in Dermaclinic Riga, Latvia, as well as via internet. “Skin sensitivity scale” (SSS-14), “Dermatology Life Quality Index” (DLQI) questionnaire were used. A questionnaire was also used with an aim to evaluate the patients’ life history, 121 both gender patients were analysed. Statistical data processing was carried out using SPSS 22 version.

**Results.** Both SSS-14 scale and DLQI questionnaires internal consistency was good (Cronbach’s  $\alpha > 0.8$ ).

Regarding the feelings mentioned in SSS-14 scale, the majority of patients (38.8%) measured in range of 10 to 20 points, with the average skin irritation among all respondents – 2.71 pt, without statistically significant differences between the gender (Kruskal-Wallis test;  $p > 0.05$ ). Majority of patients (53.7%), which were measured, admit feelings as periodic and 54.5% of the respondents associate them with the seasonality (autumn, winter period) stating as the main connection (89.4%) that the symptoms are rising or worsen in winter, but improve or disappear in summer. Most of the patients (89.2%) have no or little impact of skin condition on the quality of their life.

A medium positive correlation between amount of points of SSS-14 or sensitive skin and quality of life ( $r_s = 0.593$ ,  $p < 0.01$ , Kolmogorov-Smirnov test) showed, which proved the negative effect of increased sensitivity of the skin on quality of life.

**Consequence.** Sensitive skin is an important clinical condition that increases rapidly with a negative impact on quality of life [Laurent Misery; 2014]. Undiagnosed sensitive skin could launch a number of events. Most common are development of allergy, neurogenic inflammation, a higher predisposition to certain dermatoses and other changes reducing the quality of life [J. Escalas-Taberner, 2011; Annick Pons-Guiraud, 2012; Balázs I Tóth, 2014].

## 7. COMPARISON BETWEEN UNILATERAL AND BILATERAL OBSTRUCTION OF LACRIMAL DRAINAGE SYSTEM AND THE RISK FACTORS IN PATIENTS WITH EPIPHORA

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**Introduction.** Epiphora or tearing is a very common symptom, and is becoming even more common due to general aging of population. It is caused by disbalance between tear production and drainage. The most common reason, however, is poor drainage because of obstruction of lacrimal drainage system (LDS), which may be idiopathic, or may develop due to some risk factors.

**Purpose.** The aim of the study is to determine the frequency of unilateral and bilateral obstruction of LDS in patients with epiphora, and assess the risk factors of obstruction and their correlation with bilateral and unilateral obstruction.

**Materials and methods.** In retrospective study we analyzed dacryocystographic CT pictures of 95 patients with epiphora of Pauls Stradins Clinical University Hospital, taken within the period from March 2012 till January 2016. Associated findings of LDS obstruction were recorded: dacryocystitis, narrow bony nasolacrimal canal, malignancy, facial bone fracture, surgery, dacryoliths and sinusitis.

**Results.** Of 95 patients included 79 (83,2%) of the patients examined were females with mean age  $55,6 \pm 16,4$ . Obstruction was seen in 87 patients (91,6%), from whom 63 (66,3%) had unilateral obstruction. Of 87 patients with obstruction 32 (36,8%) and of 8 patients without obstruction 3 (37,5%) had at least one risk factor. Sinusitis was statistically significant more frequently found with bilateral (N8) compared to patients with unilateral (N7) obstruction (53,3% vs. 46,7%;  $p=0,014$ ). Bilateral obstruction was more frequent in patients with increase in age ( $r = 0,212$ ;  $p = 0,049$ ). No statistically significant correlation was found for other risk factors in relation to bilateral or unilateral obstruction.

**Conclusion.** Epiphora mostly is caused by unilateral obstruction, which, in majority of cases, is idiopathic or without any obvious reason in CT. Sinusitis from other different risk factors may facilitate bilateral obstruction. Increased age statistically significantly correlated with bilateral obstruction. However, the unilateral obstruction is more often observed in different age groups.

# GASTROENTEROLOGY, HEPATOLOGY AND GASTROINTESTINAL ONCOLOGY

## PART I

### 1. ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER – CASE REPORT

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**Background.** Gastric cancer remains an important healthcare problem. The 5-year survival in cases of gastric cancer is strongly related to the stage of the disease at diagnosis and could reach 95–96 %, if gastric cancer is diagnosed while confined to the inner lining of the stomach wall as an early gastric cancer (EGC). Endoscopic submucosal dissection (ESD) is a technique of endoscopic resection that allows for en bloc removal of EGC.

**Patient/Case report.** A 47 year old man was referred to an index upper endoscopy in 2011. Gastric biopsies were performed in antrum, incisura and corpus according to the updated Sydney classification. The histopathological examination revealed chronic atrophic gastritis and intestinal metaplasia (IM): Operative Link on Gastritis Assessment (OLGA) I and Operative Link for Gastric Intestinal Metaplasia (OLGIM) III gastritis stage, *H.pylori* positive. The patient has a family history of gastric cancer: mother at the age of 63, and mother's brother at the age of 50. *H.pylori* eradication treatment was performed. The next follow-up endoscopy was performed in 05/2015 revealing low-grade dysplasia in the antrum and incisura, *H.pylori* negative. The following upper endoscopy in 01/2016 showed a flat lesion (up to 7mm, 0-IIa-b Paris classification) in the lower corpus of the stomach and the histopathological examination confirmed high-grade dysplasia, suspicious malignant. The next follow-up gastroscopy (04/2016) with repeated biopsy from the lesion confirmed gastric adenocarcinoma G1. 2.05.2016 ESD was performed removing the gastric cancer en bloc with free lateral margins. The histopathological examinations confirmed gastric adenocarcinoma intestinal type (Lauren) pT1aNxM0.R0. The follow up gastroscopies (6.05.2016., 3.08.2016. and 15.12.2016.) showed post-ESD scar, no cancer recurrence.

**Conclusions.** Intestinal-type gastric adenocarcinoma arises through a multistep process (triggered by *H.pylori* infection) starting with chronic gastritis, progressing through stages of atrophy, IM, dysplasia and, finally, carcinoma.

As an EGC has no any typical clinical signs or symptoms, it could be prevented by detecting gastric precancerous conditions/lesions and identifying those individuals at high-risk of progressing to cancer for the follow-up.



## 2. COMPARISON OF OVERALL TEST POSITIVITY AND GENDER DIFFERENCES OF FAECAL IMMUNOCHEMICAL TEST RESULTS

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**Background.** Faecal immunochemical blood tests (FITs) are the recommended tests for colorectal cancer screening, yet the standardization of the tests, including the cut-off values and gender differences in test performance still remains an open issue.

**Purpose.** The objective is to compare the positivity between two FITs with identical cut-off values for gender subgroups.

**Materials and methods.** Within the pilot-study conducted in Latvia two target groups aged 50–74 years were offered FIT testing; 4899 individuals were offered FOB Gold (Sentinel Diagnostics, Milan, Italy), but 4871 – OC-Sensor (*Eiken Chemical Co.*, Tokyo, Japan) tests.

For the initial study purpose, a cut-off for test-positivity of 50 ng/mL was used for both tests. To allow comparisons between the study arms, the cut-off units initially expressed in ng/mL were converted to the currently recommended units, i.e. µg/g. The following conversion factor, which reflect the collection device sample mass and buffer volume, were used: 0.20 for OC-Sensor, and 0.17 for FOB Gold. Based on the converted units, further analysis considered a positive test result >10 µg/g was applied. For comparing OC-Sensor and FOB Gold test-systems the following cut-off concentrations were used: 10, 15, 20, 25, 30, 35 and 40 µg/g.

**Results.** The overall positive test rate was substantially higher ( $p < 0.001$ ) for FOB Gold compared to OC-Sensor at all identical cut-off concentrations. The proportion of test-positivity for both tests was higher in men; at the cut-off 10 µg/g the test positivity was 16.7% (CI: 14.3-19.5) for men, and 10.5% (CI: 8.9-12.2) for women with FOB Gold, but 11.4% (CI: 9.4-13.8) and 6.6% (CI: 5.5-8.0) with OC-Sensor, respectively ( $p < 0.001$  for both tests). When comparing the differences between the two tests, the positivity of FOB Gold was higher for all the cut-off concentrations in women, while for men this difference was present only at lower cut-offs (10, 15, 20 µg/g).

Test	FOB Gold							OC-Sensor						
	10	15	20	25	30	35	40	10	15	20	25	30	35	40
<b>All participants</b>	12.8*	10.1*	8.7*	7.9*	7.0*	6.4*	6.0*	8.3	6.0	5.3	4.3	4.2	3.9	3.5
(95% CI)	(11.4-14.2)	(8.8-11.4)	(7.5-9.9)	(6.8-9.0)	(5.9-8.1)	(5.4-7.4)	(5.0-7.0)	(7.2-9.4)	(5.0-7.0)	(4.4-6.2)	(3.5-5.1)	(3.4-5.0)	(3.1-4.7)	(2.8-4.3)
<b>Men</b>	16.7*	13.5*	11.8*	10.6	9.5	8.5	8.0	11.4	8.9	8.3	7.0	6.6	6.1	5.6
(95% CI)	(14.3-19.5)	(11.2-16.1)	(9.7-14.2)	(8.6-13.0)	(7.7-11.8)	(6.7-10.7)	(6.3-10.1)	(9.4-13.8)	(7.1-11.1)	(6.6-10.4)	(5.5-7.0)	(5.1-8.6)	(4.7-8.0)	(4.3-7.5)
<b>Women</b>	10.5*	8.1*	7.0*	6.3*	5.6*	5.2*	4.9*	6.6	4.5	3.7	2.9	2.9	2.7	2.3
(95% CI)	(8.9-12.2)	(6.7-9.7)	(5.8-8.5)	(5.1-7.8)	(4.5-6.9)	(4.1-6.5)	(3.9-6.2)	(5.5-8.0)	(3.6-5.7)	(2.8-4.7)	(2.2-3.9)	(2.1-3.8)	(2.0-3.6)	(1.7-3.2)

\*  $p < 0.05$  FOB Gold versus OC-Sensor

**Conclusions.** Different quantitative FIT systems may report substantially different test positivity rates at identical cut-off concentrations and gender differences in test positivity, which should be taken into account when implementing the use of FIT in national screening programs.

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### 3. THE PREVALENCE OF ANTI-PARIETAL CELL AND ANTI-INTRINSIC FACTOR ANTIBODIES, PEPSINOGENS, GASTRIN-17 AND *H.PYLORI* INFECTION IN CORPUS-RESTRICTED GASTRITIS PATIENTS

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**Purpose.** The aim of the study was to detect the prevalence and values of anti-parietal cell antibodies (anti-PCA), intrinsic factor antibodies (anti-IFA), pepsinogen ratio (PGI/II), gastrin-17 (G-17) and *H.pylori* infection in corpus-restricted gastritis and control group patients.

**Methods.** We conducted a sub-group analysis of 1978 dyspeptic patients referred for endoscopy. 5 biopsies were analysed according to updated Sydney system, *H.pylori* presence was evaluated by Giemsa stain. ELISA was used to measure PGI/II, G-17 (Biohit, Oyj., Finland), anti-PCA and anti-IFA (Inova Diagnostics, USA) in plasma samples.

**Results.** 52 patients with corpus-restricted gastritis according morphology report were included in study group and 104 patients without gastric atrophy in control group. In the corpus-restricted gastritis group 52.9% and 81.3% patients were anti-PCA positive in the positive and negative *H.pylori* subgroups respectively, mean values 38.1 and 58 units; in control group 20% and 12.1% patients were anti-PCA positive in the positive and negative *H.pylori* subgroups respectively, mean values 13.2 and 8.5 units,  $p < 0.001$ .

In corpus-restricted gastritis group 5.9% and 18.8% patients were anti-IFA positive in positive and negative *H.pylori* subgroups, the mean values 12.7 and 15.5 units; in control group positive and negative *H.pylori* subgroups 0% and 1.9% patients were anti-IFA positive, the mean subgroup values 5.6 and 6 units,  $p = 0.119$  and  $p = 0.995$  respectively.

**Conclusions.** Increased anti-PCA levels were observed in a significant proportion of patients with corpus-restricted gastritis, values were higher in the *H.pylori* negative subgroup. Anti-IFA levels were increased in a small proportion of patients, however, no statistical significance between *H.pylori* positive and negative subgroups was observed.

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#### 4. THE PREVALENCE OF ANTI-PARIETAL CELL AND INTRINSIC FACTOR ANTIBODIES IN PATIENTS WITH GASTRIC ADENOCARCINOMA

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**Background.** Gastric atrophy and *H.pylori* infection are well-known risk factors of gastric adenocarcinoma, but the relevance of autoimmune gastritis in gastric adenocarcinoma development is not entirely clear.

**Methods.** We studied anti-parietal cell antibody (anti-PCA) and anti-intrinsic factor antibody (anti-IFA) levels and their associations with Pgl/PgII levels in Caucasian patients with morphologically confirmed gastric adenocarcinoma. Plasma levels of anti-PCA and anti-IFA were measured by ELISA (Inova Diagnostics, USA). The cut-off value for anti-PCA and anti-IFA was  $\geq 25$  units. Plasma levels of Pgl and PgII and *H.pylori* IgG were measured by ELISA (Biohit, Oyj., Finland). A cut-off value of Pgl/PgII  $< 3$  was used to detect gastric atrophy. The cut-off value for *H.pylori* IgG was  $\geq 30$  units.

**Results.** Altogether 229 patients (134 men, 95 women, median age 65, range: 35–86) with confirmed gastric adenocarcinoma from Riga East University Hospital in Latvia were included to the study. Positive autoantibody (either anti-PCA or anti-IFA or both) was found in 25 (9%), the positivity results in the subgroups are provided in the Table. Significantly higher prevalence was found in the group with pepsinogen values characteristic for gastric atrophy.

	<i>H.pylori</i> IgG	Pgl/PgII $\geq 3$	Pgl/PgII $< 3$	P-value (Pg subgroups)
Positive anti-PCA (n=24)	9 (38%)	8 (33%)	16 (67%)	0.0003
Positive anti-IFA (n=6)	1 (17%)	1 (17%)	5 (83%)	0.0134
Positive both (n=5)	0 (0%)	1 (20%)	4 (80%)	0.0368
Positive anti-PCA or anti-IFA or both (n=25)	10 (50%)	8 (32%)	17 (68%)	0.0002

**Conclusions.** Only a minority of patients with gastric cancer presented with positive test results suggesting the presence of autoimmune gastritis, positive autoantibodies were observed in 1 of 9 (25/229) patients. As expected, presence of autoantibodies was higher in atrophic gastritis group.

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## 5. COLORECTAL CANCER SCREENING PROGRAMME EVALUATION – EARLY INDICATORS IN THE CANCER REGISTRY

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**Background.** Colorectal cancer (CRC) screening programme was introduced in Latvia in 2009. The target group uptake rates increased from 6.9% in 2009 up to 10.6% in 2014. The objective of the screening programme is to detect the tumour as early as possible to reduce the colorectal cancer mortality. The potential impact of screening on mortality can take decades to show a full effect; however, early indicators appear in cancer statistics, such as increase of cancer incidence and changes in the stage distribution. Since 2012 screening detected cancer cases are linked to the Latvian cancer registry. In the context of cancer screening, cancer registry play an important role to reliably assess the effectiveness of the programme.

**Purpose.** The objective of the current study was to identify changes in CRC incidence trends and to detect changes in the colorectal cancer stage distribution using Latvian population-based cancer registry.

**Materials and methods.** The study included data obtained from the Latvian cancer registry. The sample included 20494 patients age 50 and older with diagnosed and histologically confirmed colorectal cancer in the period from 1993 to 2014. Incidence changes were detected with join point regression method using the National Cancer Institute program Joinpoint Software 4.3.1.0. Data processed using MS Excel 2010 and IBM SPSS 22.0 programs.

**Results.** Trend for CRC incidence rates significantly changed once in 1997, increasing by 6.8% annually for the years 1993–1997 and by 2.6% annually for the 16-year period of 1997 through 2014. Trends for CRC incidence rates in early stages significantly changed twice, in 2005 and in 2008. Annual percentage changes (APC) in the period 1993–2005 was 5.0% ( $p < 0.05$ ), with no significant changes in trend in 2005–2008. Since 2008 trend of APC is growing rapidly, 10.1% ( $p < 0.05$ ). Trend for CRC incidence rates in the cancer stage IV changed in 2011 decreasing by 4.8% annually. During 2012–2014 220 CRC cases in the cancer registry recorded as screening detected: 17.7% at the cancer stage 0–I; 32.7% stage II; 25.5% stage III; 19.5% stage IV and 4.5% unknown stage. Early stage proportion for the screening-detected cases and for the rest of cases in the cancer registry was significantly higher in 2012 and 2013 ( $p < 0.05$ ), but not for 2014.

**Conclusions.** Colorectal cancer incidence trend does not show any changes since introduction of screening programme; however, incidence trends for early cancer stages and changes in trend for stage IV may be an indicator related to the beginning of the screening programme. Although screening detected CRC cases at early stages are higher than the rest of the registry, it could not be an eligible indicator for performance of the screening programme.

## 6. ANTIMICROBIAL RESISTANCE IN *HELICOBACTER PYLORI* ISOLATED FROM GASTRIC BIOPSIES IN ADULT POPULATION IN LATVIA

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**Background.** *Helicobacter pylori* (*H.pylori*) is a helix-shaped bacteria adapted to live in the acidic environment of the human stomach. It is responsible for the development of peptic ulcer disease as well as atrophic gastritis and gastric cancer. *H.pylori* is defined as a definite carcinogen by IARC (International Agency for Research on Cancer). The current guidelines recommend selection of the *H.pylori* eradication regimen based on local resistance patterns to antibiotics, therefore local evaluation of the patterns is critically important.

**Purpose.** To evaluate the primary susceptibility of *H.pylori* isolated from antrum biopsies in adult population in Latvia to the most important antibiotics being used in eradication regimens.

**Method.** Asymptomatic persons aged 40–64 were invited to participate in prospective population based pilot project to detect biomarkers for atrophic gastritis screening (study period 2015–2016). One antral biopsy to be used for the culture was placed into freezing media. Primary cultivation from thawed and homogenized biopsy was made on selective *Pylori* agar plate (*bioMerieux, France*) incubated at 37 °C in a microaerophilic atmosphere. Antimicrobial susceptibility of obtained strains was determined by epsilometer test (E-test, *bioMerieux, France*) method to metronidazole (MZ), clarithromycin (CL), amoxicillin (AX), tetracycline (TC), rifampicin (RA) and levofloxacin (LX) according manufactures instructions and interpreted according EUCAST clinical breakpoint standard ([www.eucast.org](http://www.eucast.org), Version 6.0).

**Results.** *H.pylori* resistance rates of 103 obtained cultures were 38% (95% CI 28,6–48,3%) to metronidazole, 8% (95% CI 3,8–15,6%) to clarithromycin, 6% (95% CI 2,4–12,9%) to levofloxacin and 11% (95% CI 5,8–18,9%) to rifampicin. No resistance was observed to amoxicillin and tetracycline. All together 10 different resistance patterns were detected – 53% showed no resistance, 27% resistant only to MZ, 3% to MZ and CL, 2% to MZ, CL and LX, 4% to MZ and RA, 1% to MZ and LX, 2% to CL, 2% to LX and 7% to RA respectively.

**Conclusions.** *H.pylori* resistance to clarithromycin is still low allowing to continue using standard clarithromycin triple therapies as the treatment of choice. At the same time, *H.pylori* resistance to metronidazole is high. Despite the fact that levofloxacin has not been widely used in the country, resistance of *H.pylori* has been observed. The study for the first time provides the results on *H.pylori* susceptibility to levofloxacin and rifampicin.

**Acknowledgements/Funding.** The study was funded by the Latvian National Research Programme “Biomedicine for Public Health” (BIOMEDICINE) 2014–2017.

## 7. IS PEPSINOGEN SCREENING IN GENERAL CAUCASIAN POPULATION JUSTIFIED? RESULTS FROM A CROSS-SECTIONAL POPULATION STUDY IN LATVIA

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**Background.** The rationale for population-based screening for precancerous lesions by detecting pepsinogens remains controversial.

**Purpose.** Our aim was to analyse the endoscopy/pathology findings in subjects being investigated based on pepsinogen test results.

**Methods.** In a population-based study settings pepsinogen, the data from 3564 study subjects were available; those with decreased pepsinogens during the recruitment were invited to undergo upper endoscopy. Pepsinogen I and II was measured in plasma simultaneously from either the initial or the follow-up sample (taken before endoscopy) by a latex-agglutination test system (Eiken Chemical Co., Tokyo, Japan). Moderately decreased pepsinogen results were considered if PgI $\leq$ 70 ng/ml and Pgl/PgII $\leq$ 3, but severely decreased if PgI $\leq$ 30 ng/ml and Pgl/PgII $\leq$ 2; the remaining cases were considered to have normal levels. *H.pylori* was assessed serologically (Mikrogen Diagnostik, Neuried, Germany).

**Results.** Results from 259 individuals (31.7% men; median age 58 years, range 22–88) were available for the analysis. The median follow-up interval was 3.5 years (range 3–6 years). Two gastric cancer cases (0.8%) and 29 dysplasia cases (11.2%) were identified. Moderately decreased pepsinogens in the initial sample were found in 133 subjects (51.4%), severely decreased – in 57 cases (22.1%).

**Conclusions.** Pepsinogen detection could be useful, however, only the minority of individuals with decreased pepsinogens have advanced gastric mucosal lesions.

# GASTROENTEROLOGY AND GASTROINTESTINAL ONCOLOGY

## PART II

### 1. GASTRIC CANCER SCREENING QUESTIONNAIRE, FINAL RESULTS

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**Background.** Various clinical guidelines, including Kyoto global consensus are recommending particular steps, including ‘search-and-treat’ strategy for *H.pylori* to prevent gastric cancer (GC), however, little of this has been implemented in clinical practice.

**Purpose.** The aim of the study was to identify how many of these recommendations have penetrated the practice.

**Materials and methods.** A web-based questionnaire was developed and distributed globally via a number of international organizations and national professional societies. Questionnaire was available online for 5 months (October 2015 – February 2016) in three languages – English, Russian and German.

**Results.** Altogether 886 responses from 75 countries were received; of the responders 570 (64%) were men; mean age 47 years. There were 606 gastroenterologists and 65 epidemiologists among the responders. The majority were involved in cancer screening (66%), performing endoscopies (67%), and prescribing *H.pylori* eradication therapies (83%).

Altogether 79.8% of the responders disagreed that the burden of GC is a disappearing problem and is not requiring any active intervention. ‘Search-and-treat’ strategy in the responder’s country was considered appropriate by 44.4%, inappropriate – by 24.3%, but 31.3% of the responders were unsure. No difference between gastroenterologists (46.9% positive responses) and epidemiologists (45.5%) was revealed ( $p=0.84$ ).

Population-based screening for GC was considered appropriate in the respective home-country by 62.2%, in other areas, but not the home-country – by 27.6%, but inappropriate – by 10.2% of the respondents. Pepsinogen detection was considered an appropriate screening strategy by 26.1% of the responders, inappropriate – by 50.3%, but the remaining 23.6% considered it useful only in particular settings. No differences were



observed in the responses of gastroenterologists and epidemiologists. When asked about volatile marker testing in exhaled air, only 23.4% considered that this approach is readily applicable for GC screening purpose; the major reason for this response was insufficient evidence (53.3%). The attitude towards *H.pylori* vaccination was as follows: 4.6% of the responders were eager to start vaccination immediately, 55.9% were supporting vaccination, but considered that more data is required; 12.0% were negative, 27.6% did not have the opinion.

**Conclusions.** In general, the attitude of the specialists corresponds well to the guidelines, yet not always to the clinical practice, particularly in the case of 'search-and-treat' strategy. No substantial differences in the attitude were revealed between gastroenterologists and epidemiologists.

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## 2. ROLE OF DIETARY HABITS IN HELICOBACTER PYLORI INFECTION IN THE LATVIAN POPULATION

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**Purpose.** Determine whether dietary habits are associated with *H.pylori* infection risk in a high risk population.

**Materials and methods.** 3444 people ages 40–64, mean age 51,53±6,74 years, were randomly selected from the population of Latvia from 2012–2016 to complete a questionnaire on lifestyle and dietary habits and were then randomly divided into control and intervention groups. *H.pylori* serological testing (Biohit PLC, Test Kit) was performed for 1229 participants in the intervention group. All analyses were performed using SPSS version 22.0 and a P-value of 0.05 was considered to be statistically significant. Descriptive data are presented as the geometric mean (95%CI) for age, BMI, salt intake, spicy foods, dairy products, products high in protein and carbohydrate, as these variables are not subject to normal distribution, and as a percentage for categorical variables. Continuous variables were examined using analyses of variance and chi-square test for categorical variables. Quartiles were categorized across the scores of each dietary pattern based on the distribution of the scores for all the participants and used for further analyses. Factor analysis was used to identify dietary patterns. Relationships between quartile categories of dietary pattern scores and *H.pylori* infection status were examined using logistic regressions.

**Results.** In the intervention group, 840/1229 (68,3%) participants tested positive for *H. pylori* -417/840 (70,6%) men, 423/840 (66,3%) women. *H.pylori* seropositivity was significantly higher for participants who consumed spicy food (72,9% (255/350) in comparison to those who did not 66,4% (579/872), p=0,0283; consumed at least 200g of milk products per week 70,4% (503/714) in comparison to less – 65,2% (331/508), p=0,0502.

Participants within the highest quartile of high-carbohydrate food consumption frequency showed a multivariable-adjusted OR (95% CI) of 1.67 (1.28–2.18) for the prevalence of *H. pylori* infection compared with those in the lowest quartile. The multiple adjusted OR for scores of the extreme quartile of high-protein food consumption pattern was 0.74 (95% CI, 0.56–0.96).

The high-carbohydrate/processed sugar pattern was positively associated with the prevalence of *H. pylori* infection (*P* for trend < 0.001) after adjustment. The high-protein pattern was associated with a lower prevalence of *H. pylori* infection (*P* for trend = 0.03) after adjustment. The multiple adjusted OR for scores of the extreme quartile of

high-protein diet pattern was 0.74 (95% CI, 0.56–0.96). No significant association was observed between balanced diet pattern and *H. pylori* infection after adjustment.

**Conclusions.** This study demonstrated that a diet rich in carbohydrates and processed sugar was positively associated with the prevalence of *H. pylori* infection, while a diet characterized by high intake of meat products, fish, dairy products and poultry was associated with a reduction in the prevalence of *H. pylori* infection in the population of Latvia.

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### 3. THE ROLE OF *PNPLA3*, *RNF7*, *MERTK* AND *PCSK7* GENE POLYMORPHISMS IN THE DEVELOPMENT OF LIVER FIBROSIS AND CIRRHOSIS

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**Background.** Liver cirrhosis is the end stage of liver diseases, which significantly reduces life quality and expectancy in patients with chronic liver diseases. The natural course of liver diseases varies considerably between separate individuals. Genome-wide association studies (GWAS) revealed a link between the risk of developing liver fibrosis (LF) or liver cirrhosis (LC) and single nucleotide polymorphisms (SNPs) of *PNPLA3*, *RNF7*, *MERTK* and *PCSK7* genes.

**Purpose.** In this study we aimed to evaluate replicate GWAS results and evaluate associations between *PNPLA3* (C>G, rs738409), *RNF7* (A>C, rs16851720), *MERTK* (A>G, rs4374383), and *PCSK7* (C>G, rs236918) SNPs and LF or LC.

**Materials and methods.** The study included 317 individuals with LC, 154 individuals with LF and 498 healthy controls. The diagnosis and etiology of liver fibrosis and cirrhosis was confirmed by laboratory tests, clinical features, liver biopsy and radiological imaging. Liver fibrosis stage in the biopsy was assessed using METAVIR score. *PNPLA3*, *MERTK*, *PCSK7* and *RNF7* SNPs in all groups were detected using real-time PCR TaqMan® method. Statistical analysis were performed using PLINK: Whole genome data analysis toolset.

**Results.** Genotypes and alleles of *MERTK* and *PCSK7* SNPs were not associated with the risk of developing LF or LC. *RNF7* rs16851720 was associated with LC in recessive model comparing CC vs. AA + CA genotype (aOD: 0.26, CI: 0.09-0.81, p=0.020). *PNPLA3* SNP was linked with higher risk of developing LF (aOD: 1.65, CI: 1.22-2.23, p=0.001) and LC (aOD: 1.92, CI: 1.49-2.48, p=5.57\*10<sup>-7</sup>). *PNPLA3* rs738409 was associated with higher risk of developing LF and LC when comparing both dominant (aOD: 1.98, CI: 1.44-2.72, p=2.20\*10<sup>-5</sup>; aOD: 1.67, CI 1.14-2.43, p=0.008, respectively) and recessive (aOD: 3.94, CI: 2.03-7.67, p=5.16\*10<sup>-5</sup>; aOD: 3.02, CI: 1.45-6.28, p=0.003, respectively) inheritance models.

**Conclusions.** *PNPLA3* rs738409 and *RNF7* rs16851720 were associated with the risk of developing LF and LC and may contribute to progression to end stage liver disease. *MERTK* rs4374383 and *PCSK7* rs236918 SNPs were not linked with the risk of LF and LC.

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#### 4. TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN TREATMENT OF PORTAL HYPERTENSION – EXPERIENCE OF ONE CENTRE

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**Background.** Transjugular intrahepatic portosystemic shunt (TIPS) is an effective treatment modality for the life-threatening complications of portal hypertension (PH). However, the use of the procedure is limited by a high rate of post-procedural hepatic encephalopathy (HE) (10–55%) and early mortality (25–30%).

**Purpose.** The objective of the current study was to evaluate the efficacy of TIPS, rate of short-term complications and factors predicting patient survival after TIPS procedure.

**Materials and methods.** A retrospective analysis included 56 patients with refractory ascites/hydrothorax, recurrent variceal bleeding and Budd-Chiari syndrome who underwent TIPS procedure between 2002 and 2015 at the Department of Gastroenterology of Lithuanian University of Health Sciences Hospital. The efficacy of the procedure, rate of HE and stent dysfunction and mortality were evaluated 30 days after the procedure. Child-Pugh class, Model of end stage liver disease (MELD) score, serum bilirubin, creatinine, albumin, and international randomized ratio (INR) before TIPS (pre-TIPS) were assessed as possible prognostic factors of early mortality.

**Results.** The mean age of the study group was 53.0 years (range 26–82 years); 58.9% (33) were male. TIPS was performed on elective basis in 66.1% (37) of our patients. Most common indications for TIPS placement were refractory variceal bleeding 51.9% (29) and refractory ascites 33.9% (19). Variceal bleeding was controlled in all the patients, whereas the control of refractory ascites and hydrothorax improved in 96.2% (54) of patients. The rate of early stent dysfunction was 3.7% (2) and worsened or newly developed HE was observed in 39.3% (22). 30-day mortality in our study after TIPS placement was 26.8% (15). Univariate analysis showed that Child-Pugh class C, pre-TIPS Child-Pugh score >11, pre-TIPS MELD score >18, pre-TIPS creatinine level >176  $\mu\text{mol/l}$  and infectious complications, newly developed or worsened hepatic encephalopathy after TIPS placement were predictors of 30-day mortality. We found that with one point increase in Child-Pugh score, the risk of death increased 1.9 times ( $p < 0.04$ ; 95% CI 1.1–3.02).

**Conclusion:** TIPS is an effective treatment modality for the complications of PH. Hepatic reserve, renal function and presence of infection and hepatic encephalopathy after the procedure can predict 30-day mortality after TIPS placement.

## 5. UPPER GASTROINTESTINAL ENDOSCOPY FINDINGS AND INCIDENCE OF GASTRIC PRECANCEROUS CONDITIONS IN AMBULATORY PATIENTS

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**Background.** Purposefully performed upper endoscopy evaluates the esophageal, gastric and duodenal mucosa.

**Purpose.** To determine at what age upper endoscopy is performed most often and in what order gastric biopsies are taken. To analyze findings of upper gastrointestinal examination including gastric precancerous conditions.

**Materials and methods.** Patients, who had their upper endoscopy done at Digestive Diseases Centre "GASTRO" in 2013, were included in the research. Data were obtained retrospectively from database programme "Ārstu birojs". Histological data were analyzed from patients, from whom biopsies were taken according to the scheme, which has been recommended by guidelines of MAPS (Management of precancerous conditions and lesions in the stomach). Histological data were grouped according to the classification system of OLGA (Operative Link on Gastritis Assessment) and OLGIM (Operative Link on Gastric Intestinal Metaplasia Assessment).

**Results.** Upper endoscopy was performed on 7061 patients – 32,6% male and 67,4% – female (average age 49,6±17,4 years). 58,2% were older than 45 years. Peptic ulcer in active stage was diagnosed in 92 (1,3%) patients, from whom 50 (55,6%) had *H.pylori* infection, whereas ulcer scar – 114 (1,6%) patients. Gastric cancer was diagnosed in 60 (0,9%) patients, but esophageal cancer – 15 (0,2%). 336 (4,8%) patients had previously done gastrectomy or gastric resection. Barrett's esophagus was diagnosed in 38 (0,5%) patients. Gastric biopsies were taken from 2088 patients, however, only 1270 or 18% of them were done accordingly to the scheme of gastric precancerous conditions guidelines. These 1270 patients were divided in different level risk groups. High and low grade dysplasia was found in 56 (4,4%) patients, 47 (83,9%) were older than 56 years. 116 (9,1%) patients' histological data corresponded with either OLGA/OLGIM III/IV, OLGA III or IV and OLGIM III or IV classification system, 101 (87%) were 56 years and older. Thereby high risk precancerous conditions were found in 172 (13,5%) patients, from whom standard biopsies were taken.

**Conclusions.** In most of the cases, upper endoscopies are performed on patients, who are over 45 years old. Only a small part of patients have their biopsies taken accordingly to the scheme by the guidelines, thereby histologically condition of gastric mucosa is not evaluated according to the guidelines for most of the patients.

## 6. ASSOCIATION OF INTRATUMORAL INFILTRATING LYMPHOCYTES WITH THE DEGREE OF DIFFERENTIATION AND GROWTH PATTERN OF GASTRIC CARCINOMA

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**Background.** Gastric cancer (GC) is one of the most common malignancies and the second most frequent cause of cancer-related death worldwide. It has the highest incidence in China, Japan, Korea and eastern Asia. The overall prognosis is poor with a 5-year survival rate below 30% in most countries; poor prognosis is due no specific signs on the early stage of disease that is why disease is usually diagnosed in the advanced stage. Therefore, there is an urgent need for the morphofunctional and prognostic characteristics of GC.

**Purpose.** The purpose of our study was to evaluate the correlation between differentiation degree (*Grade*), *Lauren* classification and peritumoral lymphocytes in the patients with C.

**Materials and methods.** Altogether, 300 patients undergoing GC surgery at Riga East University Hospital in 2012–2014 were enrolled in the study. The study was approved by a local ethical committee. The histopathological examination of GC tissue was performed. The results were analyzed by SPSS 21. version software.

**Results.** Obtained results showed that *Grade* I carcinoma was found in 8 cases, *Grade* II carcinoma in 70 cases and *Grade* III in 222 cases. Additionally, according to *Lauren* classification the 80 patients had intestinal type carcinoma, 93 patients had diffuse type carcinoma, 38 patients had a mixed type carcinoma and 15 patients had an undetermined type carcinoma.

Furthermore, obtained results demonstrated increased infiltrating peritumoral lymphocytes in patients with intestinal type carcinoma compared to diffuse type carcinoma, mixed type carcinoma undetermined type carcinoma ( $p < 0.05$ ). In addition, the positive correlation between the degree of differentiation and infiltrating peritumoral lymphocytes was revealed ( $p < 0.001$ ).

**Conclusions.** In conclusion, our data indicated that peritumoral lymphocytes are important in establishing the tumor microenvironment for GC; intratumoral lymphocytes are associated with tumor differentiation degree and growth pattern according to *Lauren* classification.

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# BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY AND REGENERATIVE MEDICINE

## PART I

### 1. DNA LESIONS IN HEALTHY SUBJECTS: A LITERATURE REVIEW

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**Background.** DNA damage is a valuable biomarker in human molecular epidemiology being associated with many diseases and also aging. However, the level of DNA damage is also influenced by lifestyle, habits and environmental factors.

**Purpose.** The objective of the current study was to summarize literature data on DNA breakage level of DNA in healthy subjects depending on their lifestyle, habits and environmental factors as a preliminary work for vast study of above parameters in the Latvian population.

**Materials and methods.** Publications cited in PubMed database and sorted out using key words “comet assay, aging, smoking, alcohol, coffee, tea”, etc. were analysed, as well as the publications of participants of the *CA COST Action CA15132* “The comet assay as a human biomonitoring tool (hCOMET)”.

**Results.** Some gene polymorphisms are associated with increased level of DNA damage, however, it is believed that environmental factors are more important. Data on the role of gender are contradictory and depend on race. In tall individuals, DNA breakage level is higher. It also depends on the latitude and season: in southerners DNA is damaged to a larger extent than in northerners, breakage increases during hot season. Physical activity favours DNA breakage. Data on single-strand DNA breaks in aged persons are contradictory, but double strand breaks evidently increase with age. Smoking heavily damages DNA, and so does alcohol, however, DNA cross-links formed by acetaldehyde can mask DNA breaks. Consumption of coffee, black and green tea decreases the level of DNA breaks and favours DNA repair. Consumption of roasted meat increases level of DNA breaks, at the same time, in vegetarians the level of DNA breaks is not significantly lower compared to omnivorous persons. Moreover, a high consumption of tomatoes favours DNA breakage, but the fruit protect DNA only in women and when consumed in large quantities. Mouth washes damaged DNA in buccal epithelium cells.

**Conclusions.** Levels of DNA damage are variable in healthy persons.

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## 2. PSMA6 GENE POLY(DA:DT) TRACT GENETIC VARIATIONS ARE ASSOCIATED WITH AUTOIMMUNITY RELATED PATHOLOGIES IN LATVIANS

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**Background.** The ubiquitin-proteasome systems (UPS) are a key player of proteostasis network in the body. Deregulation of this system implicated in several human pathologies can depend on the structural variations in the genes encoding the proteasome subunits.

**Purpose** was to investigate the structure of *PSMA6* promoter poly (dA:dT) tract and to evaluate possible associations with autoimmune disorders in Latvians.

**Materials and methods.** The *PSMA6* poly(dA:dT) tract was investigated by fragment length analysis in cases/control study including 156 juvenile idiopathic arthritis (JIA), 103 bronchial asthma (BA), 108 childhood obesity (OB), 280 multiple sclerosis (MS), 152 type 1 diabetes mellitus (T1DM) patients and 341 controls. The rs71640264 was genotyped by sequencing in 36 samples randomly selected from all collections and compared to previously published genotyping data of rs2277460 (Sjakste *et al.*, 2014; 2015; Paramonova *et al.*, 2014; Kalnina *et al.*, 2014). The results from individual disease studies were combined to autoimmune diseases group with the aim to reveal the overall autoimmune effect.

**Results.** It was shown that the *PSMA6* poly(dA:dT) tract is unchangeable and always consists of A24 repeats. Thus the formerly observed variability of the site length depends on insertions rs200541481 (-/AC) and rs200298313 (-/C) *upstream the tract*. Three microsatellite length variations: 216bp (without *insertions*), 217bp (with rs200298313 included) and 218bp (with rs200541481 included) were observed with frequency more than 5% in sum in both case and controls. Alleles 216bp, 217bp were equally presented in cases and controls (about 43% and 54%, respectively). Alleles and genotypes including 218 bp appear to be autoimmunity disease susceptible ( $P < 0.0001$ , OR=3.360 [1.873–6.038] for alleles and  $P < 0.001$ ) for genotypes in Latvians. The SNP rs71640264 (A/C) in downstream part of microsatellite *does not affect the microsatellite length and* was observed with rs2277460 in complete ( $D' = 1$ ,  $r^2 = 1$ ) or slightly disrupted LD in European populations and in Latvians. Therefore, rs71640264 may contribute to the risk of JIA and BA in Latvians (Sjakste *et al.*, 2014, 2015).

**Conclusions.** We provide evidence that *PSMA6* poly(dA:dT) microsatellite variations may contribute to the risk of autoimmunity related diseases in Latvians.

**Acknowledgements/Funding.** *The study was funded from the UL-funded project “Proteasome genes structure, expression and pharmacogenomics study”.*

### 3. STUDY OF ANTIOXIDANT PROPERTIES AND INTERACTIONS WITH DNA OF 1,4-DIHYDROPYRIDINE DERIVATIVES USING SPECTROSCOPIC METHODS

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**Introduction** Synthetic derivatives of 1,4-dihydropyridine (1,4-DHPs) possess important biochemical and pharmacological properties. Some of them have antioxidant and antimutagenic activity, ability to enhance the repair kinetic after oxidative stress, and to interact with DNA molecule.

**Purpose.** The aim of our study was to evaluate the ability of different 1,4-DHPs to interact with DNA molecule, to evaluate possible base-specificity of binding, to assess the ability of the compound to scavenge the peroxynitrite.

**Materials and methods.** UV-VIS spectra of the tested compounds were recorded on Perkin Elmer Lambda 25 UV/VIS spectrophotometer in absence of DNA and presence of increasing amounts of DNA. Possibility to interact with different bases was studied in the same way. To evaluate role of ionic and hydrogen bonds in interactions with bases and DNA, titration was performed in solutions of 1M NaCl and 8M Urea. Observation of hyperchromic or hypochromic effects produced by DNA indicated interactions of the substance with minor groove of the DNA or intercalation of the substance between the DNA strands. Binding constants were calculated as described (Buraka *et al.*, 2014). The peroxynitrite decomposition was detected, measuring the absorption changes at 302 nm wavelength in the presence of different 1,4-DHPs at alkaline conditions. The average rate of reactions were calculated with  $V = \pm ((C_2 - C_1) / (t_2 - t_1)) = \pm (\Delta C / \Delta t)$

**Results.** Ability of several 1,4-DHPs to interact with DNA was different. E-2-84, I-6-180-2 and I-4-105 interacted more intensively compared to PP-544-NH<sub>4</sub>, E-2-84, V-7-17-1 and J-9-125. Salts of AV-153 (Ca, Mg, Li, Rb, K) could interact with the four DNA bases, however without significant difference. Interestingly, interaction intensity of K salt with DNA and bases was significantly different when determined in 1M NaCl and 8M urea. The binding constant of K salt with adenine in 8M urea was 1.85 times greater than in 1M NaCl. The peroxynitrite decomposition rate was greater in the presence of J-9-125, J-4-96, J-3-86 and AV-154-Na compared to PP-150-Na, glutapyrone and tauropyrone.

**Conclusions.** 1. Several 1,4-DHPs can interact with DNA molecule with different intensities 2. The Ca, Mg, Li, Rb and K salts of AV-153 manifest similar affinity to the four DNA bases interact with four DNA bases. 3. Several 1,4-DHPs catalyse the decomposition rate of peroxynitrite.

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## 4. THE INTRACELLULAR INTERACTION OF AV-153-NA

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**Background.** A lot of interest among scientists encourages compounds with antimutagenic properties, and AV-153-Na is one of them. AV-153-Na is 1,4-dihydropyridine (1,4-DHP) analogue which is capable of interacting with DNA molecule through intercalation. The fact that AV-153-Na is a fluorescent gives an opportunity to visualize its intracellular distribution and determine interactions with cell nuclei that is important for a better understanding of compound functions.

**Purpose.** The objective of our study were to evaluate the AV-153-Na ability to enter the cell, as well as to visualize this 1,4-DHP analogue possible interaction with DNA molecule.

**Materials and methods.** We analyzed the AV-153-Na ability to interact with live and fixed HeLa and EA.hy926 cells. Interactions with cell nuclei and with DNA *halo* were also studied (under oxidative stress condition and without it). The concentration of AV-153-Na at all experiments was constant (10 mM). As a DNA marker was used propidium iodide. Results were analyzed using confocal and fluorescent microscopy methods.

**Results.** AV-153-Na can enter the cell and its fluorescence was visualized in living and in fixed cells. Compound fluorescence was detected in cell cytoplasm and cell nuclei. AV-153-Na interaction with isolated cell nuclear structures was also visualized, but Fenton reaction condition and following DNA breaks did not influence intensity of AV-153-Na fluorescence.

**Conclusions.** Summarizing the obtained results and already published data, we conclude that AV-153-Na can enter the cell and interact with DNA molecule.

**Acknowledgements/Funding.** *The study was funded from the University of Latvia project “Proteasome genes structure, expression and pharmacogenomics study”.*

## 5. NITRATE CONCENTRATION CHANGES IN TYPE 1 DIABETES IN THE PATIENT'S BLOOD AND URINE

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**Background.** Many scientific researches have proven that development of type 1 diabetes mellitus (1TDM) can be stimulated by inflammatory factors and also by free radicals, including nitric oxide (NO). Increased production of free radicals can result in DNA damage, protein degradation, and lipid peroxidation. Those processes can cause for mutations and cell death. Between oxidative, nitrosative stress and complications of 1TDM is statistically significant association – increase of nitrosative stress results with poor disease prognosis.

NO reacts with molecular oxygen forming nitrites ( $\text{NO}_2^-$ ), nitrates ( $\text{NO}_3^-$ ) and nitrogen dioxide. For that reason, based on data about  $\text{NO}_2^-$  and  $\text{NO}_3^-$  levels in biological materials, it is possible to talk about NO concentration and nitrogen metabolism in organism.

**Purpose.** The objective of the current study was to find out if there is an association between changes of  $\text{NO}_2^-$  concentration in blood and urine, and clinical biochemistry data of 1TDM patient and control group.

**Materials and methods.** Clinical, quantitative, analytic, retrospective cohort research was done. The biological materials of 55 control and 180 patients with diagnosis 1TDM was used.  $\text{NO}_2^-$  concentrations was measured using *Sievers'* nitric oxide analyser (Model 280i). Data statistical analysis was done using statistical software "R (3.2.0)" with general linear model (GLM) regression analysis, calculation of Kendall rank correlation coefficient and Wilcoxon signed-rank test.

**Results.** There is no statistically significant difference in  $\text{NO}_2^-$  concentration between serum and urine in case ( $p=0.08$ ) and control ( $p=0.44$ ) group. Kendall rank correlation test found out that between  $\text{NO}_2^-$  concentration in serum and eGDR ( $p=0.04$ ,  $\tau = -0.09$ ), creatinine ( $p=0.04$ ,  $\tau = 0.10$ ) there is a statistically significant correlation. It has been found out that between  $\text{NO}_2^-$  concentration in urine and the entire cholestenone level ( $p=0.02$ ,  $\tau = -0.12$ ), LDL ( $p=0.02$ ,  $\tau = -0.13$ ), ALAT ( $p=0.004$ ,  $\tau = -0.15$ ) and albuminuria ( $p=0.03$ ,  $\tau=0.12$ ) there is a statistically significant correlation. GLM analysis showed that none of the researched factor combinations are statistically significant associated with  $\text{NO}_2^-$  concentration changes in the samples.

**Conclusions.**  $\text{NO}_2^-$  concentration changes in serum and urine are statistically significant associated with other biochemistry data (entire cholestenone level, LDL, ALAT, creatinine, albumin. level).

**Acknowledgements/Funding.** *The study was funded from the University of Latvia project "Proteasome genes structure, expression and pharmacogenomics study".*

## 6. S-PHENYLPYRACETAM BINDS TO DOPAMINE TRANSPORTER AND REDUCES BODY WEIGHT GAIN IN OBESE ZUCKER RATS AND HIGH FAT DIET-FED MICE

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**Background.** Obesity is a multifactorial condition that increases risk of premature death, reduces the overall quality of life and is a major risk factor for diabetes mellitus, cardiovascular diseases and stroke. World Health Organization data show, that the prevalence of obesity worldwide has more than doubled in the last decades. The most widely used medications for body weight reduction are nonselective inhibitors of monoamine uptake or re-uptake (such as modafinil, amphetamine, tesofensine), which rise the extracellular concentrations of dopamine (DA), norepinephrin and/or serotonin.

**Purpose.** The aim of this study was to determine the S-phenylpiracetam binding affinity to dopamine transporter (DAT) and examine the effect of S-phenylpiracetam on body weight gain, locomotor activity and blood glucose level in obese *Zucker* rats and high fat diet (HFD)-fed mice.

**Materials and methods.** In this study, we assessed the binding affinity of S-phenylpiracetam to DAT using a [<sup>3</sup>H]WIN-35428, radiolabeled selective DAT inhibitor. The weight reduction effects of S-phenylpiracetam were detected using the *Zucker* rats and mice that received a HFD. Obese *Zucker* rats were treated daily with peroral administration of S-phenylpiracetam (50 mg/kg) for 12 weeks (n=6). Obese *Zucker* control (n=10) and lean *Zucker* control (n=8) rats received water. HFD-fed mice, which were divided into 3 groups (equal number of animals in each group, n=9): normal diet, HFD and HFD with S-phenylpiracetam (50 mg/kg, per os) treatment daily for 8 weeks. The HFD control and normal diet mice received water via the same route. Weight gain and plasma metabolites reflecting glucose metabolism were measured. We used the open-field test to detect locomotor activity.

**Results.** Binding experiments using rat brain membrane preparations revealed that the equilibrium dissociation constant ( $K_i$ ) for S-phenylpiracetam was 56 $\mu$ M. We found that after 12 weeks treatment with S-phenylpiracetam, body weight gain in the obese *Zucker* rats decreased by 16% as compared to obese control group. Moreover, after 8 weeks the HFD mice which received S-phenylpiracetam showed by 25% lower body weight gain compared to HFD control group. In addition, S-phenylpiracetam reduced the plasma glucose concentration and lowered hyperglycemia in a glucose tolerance test in both models. Additionally, S-phenylpiracetam did not affect locomotor activity in both models.

**Conclusions.** Overall, our results demonstrate that S-phenylpiracetam treatment reduces body weight gain and improves adaptation to hyperglycemia without stimulating locomotor activity. Furthermore, our data suggest that weak dopamine re-uptake inhibitors, such as S-phenylpiracetam could be potentially useful for treating overweight and obesity in clinical practice.

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## 7. OPTIMIZATION AND VALIDATION OF *IN VITRO* MONOCYTE-MACROPHAGE DIFFERENTIATION MODEL

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**Background.** Macrophages are part of the body's innate immune system and are particularly active in inflammation and infection. Under such conditions, monocytes migrate to tissue where they differentiate into macrophages. Classically, macrophages were seen as pathogen-removing agents owing to their phagocytic and antigen-presenting activity. However, it is now known that under certain conditions macrophages mediate immunosuppression and promote cell proliferation and angiogenesis. Based on those properties, macrophages are separated into two subclasses: M1 are classically activated macrophages that are pro-inflammatory, tumoricidal and with high phagocytic activity, but M2 are alternatively activated macrophages that are anti-inflammatory, with low phagocytic activity and pro-tumorigenic. These subclasses are characterized by specific *in vitro* morphology, phenotype and cytokine secretion profile.

**Purpose.** The purpose of the present study was to optimize and validate *in vitro* monocyte-macrophage differentiation model suitable for further studies of different pharmacologically active substances and other biological factors.

**Materials and methods.** Human monocytic THP-1 cells were differentiated into inactivated macrophages using phorbol 12-myristate 13-acetate (PMA). Macrophages were then polarized into M1 macrophages by incubation with of bacterial lipopolysaccharides (LPS) and interferon- $\gamma$  (IFN- $\gamma$ ). M2 polarization was induced by incubation with interleukin-13 (IL-13) and interleukin-4 (IL-4). Cell morphology was analyzed using phase-contrast microscopy. Cell phenotype was analyzed using flow cytometry.

**Results.** Monocytes differentiated into inactivated macrophages (M0) in the presence of phorbol 12-myristate 13-acetate. The differentiation was confirmed by plastic adherence of the cells in culture and by increase of CD14 expression. Monocyte-derived macrophages differentiated into M1 macrophages in the presence of LPS and IFN- $\gamma$ . The differentiation was confirmed by cell morphology changes to typical "fried egg" pattern and increased expression of marker HLA-DR. Inactivated macrophages differentiated into M2 macrophages in the presence of IL-4 and IL-13, and the differentiation was confirmed by cell morphology changes into more elongated, fibroblast-like form and by increase in marker CD206 expression.

**Conclusions.** We have optimized and validated THP-1 monocyte-macrophage *in vitro* differentiation model including polarization of M0 macrophages into M1 macrophages using LPS and IFN- $\gamma$  or into alternatively activated M2 macrophages using IL-4 and IL-13. CD-14 is a marker for inactivated macrophages (M0), HLA-DR is a marker for M1 macrophages and CD206 is a marker for M2 macrophages.

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# BASIC MEDICAL SCIENCES, PATHOLOGY, PHARMACOLOGY AND REGENERATIVE MEDICINE

## PART II

### 1. SELECTION OF SSDNA APTAMERS TARGETING METASTATIC RENAL CELL CARCINOMA USING CELL-SELEX TECHNOLOGY

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**Background.** Aptamers are oligonucleotides that bind to specific molecular targets based on their tertiary structure interactions with target molecule. Identification of aptamers for specific target is achieved using SELEX (systematic evolution of ligands by exponential enrichment) method. Aptamers have been proven to be promising technique for use in theranostics and have been compared to antibodies with respect to their high specificity and mechanism of action. Cell-SELEX is a variation of SELEX method that uses live cells as a target. Aptamers that are selected against specific type of cells can be further modified to be used as a targeting moiety in therapeutics or diagnostic devices. Renal cell carcinoma has several well described molecular targets, but still lacks easy and reliable early diagnostic method, however, no research has been reported in this field using aptamers.

**Objectives.** The objective of current study was to enrich oligonucleotide starting library with sequences that specifically bind to renal cell carcinoma cells (RCC-MF) using cell-SELEX technique.

**Materials and methods.** Clear cell renal cell carcinoma cell line RCC-MF established from the kidney clear cell carcinoma (lung-metastasis) of a 63 years old male (*Cell Lines Service GmbH*) was used as a target cell line and epithelial kidney cell line RC-124 established from non-tumor tissue of a 63-years-old man diagnosed with kidney carcinoma (*Cell Lines Service GmbH*) was used as a negative control cell line. Randomized DNA aptamer library with sequence 5'-ATCCAGAGTGACGCAGCA-40N-TGGACACGGTGGCTTAGT-3' (*Metabion*) was used as a starting library. After each selection cycle, selected library was multiplied with PCR. ssDNA was prepared by binding biotin labelled primer 5'-biotin-ACTAAGCCACCGTGTCCA-3' (*Metabion*) to streptavidin beads (*GE Healthcare*) and subsequent separation of DNA strands with 0.2 M NaOH. FITC labelled primer 5'-FITC-ATCCAGAGTGACGCAGCA-3' (*Metabion*) was used for monitoring with flow cytometry (*Guava, Millipore*).

**Results.** After eight cell selection cycles, 31.8% of aptamer fraction bound to RCC-MF whereas binding to non-malignant control cells was 3.6%, as demonstrated by flow cytometry analysis.

**Conclusions.** Successful enrichment of RCC-MF specific oligonucleotide sequences in aptamer library after eight cycles confirm that Cell-SELEX method may be used for renal carcinoma targeted aptamer selection.

Further enrichment of renal carcinoma specific aptamer library will be carried out and aptamers in pool will be identified by sequencing.

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## 2. QUANTUM DOT TRANSFER FROM MESENCHYMAL STEM CELLS TO BREAST CANCER CELLS IN 3D CO-CULTURE MODEL

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**Introduction.** Mesenchymal stem cells (MSCs) could be used as nanoparticle vectors for diagnostic or therapeutic use due to their ability to migrate to the sites of inflammation and /or tissue damage, e.g., tumour. Quantum dots (QDs) are fluorescent nanoparticles with stable and bright fluorescence, wide excitation and narrow emission spectra. The surface of QDs can be conjugated with bioactive molecules, making them promising candidates for diagnostic and therapeutic applications.

**Objectives.** The objective of the study was to determine the endocytic pathway of QD uptake in MSCs and to analyse whether MSCs could transfer QDs to breast cancer cells in 3D co-culture model.

**Materials and methods.** Endocytosis inhibitors for micropinocytosis, phagocytosis, lipid-raft, clathrin and caveolin mediated pathways were used to analyse endocytic pathway of QDs in MSCs by fluorescence microscopy. Method for 3D co-cultures of skin MSCs and breast cancer cell lines MCF7 and MDA-MB-231 on polyHEMA coating was established. CD90 was chosen as selective marker for MSCs. The transfer of QDs from MSCs to cancer cells was analysed by flow cytometry

**Results.** MSCs internalized QDs through clathrin-mediated endocytosis in serum-supplemented cell culture medium, whereas in serum-free conditions QD uptake occurred via clathrin- and caveolin/lipid-raft mediated endocytosis. In 3D co-culture 18% of MCF7 and 30% of MDA-MB-231 cells internalized QDs from MSCs.

**Conclusions.** MSCs could be potentially used as a cellular carrier to transfer QDs or QD linked anti-cancer drugs to tumour cells.

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### 3. IZOLĒTU (*NICOTIANA TABACUM L.*) HLOROPLASTU IZMANTOŠANAS IESPĒJAS CILVĒKU ŠĒNU KULTIVĒŠANA *IN VITRO*

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**Ievads.** Augu šūnu hloroplasti var tikt ģenētiski transformēti tā, lai tie ekspresētu dažādas ekonomiski nozīmīgus proteīnus. Arī mūsu iepriekšējos pētījumos ir izdevies ģenētiski modificēt hloroplastu un ekspresēt iekšējās membrānas un stromas proteīnus. Šādi proteīni varētu tikt izmantoti cilvēku šūnu kultūrās augšanas, diferenciacijas un citu procesu regulācijai.

**Darba mērķis.** Noskaidrot cilvēku šūnu kultivēšanas iespējas hloroplastu klātbūtnē un pārbaudīt iespējamo negatīvo ietekmi, ņemot vērā hloroplastu bakteriālo izcelsmi.

**Materiāli un metodes.** Izolētu hloroplastu suspensijas pagatavoja no *Nicotanium tabacum* un lapām un pievienoja Murashige and Skoog barotni ar Gamborga vitamīniem (Sigma). Darbā tika izmantotas FM-55 cilvēka melanomas (primārā audzēja) šūnas u.c. šūnas, kas saņemtas no Latvijas Universitātes Bioanalitikas un biodozimetrijas laboratorijas šūnu bankas. Šūnas tika kultivētas šūnu barotnē, ko veidoja 90% DMEM (VLE-DMEM FG 1445 Biochrom GmbH) ar pievienotām antibiotikām (penicilīns-streptomcīns, Gibco Pen Strep 15140-122 un 15140-163, 5 ml pievienoti 500 ml DMEM) un 10% FBS. Barotnei tika pievienota hloroplastu suspensija vai arī tīri hloroplasti dažādās koncentrācijās. Šūnas tika inkubētas 2 dienas 37°C, 5% CO<sub>2</sub> koncentrācijā un periodiska apgaismojuma apstākļos (12 h 418 lux un 12 h tumsā). Pēc šī perioda nekrāsotas šūnas tika apskatītas ar Leica DM IL mikroskopu un noteikta konfluēnce. Tālāk šūnas tika fiksētas un krāsotas ar propīdija jodīdu un analizētas ar konfokālo lazerskenējošo mikroskopu (Leica DM RA-2 ar konfokāli skenējošo galvu TCS-SL), lai noteiktu šūnu, šūnu kodolu un barotnē esošo hloroplastu morfoloģiskās īpatnības.

**Rezultāti.** Analizējot FM-55-P melanomas šūnu konfluēnci varēja konstatēt, ka hloroplastu klātbūtnē ir līdzīga šūnu konfluēnce. Arī vārsptveida un dendrītisko šūnu sastopamība šajos variantos būtiski neatšķirās. Maksimālās hloroplastu koncentrācijas gadījumā samazinājās apaļas un eliptiskas formas kodolu skaits, bet palielinājās kodolu skaits ar invaginācijām. Parādījās arī fragmentēti kodoli. Šādas hloroplastu koncentrācijas gadījumā palielinājās noapaļotu šūnu skaits un šādas šūnas zaudēja savas adherentās īpašības. Daudzos gadījumos varēja vērot, ka dendrītisko šūnu izaugumi satur hloroplastus, kas uzņemti ar fagocitozes palīdzību. Daudzos gadījumos šie ieslēgumi saturēja hlorofilu, bet bija mazāki par hloroplastiem. Hloroplastu fluorescēnce un morfoloģiskās īpašības nemainījās, neraugoties uz 37°C temperatūru un antibiotiku klātbūtni barotnē.

**Secinājumi.** Hloroplastu neatstāj kaitīgu ietekmi uz pētīto melanomas šūnu proliferāciju un morfoloģiju. Tas nozīmē, ka tie ir izmantojami kā svešu proteīnu avots šūnu barotnēs. Fluorescējošu hloroplastu atrašanās pētītājā melanomas šūnu līnijā liecina par endosimbiozi, kuri jāpievērš uzmanība tālākajos pētījumos.

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## 4. SEARCH FOR STRUCTURES OF HYPOXIA-INDUCED EXOSOMAL PROTEINS IN DATA BASIS

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**Background.** Emerging evidence indicates that the effect of hypoxia on malignant progression is mediated by a series of hypoxia-induced proteomic and genomic changes. Thus, expansion of new (and more aggressive) clones become the dominant tumour cell type. Expanding cells release exosomes (Ex), which through the endosomal pathway may constitute a hypoxia-dependent intercellular signalling during tumour development. Ex proteome analysis may therefore be of value in disease diagnosis and monitoring in a variety of settings.

**Purpose.** The objective of the current study was to analyse protein profile of Ex secreted under hypoxic and normoxic conditions by colorectal cancer (CRC) cell lines SW480 and SW620 derived from a primary and metastatic CRC, respectively.

**Materials and methods.** Ex were received from researchers of Latvian Biomedical Research and Study centre. Ex surface and total protein fractions were separated using XPEP Ex Mass Spec kit (System Biosciences). Ex<sup>Hyp</sup> and Ex<sup>Norm</sup> proteome was analysed by UPLC-TOF MS technique and corresponding to mass spectra protein structures searched in UNIPROT-SPROT + UNIPROT-TREMBL and ExoCarta data basis with taxonomy – *Homo sapiens* (human), enzymatic cleavage = trypsin, fixed modifications = carbamidomethyl (C), variable modifications = oxidation (M), monoisotopic mass, peptide tolerance = 1.5 Da, MS tolerance = 0.8 Da, one missed cleavage, charge positions = 1+, and 2+, instrument = ESI-QTOF.

**Results.** We have found fragments of different Ex proteins that were overexpressed in Ex<sup>Hyp</sup> surface protein samples, whereas protein profile in total protein samples of Ex<sup>Hyp</sup> and Ex<sup>Norm</sup> was similar. Finding of one fragment from the structure of proteins allow us to classify deciphered proteins as putative ones. ExoCarta data basis shows that all these proteins are found in CRC-derived Ex.

**Conclusions.** The protein expression changes in Ex surface protein fraction are consistent with a hypoxic response. We have found distinct hypoxia-induced candidate proteins in Ex<sup>Hyp</sup> secreted by both cell lines SW480 and SW620.

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## 5. COMPOSITION PROFILES OF VARIOUS CONIFER POLYPRENOLS

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**Background.** The polyphenols (PPs) are polyisoprenoid alcohols that contain multiprenyl (polyphenyl) chains build-up from 5 to 25 and more prenyl units with a hydroxyl group placed at the end and can be characterized by the general formula  $H-(C_5H_8)_n-OH$  where  $n$  is the number of isoprene units (Rezanka T. *et al.*, 2001). The stereospecific head-to-tail assembly of the prenyl units creates polymers that differ as to the chain length and/or geometrical configuration. The other important structural modification of PPs is related to saturation of one or more residues, e.g. the dolichols (Ciepichal *et al.*, 2007). PPs and dolichols can be found in plants, animals and other eukaryotic organisms having important roles in the synthesis of glycoproteins and as the components of cell membranes (Bauersachs *et al.*, 2010).

**Purpose.** The objective of the study was to investigate the structure of PPs from various *coniferophyta* sources, obtained by different extraction methods.

**Materials and methods.** Norway spruce (*Picea abies* L.) PPs (acquired from a local producer AS “Biolat”) were extracted using non-polar hydrocarbon mixture solvents. Siberian fir (*Abies sibirica*) PPs (acquired from a Russian producer “Solagift”) were extracted by  $CO_2$  at 18–25°C. Scots pine (*Pinus sylvestris* L.) PPs were acquired via ASE (accelerated solvent extraction) using hexane and ethyl acetate by increasing solvent polarity (at  $T=90^\circ C$ ,  $P=1500$  psi  $N_2$ ). Molecular structure of all PPs was determined by UPLC-TOF (ultra-performance liquid chromatography time of flight mass spectrometry).

**Results.** Norway spruce extract was purified to  $\geq 95\%$  (by column chromatography) and Siberian fir extract to 75–82% (using molecular distillation). The Scots pine needles, collected in Latvian forest, were air-dried before extraction and the PPs content was determined to be approx. 20%. All the obtained conifer needle PPs consisted of a mixture of PP homologues with isoprene unit numbers ranging from  $n = 9$  to 22 (from  $C_{45}H_{74}O$  to  $C_{110}H_{178}O$ ), however, some variance depending on the conifer species and extraction methods was observed, specifically as pertains to the dominant chain lengths: Norway spruce – P13-P19 ( $C_{65}H_{106}O$  to  $C_{95}H_{114}O$ ), Siberian fir – P14-P17 ( $C_{70}H_{114}O$  –  $C_{85}H_{138}O$ ) and Scots pine – P17-P18 ( $C_{85}H_{138}O$  –  $C_{90}H_{146}O$ ).

**Conclusions.** Several conifer species were compared according to their PP chain length divergence. We found  $CO_2$  and ASE extractions to be more cost effective than the conventional extraction with an organic solvent. Further studies as to the different length PP impact on pharmacological activity should be carried out.

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## 6. DEVELOPMENT OF POLYPRENOL PROLIPOSOMES

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**Background.** Polyrenols are natural long-chain isoprenoid alcohols of the general formula  $H-(C_5H_8)_n-OH$  where  $n$  is the number of isoprene units. The needles of conifer trees are one of the richest sources of polyrenols therefore conifer polyrenols are studied most often. Polyrenols are fully soluble only in lipids, thus for the entrapment, delivery and release of polyrenols, a liposome formulation (containing both lipid and aqueous phases) could be successfully utilized. Proliposomes offer an alternative to the conventional liposomal formulations and are defined as dry, free-flowing particles that immediately form a suspension, when they come in contact with water. Such lipid vesicles are currently under intensive research and development as nanocarrier systems for the protection and delivery of bioactive agents (Mozafari M.R. *et al.*, 2008). Other encapsulation systems, such as soft-gel capsules either fail to achieve the needed active ingredient bioavailability in the organism or in the case of hard-gel capsules – can only accommodate hydrophilic substances.

**Purpose.** The objective of the current study was to create novel conifer polyrenol proliposomes, which can be further used for specific pharmacological investigations.

**Materials and methods.** Conifer polyrenols with purity 75–82% were acquired from a local producer AS “Biolat”, phospholipid mixture Phosal 40 IP (contains at least 25–75% of phosphatidylcholine) was purchased from “Lipoid”. The proliposomes were prepared according to a modified method originally from (Song *et al.*, 2002). Polyrenols and Phosal 40 IP (1:15, v/v) were dissolved in organic solvent mix (methanol: chloroform = 2:1, v/v) and the flask was then rotated until the solvent was completely evaporated.

**Results.** 2 kg of polyrenol proliposomes were successfully prepared. The encapsulation efficiency of polyrenol proliposome was assessed to be not less than 80%. Polyrenol content in proliposomes was determined by HPCL-MS as 7.80% (w/w).

**Conclusions.** We have prepared phospholipid proliposomes as conifer polyrenol carrier formulation.

**Funding:** Research project No. 1.2.1.1/16/A/005 “Technology development for the incorporation of biologically active substances into phospholipid liposomes” in cooperation with SIA “Smart material and technology competence centre” and CFLA. University of Latvia base and achievement project No. Y9-B050-ZF-N-840.

## 7. IDENTIFICATION AND MEASUREMENT OF DOLICHOL LEVELS IN RAT ORGANS

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**Background.** Dolichols (Dol) belong to a group of hydrophobic long-chain isoprenoid compounds which are made up of varying numbers of isoprene units. Dol in all living organisms, including humans, play a role in the co-translational modification of proteins. Additionally, Dol have been suggested to be used as a biomarker for aging. Dol identification and measurement of their levels in tissue may therefore be of value in studies on aging or neurodegeneration.

**Purpose.** The objective of the current study was to simplify Dol extraction procedure and to identify and measure level of dolichols in rat organs, as well as to evaluate dolichol preservation in freezer one and half year after rat sacrifice.

**Materials and methods.** Rat tissue were homogenized in liquid nitrogen and homogenate was resuspended in methanol and centrifuged. Then Dol were extracted from supernatant with hexane. The extract was dried under nitrogen and pellet suspended in propanol-2 and centrifuged. Obtained clear supernatant was analysed with ultra-performance liquid chromatography, time of flight-massspectrometry (UPLC-TOF MS (Agilent)). Dol with 13-21 isoprene units (Aventis Polar Lipids, Inc.) were used as standards.

**Results.** We have skipped step of Dol saponification and extraction with chloroform, and thus simplified Dol extraction procedure. In rat muscles we have found Dol with 18 and 19 isoprene units (D18 and D19), in liver – D15, D17, D18, D19 and D20 whereas in kidney dominant Dol were D16, D17, D18 and D19. However, measured level of Dol reflected individual animal variations. Therefore, average level of Dol mix was compared. Liver was the most Dol rich rat organ (in average approximately, 40µg/g), then follows kidney (approximately, 10µg/g) and muscle (approximately, 4µg/g). We have found that Dol are well preserved one and half year after rat sacrifice if samples are stored in freezer at temperature of -80 C°.

**Conclusions.** It is possible to detect and quantify Dol in frozen tissue at least one and half year after rat decapitation. UPLC-TOF MS assay allows to identify and quantify Dol in presence of other lipids in less purified tissue extracts. In all investigated tissue Dol with 17-19 isoprene units dominated. The liver was the most dolichol-rich rat organ.

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## 8. QUANTIFICATION OF GLYCOALKALOID LEVELS IN EXTRACTS OF PEELED POTATO SKIN

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**Background.** Glycoalkaloids are nitrogen-containing secondary plant metabolites found in many plants, including potatoes. Glycoalkaloids are toxic to humans if consumed in high concentrations. However, people are rarely exposed to levels of glycoalkaloids that cause serious health effects. Glycoalkaloids concentrate in the sprouts, peel and the area around the potato 'eyes'. Peeling of the skin from potatoes reduces glycoalkaloid levels. Cooking (i.e., microwaving) does not significantly reduce the levels of glycoalkaloids in foods. It is estimated that every year in the world are produced about 70 to 140 thousand tons of potato peel as the waste that are dumped in landfills, which, in turn, may affect the environment. Human poisoning risk arises from the fact that eating potato with skin has gained popularity and fried potato peels have become a popular snack. Therefore, studies on content of glycoalkaloids are important to call attention to possible hazards of eating or throwing out too many potato peels.

**Purpose.** The objective of the current study was to analyse glycoalkaloid levels in extracts of potato skin peeled in three different ways.

**Materials and methods.** Samples of peeled potato skins were received from researchers of Latvian University of Agriculture. Potatoes were peeled using abrasion peeling method and different size peels – 1–1.5 cm, 3–5 mm and very tiny flakes were obtained. The levels of glycoalkaloids  $\alpha$ -solanine and  $\alpha$ -chakonine in 21 sample were measured using high performance liquid chromatography-mass spectrometric method.

**Results.** We have found variable levels of glycoalkaloids. The levels of  $\alpha$ -solanine ranged from 3.14 to 1138.78 mg/kg, of  $\alpha$ -chakonine – from 0 to 1149.45 mg/kg. Content of glycoalkaloids in nine samples exceeded consumption safety level, which is 200 mg/kg. Additionally, we observed that peeling way and storage conditions influence the level of glycoalkaloids.

**Conclusions.** We suggest monitoring of glycoalkaloid levels in potato processing waste, as well as recommend potato skin size to be 1–1.5 cm, if these skins are peeled for later use as food product. In a broader sense, studies on composition of edible plant products and finding new solutions to use them contribute to strengthening of the Latvian bio-product market niche.

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## 9. MECHANISMS OF NEUROPROTECTIVE ACTION OF MUSCIMOL

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**Introduction.** Neuroinflammation which is a typical event in neurodegenerative diseases, such as Alzheimer's disease (AD), is manifested as activated innate brain immune cells (glial cells and macrophages). The oversecretion of cytokines, chemokines and excitotoxins leads to cell damage, neuronal demyelination and degeneration (Crowley *et al.*, 2016) resulted in gradual decline in cognitive functions. Therefore search for non-toxic anti-inflammatory agents might serve as a new therapeutic or preventive strategy in early AD. One of approaches could be to focus on neuronal survival by balancing the neurotransmitter functioning. Previously (Pilipenko *et al.*, 2015) have found that low doses of GABA-A receptor agonist muscimol is capable to reverse memory deficit in AD model-rats.

**Purpose.** To determine whether low doses of muscimol may influence neuroinflammation, as well as GABA and acetylcholine systems in AD model rats.

**Materials and methods.** Non-transgenic AD rat model was created by intracerebroventricular (icv) injection of streptozotocin (STZ, 750 µg in 10 µL). Muscimol (0.01 or 0.05 mg/kg) was administered intraperitoneally for 3 days. On day 4, STZ was injected. Saline served as control. The following biomarkers were used: glial fibrillary acidic protein (GFAP), glutamic acid decarboxylase 67 (GAD 67) and acetylcholine esterase (AChE). Appropriate protein expression was assessed in the hippocampus and cortex immunohistochemically or histochemically.

**Results.** Cortical and hippocampal GFAP and AChE density was markedly increased following STZ treatment, while muscimol at both doses reversed this effect to the control group values. STZ-induced significant decrease in GAD67 density also was normalized by muscimol.

**Conclusions.** At low doses muscimol decreases astrogliosis and acetylcholine cleavage, as well as regulate GAD67 expression. These data indicate that muscimol memory-enhancing effect to a great extent is based on its anti-inflammatory effects, as well as on promotion of GABA synthesis and Ach accumulation. These events are crucial for cell survival and functioning, and thus for neuroprotection and the improvement of memory processes.

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## 10. BACLOFEN, A GABA-B RECEPTOR AGONIST, SHOWS MEMORY IMPROVING AND ANTI-INFLAMMATORY ACTIVITY AND INCREASES CHOLINERGIC ACTIVITY IN ALZHEIMER'S DISEASE MODEL-RATS

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**Background.** Early signs of Alzheimer's disease (AD) include impairments of spatial memory, neuroinflammation, increased acetylcholine cleavage and decreased GABA levels. Recently, a compensatory role of  $\gamma$ -aminobutyric acid (GABA) in the pathogenesis of AD has been stressed as one of key factors capable to protect cell survival and, thus, halt early symptoms of AD (Nava-Mesa *et al.*, 2014). Previously, we have shown memory-enhancing and anti-neuroinflammatory effects of very low doses of muscimol, a GABA-A receptor agonist, in non-transgenic AD model rats (Pilipenko *et al.*, 2015).

**Purpose.** In the present study, we examined the effects of very low doses of GABA-B receptor agonist baclofen, previously known as muscle relaxant and an antispastic agent, in non-transgenic AD model rats obtained by intracerebroventricularly (icv) injected streptozocin (STZ).

**Materials and methods.** Male Wistar rats (280 $\pm$ 20 g) were pre-treated for 3 days with baclofen (0.025 and 0.05 mg/kg intraperitoneally, ip). Saline served as control. On day 4, STZ was injected bilaterally (750  $\mu$ g in 10  $\mu$ l aCSF total per rat). After two weeks, baclofen was injected again (daily for 4 days), and spatial learning/memory were assessed in the water maze test (4 trials/day for 4 days). A probe trial was carried out 24 h after the last training trial. *Ex vivo*, in the cortex and hippocampus, markers of astroglial and microglial neuroinflammation (GFAP and IBA-1, respectively), production of GABA (GAD67) were assayed immunohistochemically, and acetylcholine degradation (AChE) – histochemically.

**Results.** STZ produced about a 4-fold increase in GFAP- and around 3-fold increase in IBA-1-positive cell density in both cortex and hippocampus. Approximately 3-fold increase in AChE fiber density and a significant decrease in GAD67-positive cells was observed in both structures. Treatment with baclofen at both doses significantly decreased the densities of GFAP and IBA-1 in both structures, demonstrating a reversal of STZ effects. Baclofen also normalized AChE fiber density to the control group values, however only tendency to reverse STZ-induced decrease in GAD67 density was observed.

**Conclusions.** In STZ model-rats, baclofen at very low doses of 0.025 and 0.05 mg/kg improved spatial memory, prevented astro- and macrogliosis, decreased acetylcholine degradation. No significant influence on the production of GABA was shown. These data indicate that GABA-B receptor agonists might serve as prototype molecules to design effective neuroprotective compounds for the treatment of AD in its early stages.

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## 11. AN IMPROVED METHODOLOGY FOR LONG-TERM CONTINUOUS INTRACEREBRAL INFUSION OF EXPERIMENTAL SUBSTANCES BY ALZET MICROOSMOTIC PUMPS

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**Background.** One of the therapeutic approaches in neurodegenerative disease research is a long-term continuous intracerebral infusion of test substances (Tsung Tan *et al.*, 2011). The Alzet microosmotic pump is a miniature infusion system that can be used for continuous systemic infusion for targeted delivery of test substances into specific sites. However, there is a need for an improved methodology for a long-term continuous intracerebral infusion in mice models that can be followed by behavioural/cognitive and immunohistochemical (IHC) studies.

**Purpose.** To develop an improved methodology for a long-term continuous intracerebral infusion of test substances by Alzet microosmotic pumps that provides stability of the cannula and precise distribution of experimental compounds.

**Materials and methods.** For better fixation of the intracerebral cannula (mouse brain infusion kit, Alzet), a gypsum-skull was prepared based on a skull from a 50 days old C57BL/6J mouse. This was used to produce perfectly fitting silicone bases with a flat top to provide permanent and reproducible fixation of the cannula. To do so, a silicone sheet of 6 skull-prints was prepared by using a mold-system, which consisted of 6 gypsum skulls glued onto the glass surface and a molding chamber filled with medical-grade silicone. Stability of the cannula fixation was assayed by IHC using hematoxylin/eosin and NeuN staining's. Black India ink was infused and precise distribution of long-term continuous infusion was detected after 1, 2 and 3 weeks by microscopic image analysis.

**Results.** Previous studies of long-term continuous infusion experiments showed that an inappropriately fixed cannula can harm the mouse's brain (Sike *et al.*, 2016, Abstract) and therefore might even lead to a failed study. The study presented here shows that the new fixation method has stabilized the cannula onto the mouse skull and that this improvement gives a strong and permanent fixation of the Alzet pump cannula and a precise distribution of long-term intracerebral continuous infusion treatment of test substances.

**Conclusion.** This new methodology helps to generate consistent injection points by strongly fixed Alzet pump cannula and shows that it is a crucial and necessary step for long-term continuous intracerebral infusions that can be followed by further *in vivo* studies.

**Funding:** *This study was funded from Norwegian Financial Mechanism 2009–2014, and co-financed from project No. NFI/R/2014/023.*

## 12. THE EVALUATION OF ACUTE TOXICITY OF PENICILLIUM VIRIDE LANOSO-AMP DEAMINASE FOLLOWED BY IV ADMINISTRATION IN MICE

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**Background.** Adenylate deaminase (AMPD) is an immunomodulatory glycoprotein produced by the microscopic filamentous fungus *Penicillium lanoso - viride*. Previous *in vitro* studies and *in vivo* studies on rodents have demonstrated that purified AMPD has diverse immunomodulating and wound healing properties, however, the exact mechanism of immunomodulation has not been elucidated yet. In addition, a comparison with known inducers of immune response is desirable to characterize the biological activity.

**Purpose.** To evaluate the acute effects of AMPD on immune cell counts and secretion of cytokines after IV administration in mice.

**Materials and methods.** ICR male mice received a single intravenous injection of AMPD (0,45 and 4,5 mg/kg), lentinan (4,5 mg/kg), lipopolysaccharide (LPS; 500 ng/kg) and phosphate buffered saline (PBS; used as control). Before i.v. injection and 4, 8 and 24 hours after, the body temperature of mice was measured. Blood samples for the white blood cell counts and cytokine level analysis were taken 4, 8 and 24h after administration of the substances. Concentrations of G-CSF, GM-CSF, IFN- $\gamma$ , IL-10, IL-1 $\beta$ , IL-6, TNF- $\alpha$  in mice plasma were detected using Milliplex MAP Mouse Cytokine/Chemokine Magnetic Bead Panel.

**Results.** Body temperature was significantly reduced 2 and 4 hours after a single AMPD (0,45 and 4,5 mg/kg) i.v. injection in mice. The statistical significance was not seen 8 and 24 hours after AMPD, LPS and lentinan i.v. administration compared to the control animal group. Four hours after intravenous injection a pronounced, dose dependent decrease of lymphocyte counts and increase in neutrophil counts in both AMPD groups was found. This trend is similar to that observed in LPS group, however only slight changes in neutrophil and lymphocyte counts were observed in lentinan group. There was also a considerable statistically significant dose dependent increase in IL-6 secretion 4h after injection in AMPD groups. Highest AMPD dose yielded also statistically significant increase of IL-10, TNF- $\alpha$ , IFN- $\gamma$ . The effect of LPS and lentinan was less pronounced than that of AMPD. Concentrations of most cytokines returned to control level already at 8h after i.v. injection of the substances.

**Conclusions.** AMPD is a potent stimulator of immune response by regulation of immune cells and induction of cytokine secretion. Meanwhile, the safety profile is optimal as no pyrogenic effect was observed and cytokine levels were efficiently balanced within 8 hours.

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# INTEGRATIVE MEDICINE

## PART I

### CONTRASTING STRATEGIES OF TREATMENT OF CHRONIC DISEASE IN MODERN AND TRADITIONAL MEDICINE

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Recent research on Yoga Medicine and other systems of Traditional Complementary and Alternative Medicine show that they achieve results in a completely different way from the chemical drug based approach of modern medicine. The aim of Yoga Medicine and systems of meditation that are effective at reducing stress is to improve the quality of health by removing the effects of stress. This allows them to have long term effects which extend long after treatment programs are finished. Also, the larger the initial deviation from normal range of particular variables such as SBP and DBP in the case of hypertension, and FBS and PPBS in the case of Type 2 Diabetes, the larger will be the effect of Yoga practice or meditation – particularly Transcendental Meditation. Thus, when a trial of such an intervention is conducted, the initial distribution of subjects in the treatment group may reduce in variance with similar or even greater statistical significance than the shift in mean. Similarly, Yoga lifestyle programs will normalize BMI values, for those with both high and low initial values, though in this case slightly different programs may be prescribed. Even a group of seemingly healthy subjects can have variances in many different variables reduced, while variances in control groups will tend to increase. Such results suggest that without ongoing health improvement programs, quality of health tends to degrade. Similar results obtain for psychological variables, particularly measures of stress, such as STAI tests of anxiety. Electrodermal measures of acupuncture meridian activities yield parallel results corroborating these ideas. Several examples of increased variance for pathology groups over control groups are given, together with theoretical reasons. In the case of Ayurveda, similar results obtain, but can be more dramatic. The aim of Ayurveda treatment is often to restore balance to underlying variables derived from systems biology, applying at various levels of the organism – cells, tissues, organs, organ systems and the whole organism. Restoration of balance prevents different pathologies continuing to develop after a particular pathology has been treated. For example, diagnosis of PCOS may lead to removal of one or both ovaries, but the patient may continue to develop other pathologies in the metabolic disorder spectrum on a regular basis, every year or two. Restoring the Ayurvedic *doshas* to balance, particularly in this case, *Kapha dosha*, prevents this occurring because most metabolic disorder related pathologies fall in the category of '*Kaphaja Rogas*', *Kapha* imbalance driven disorders and illnesses. When *Kapha* has been brought back in balance, health can be re-established on a long term basis. To discuss these results at a deeper level, three 'Laws of Regulation' are presented, along with principles of systems biology underlying them.

These establish the basic law of health: level of health related to quality of regulation of the system, so that optimal regulation maintaining optimal function equates with health. As a complex system, the human (and animal) physiology presents an intricate structure that can maintain itself at optimal levels of function, and optimal regulatory response to external challenge. Poor personal habits and lifestyle factors slowly degrade quality of regulation e.g. by accumulating stress, and/or moving *Doshas* out of balance. Conversely, health improvement strategies that restore *Doshas* to balance have long term health implications that studies over 3 months, 6 months, or even 1 year, can hardly begin to assess. Ayurveda treatments require a completely different strategy of assessment. In conclusion, all studies performed on the ability of TCAM systems of medicine to treat various pathological conditions require re-evaluation. New protocols are required to demonstrate the kind of effects described above.

# REVERSE PHARMACOLOGICAL APPROACH TO UNDERSTAND AYURVEDIC FORMULATION IN MANAGEMENT OF CHRONIC DIABETIC FOOT ULCER

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**Background.** An incidence of 25% of diabetic foot ulcers is estimated among all diabetics in their life time, with high reoccurrence rate of 60.5% within 31.5 months and among these 84% undergo lower leg amputation with a mortality rate of 46% after one year and 79% – after five years. Natural process of wound healing is a complex web of interconnected biomolecular events that includes homeostasis, modulation of inflammation, proliferation, angiogenesis and remodelling. *Sushruta* in his classical work of *Chikitsa sthana dwivraniyaadhyaya* has defined the wound (*Vrana* in Ayurveda) as destruction, break, rupture or discontinuity in any body tissue or part of the body. Case studies have shown that an effective option in management of diabetes foot ulcers is through Ayurvedic formulations.

**Materials and methods.** We evaluated existing knowledge on different types of endogenous or exogenous, acute and infected or non-infected granulating healing wound and traumatic wounds.

**Results.** In Ayurveda classical texts we found references on more than 60 different types of intervention, 164 medicinal plants, 24 metals and minerals, and 18 animal products. A very strong reference on increased incidence of diabetic wound due to diabetes complication called *Prameha Pitaka* has been mentioned. Web-based literature search has showed that there are an ongoing research programmes aiming to meet challenges of identifying the active fractions in the plants as well as formulation and to create research-based evidence on whether whole herbs or extracted compounds are better. The use of new technologies, in field of molecular biology, analytical chemistry and experimental pharmacology is giving more and more convincing rationale behind the traditional science. Inspired by this case study and by utilising the concept of reverse pharmacology we designed an elaborated preclinical and clinical study.

**Conclusions.** Ayurveda probably is one of the earliest codified systems of biomedicine in the world history. A major hypothetical advantage of botanicals over conventional single-component drugs is the presence of multiple active compounds that together can provide a potentiating effect that may not be achievable by any single compound.

# THE FIRST *IN VITRO* STUDY ON AYURVEDIC FORMULATION IN EUROPE

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**Background.** With the increasing implementation of integrative medicine there is an obvious need for scientifically validated studies on Ayurvedic formulations in Europe. *Jathyadi Thailam* is polyherbomineral formulation used since ancient times for chronic wound, incl. diabetic foot, treatment.

**Purpose.** The aim of this study is to initiate an effective collaboration between academic research and industrial partner, involving specialists in Ayurveda, to explore the efficacy of the traditional Ayurvedic formulation and its modifications. The preliminary results indicated the need for modification of *Jathyadi Thailam* for further studies *in vitro*.

**Materials and methods.** The extracts of formulation were obtained using the reverse pharmacology method and processed further for microbiological and cellular studies *in vitro*. The original formula was modified by preparing the lamellar gel phase emulsion and change in active herbal compounds.

**Results.** Initially, the antibacterial and cell proliferating effect was shown *in vitro* for several fractions of *Jathyadi Thailam*. Lamellar gel emulsion was more applicable for *in vitro* studies, however, that phase of the study needs more investigations.

**Conclusions.** As the next phase, the preclinical and clinical studies will be carried out on Latvian patients with diabetic ulcers.

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## ANTI-INFLAMMATORY EFFECTS OF *JATYADI THAILAM* PLANT EXTRACTS *IN VITRO*

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**Introduction.** Diabetic foot ulcer is one of the most common complications of diabetes mellitus. In the diabetic foot the process of wound healing is impaired and associated with inflammation, immune cell infiltration and increased production of proinflammatory cytokines and chemokines. *Jatyadi Thailam* is Ayurvedic herbal oil with antimicrobial properties which has been used in traditional medicine for the treatment of non healing wounds, burns, ulcers and eczema.

**Objective.** The present study evaluated the effects of polar and nonpolar plant extracts of *Jatyadi Thailam* on anti-inflammatory activities in lipopolysaccharide (LPS) stimulated peripheral blood mononuclear cells (PBMC).

**Methods.** PBMC were freshly isolated from peripheral blood of healthy donors using vacutainer cell preparation tubes. Cells were seeded into cell culture plate at the density  $2 \times 10^6$  cells/well and stimulated with  $1 \mu\text{g/ml}$  LPS in the presence or absence of *Jatyadi Thailam* nonpolar ( $50 \mu\text{g/ml}$ ) and polar ( $10 \mu\text{g/ml}$ ) plant extracts for 4h. Inflammatory cytokines and nuclear factor-kappaB (NF- $\kappa$ B) transcription factor gene transcripts were evaluated by quantitative real time PCR.

**Results.** LPS stimulation markedly upregulated proinflammatory cytokines interleukin- 6 (IL-6), IL-8 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) gene expression in PBMC. Nonpolar extracts of *Jatyadi Thailam* almost completely abolished the LPS- stimulated IL-6 (by 98%), IL-8 (by 90%) and TNF- $\alpha$  (by 97%) expression. Furthermore, nonpolar extract treatment led to the suppression (by 40%) of LPS- induced expression of inflammation associated transcription factor -NF- $\kappa$ B.

However, the polar plant extract of *Jatyadi Thailam* was not able to modulate cytokine expression.

**Conclusions.** These findings indicate that nonpolar fraction of *Jatyadi Thailam* plant extracts exhibited potent anti-inflammatory properties by suppressing LPS- stimulated proinflammatory gene expression.



# INTEGRATIVE MEDICINE

## PART II

### STRENGTHS AND WEAKNESSES OF INTEGRATION

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Prevailing discussions of what we call “Integrative Medicine” are based on a poorly thought out concept of what integrative medicine actually is.

This presentation will attempt to take the discussion to a deeper level.

The author proposes that what most people call “Integrative Medicine” is actually Holism, rather than a true amalgamation of Holism and Reductionism, and he suggests how to combine them to create a truly Integrated Medicine.

# CAN WE USE EXPANDED CATEGORIES BASED ON INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH (ICF) FOR QUICK UNDERSTANDING OF TRADITIONAL CHINESE MEDICINE (TCM)?

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**Background.** TCM and Western medicine adopt different viewpoints and methods to conduct research and explore the science of human life patterns. In comparison with Western medicine and modern science, the basic characteristics of TCM theory are abstract and indistinct, based on the notion of harmony and balance, and employing the ideas of moderation and prevention. For western medicine doctors, it is complicated to understand the TCM philosophy and diagnostics, even more for research. ICF is commonly used to define and measure the components of health, its main determinants of health include the social and economic environment, the physical environment, and the person's individual characteristics and behaviors. Taking diabetes mellitus as example, we tried to expand the usage of ICF categories for quick diagnostics and prescriptions in TCM and even for integrative research.

**Purpose.** The aim of the current study is to make the connection between the clinical symptoms of TCM to the expanded category of ICF, so that to establish one more effective way for diagnosis and treatment.

**Materials and methods.** The ICF Core Set for Diabetes Mellitus is used as the base for expanded categories, since it is developed by World Health Organization as a standard language and framework for the description of health and health-related states. The "Clinical Fundamentals of TCM" published by State Administration of TCM of the Peoples Republic of China was used as standard language to describe specific symptoms of diabetes mellitus of TCM.

**Results.** According the traditional Chinese medicine theory, TCM "Zheng" (or pattern) is an analysis on disease presentation by TCM practitioners. "Zheng" classification is a traditional diagnostic method to categorize patients' syndromes based on their presented conditions. By splitting all the related syndromes of "Zheng", we make the connection between each of that to the expanded category of ICF.

**Conclusions.** Eventually it is possible for anyone to use the expanded categories to make the TCM diagnostic pattern for clinical use or research application, simply by recording the exact symptoms of diabetes patient. Our finding gives the opportunity to western medicine doctors to be more effective for diagnosis and treatment so as to promote the development of the theories of TCM.

# IMAGE MEDICINE AS A PART OF QIGONG THERAPY AND TRADITIONAL CHINESE MEDICINE

*Edgars Vasilevskis*

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Image medicine (IM) is considered as a old family and natural medicine system and the part of Traditional Chinese medicine (TCM). IM is often used by qigong practitioners. Image Medicine like TCM is based on integration of energy, information and physical body. IM includes three parts: theory, system of diagnostics and treatment system and is based on such methods and theories of famous doctors Bian Que and Hua Tuo as the “inner vision” and “image pulse diagnosis”. Diagnostics and treatment methods of IM are simple, painless, harmless, no side effects and reactions.

The IM and qigong practitioners developps his own abilities to visualize images and transfer information with help of images. During the pulse diagnosis Image therapist make a diagnostics of internal organs images, structures and functions of organism. After obtaining and analyzing images, IM treatment is based on simultaneous changes of energy and image in different structures of the body.

In 2015, we performed a controlled clinical study in Latvia to evaluate the IM treatment effect in 4 disease groups: diabetes, asthma, migraine and arterial hypertension. The results confirmed the high efficiency of IM.

# PANCHABHAUTIK APPROACH IN AYURVEDIC DIAGNOSIS

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According to the principles of Ayurveda, the universe is made up of the Panmahabhutas i.e. the 5 elements – namely Ether, Air, Fire, Water and Earth. These elements are the building blocks of the nature and are responsible for all the physical existence. Human body is also a part of this physical existence and is made up of these 5 elements.

Though the functioning of human body and its anomalies are explained by “Tridosha Siddhanta”, the foundation of Ayurveda, a Panchabhautik (5 elemental) approach makes it easier to understand the basic principles of Ayurveda. This approach also assists in understanding, diagnosing and treating the diseases from an Ayurvedic perspective.

Through this presentation, the relation between the Tridoshas and the Panmahabhutas is explained. Furthermore, the Panmahabhautik approach and its application in the diagnosis and treatment of the diseases are also explained.

# INTEGRATING AYURVEDA MEDICINE AT THE CHARITÉ MEDICAL UNIVERSITY BERLIN

***Elmar Stapelfeldt***

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Over the last two decades, Ayurveda Medicine developed considerably in European countries. But in order to gain recognition by the scientific fraternity and consequently by the authorities of national health care systems, it is a must to establish Ayurveda in medical universities. At the Charité Berlin – Europe’s largest Medical University – first steps in this direction have been taken.

Financed by the Indian Government (Ministry of AYUSH) a clinical trial on osteoarthritis of the knee has been conducted with rigorous EBM standards. Over a period of 4 years, 150 patients have been treated. The results are highly significant and are in the process of publication in a renowned research journal. This trial might serve as a blueprint to generated data on the effectiveness of Ayurveda Medicine in order to foster its development in Western countries. The lecture will summarize the design, execution and results of the trial. Furthermore, it will discuss the key learnings on how Ayurveda can be integrated in Western University settings.

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# INTEGRATIVE MEDICINE

## PART III

### **VASTU SHASTA – THE AYURVEDA FOR LIVING AND WORKING SPACES.**

***Mark Rosenberg,***

*CEO, European Academy for Ayurveda, Birstein, Germany*

The concept of *Vastu Shastra* assumes that the energy of a space influences the well-being of the people who live and work in it. Factors such as the compass direction, the proportions of a house and the building site play a role, as do the materials used. And just like in Ayurveda, *Vastu Shastra* considers the balance of elements as vital for a good state of health. As a result, *Vastu Shastra* experts strive for harmonizing the distribution and characteristics of elements when they work with clients in the context of a therapy. This is possible because the elements are assigned to both the cardinal points and the Doshas (the three biodynamic energies known in Ayurveda). Thus, the right placement of rooms can support certain activities or a person's individual constitution. For instance, a bedroom in the southwest promotes a restful sleep, while an office in the northwest facilitates communication and sales activities. Even Dosh disorder can be balanced to a certain extent by moving a sleeping room, to a balancing position in the *Vastu* matrix. Health can be promoted by the space around us. As such it is a tool of therapy in the traditional Ayurvedic system of Healthcare in India.

In his lecture, Mark Rosenberg will explain the basic principles of designing living spaces by *Vastu Shastra*, as the benefits of this ancient science are worth being integrated into modern times.

## AYURVEDIC DIET: FOOD AS FOOD – FOOD AS MEDICINE

***Kerstin Rosenberg***

*European Academy for Ayurveda, Birstein, Germany*

A balanced nutrition is an important element in Ayurvedic medicine. Ayurvedic dietetics comprise differentiated knowledge about the effect, quality and influence of the food on the Doshas, Agni and Dhatus, thus providing an effective therapy for the treatment of physical and mental disorders. In the process, the selection of the appropriate food has to be considered alongside with the preparation method and the composition both of the menu and of the individual food products. For the European doctor or therapist, it is an additional challenge to transfer an authentic Ayurveda diet to domestic foods as well as to modern nutritional and lifestyle habits.

The experienced Ayurveda specialist and book author Kerstin Rosenberg has a long-time experience in the practical application, implementation and teaching of Ayurvedic nutrition, cookery and dietetics. In her lecture “Food as food – food as medicine”, she will introduce the basic principles and systematics of Ayurveda dietetics and show how the traditional Ayurveda nutrition and health recommendations can be applied to domestic food, herbs and nutritional habits.

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# SURGERY, GYNECOLOGY, ANESTHESIOLOGY, ONCOLOGY

## 1. EVALUATION OF POST OPERATIVE ANALGESIA METHODS FOR TOTAL SHOULDER REPLACEMENT SURGERY

*Rūdolfs Jānis Vīksne*<sup>2</sup>, *Māra Klibus*<sup>1</sup>, *Aleksejs Miščuks*<sup>2,3</sup>, *Iveta Golubovska*<sup>1,2,3</sup>,  
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**Background.** Total shoulder replacement surgery is associated with mild to severe post-operative pain that lasts for up to 48 hours and is particularly severe during movement. Local infiltration analgesia (LIA) technique is one of the analgesic methods along with brachial plexus block. LIA technique involves infiltration of the wound during surgery with local aesthetic (Ropivacaine) along with an adjuvant (e.g. epinephrine). Brachial plexus block technique involves injection of local analgesic in close proximity to the nerves of the brachial plexus.

**Purpose.** Evaluate methods of multimodal post-operative analgesia after total shoulder replacement

**Materials and methods.** 37 patients scheduled for total shoulder replacement surgery were randomized into one of the 3 groups. First group consists of 15 patients with plexus brachialis block (Ropivacaine 0.2% 40ml) and general anesthesia. Second group consists of 12 patients with LIA method receiving general anesthesia + Ropivacaine 0,2% 112-187 ml combined with Epinephrine. The third group with 10 patients received general anesthesia only. After surgery all three groups received multimodal analgesia which included Acetaminophen, Naproxen and also Morphine only if VAS (visual analogue scale) scale was higher than 4 (0-10).

**Results.** Our results show that 2 hours after surgery patients in plexus brachialis block group required less morphine than the control group ( $p=0.029$ ).

Patients in plexus brachialis group felt less pain than the control group 8 hours after the surgery ( $p=0.045$ ).

**Conclusions.** The results are still preliminary and indicate that brachial plexus group provides slightly better analgesia in first few hours after surgery. Due to small amount of annual total shoulder replacement surgeries, the research is still ongoing and requires more data to distinguish the best method of analgesia.



## 2. EFFICIENCY OF THE TRUST PERIOPERATIVE BLOOD TRANSFUSION PREDICTING SCALE IN PATIENTS UNDERGOING OPEN HEART SURGERY

*Leonids Solovjovs<sup>1</sup>, Agnese Ozolina<sup>1</sup>, Agnese Zdanovska<sup>1</sup>, Tatjana Mikijanska<sup>2</sup>, Eva Strike<sup>1,3</sup>*

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**Background.** Allogenic blood transfusions are associated with poor outcomes in terms of postoperative morbidity and mortality. In elective cardiac surgery, preoperative risk assessment is essential. It allows to avoid allogenic blood transfusion and may inform optimal and consistent application of blood management.

**Purpose.** To evaluate efficiency of the TRUST scale in elective patients undergoing open heart surgery.

**Materials and methods.** After ethical approval, totally 172 adult patients (mean age  $66 \pm 11$  years) scheduled for elective cardiac surgery in Pauls Stradins Clinical University Hospital, were enrolled into a retrospective study. Data were collected from medical histories. Exclusion criteria: cardiopulmonary bypass time  $>120$  minutes; reoperation; thrombocytopenia and/or coagulopathy; off-pump cardiac surgery. Parameters in TRUST scale were recorded: type of surgery, age and body weight, preoperative haemoglobin (Hb) g/dl, gender, creatinin in parallel with requirement of haemotransfusions and length of stay in intensive care unit (ICU) and in hospital. For each patient TRUST score was calculated. Descriptive statistics for analysis of baseline demographics and clinical data were used. We evaluated the sensitivity and specificity of TRUST scale to predict allogenic blood transfusions by using receiver operating characteristic (ROC) curve analysis. Person correlation coefficient was applied. We defined  $P < 0.05$  as statistically significant. As a primary outcome allogenic blood transfusions during the perioperative period were analysed. A secondary outcome, the length of stay in ICU and hospital were determined.

**Results.** 47 patients were excluded. Of the 125 (females 68) remaining patients 54 (43.2%) had aortocoronary bypass grafting, 47 (37.6%) valve replacement, 11 (8.8%) combined and 13 (10.4%) other type of surgery. Fourteen out of 125 had TRUST score 0 points, 19–1 point, 30–2 points, 29–3 points, 24–4 points, 7–5 points and 2–6 points. The highest rate of hemotransfusions was detected in patients with 4 and 5 TRUST score points, (24/14) 56% and (7/5) 71% received allogenic blood transfusions, respectively. Totally 30 patients (24%) received haemotransfusions, presenting preoperatively older age ( $p = 0.005$ ), lower body weight, Hb, Ht levels ( $p < 0.001$ ), lower red blood cell ( $p = 0.001$ ) and platelet count ( $p = 0.016$ ). Age  $<67$  years (AUC = 0.7;  $p=0.01$ ), body weight  $<75$  kg (AUC = 0.8;  $p < 0.001$ ), Hb  $<133.5$  g/dL (AUC = 0.8;  $p < 0.001$ ) and female sex (AUC = 0.7;  $p < 0.001$ ) were independently associated with postoperative haemotransfusions. Creatinin showed AUC = 0.56 without reaching statistical significance ( $p=0.3$ ) in predicting haemotransfusions. The transfusion rate of red blood cells (RBC) correlated with TRUST score rate,  $r = 0.408$ ,  $p<0.001$ . Higher TRUST score were not associated with longer stay in ICU  $r = 0.17$   $p>0.1$ , but associated with longer hospital stay  $r = 0.182$   $p<0.05$ .

**Conclusions.** TRUST score could be a helpful tool in assessment of elective open heart surgery patients. Age, body weight and preoperative Hb levels may be the most informative values.

### 3. FEATURES OF THE PATHOGENESIS AND DEVELOPMENT OF LOCOREGIONAL RECURRENCE OF BASAL CELL CARCINOMA IN THE CERVICAL – FACIAL REGION

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**Background.** Basal cell carcinoma (BCC) is one of the most topical problems of modern oncology. In recent years, the frequency of the disease in many countries is increasing, and despite the diversity of treatments BCC recurs in 20%–40% of cases within the first two years, regardless of the chosen method of treatment.

**Purpose.** The aim of our work is to study the features of the pathogenesis and recurrence of BCC in cervical – facial region, analyzing dermatoscopically and morphologically tumor and perifocal tissues. Identify the relationship between prone to recurrence morphological types of tumor and histological features, which will allow to reduce the risk of recurrence in the future.

**Materials and methods.** Investigated 35 biopsies taken from the surgical specimens of patients with BCC. Clinically, in 11 cases were diagnosed nodular form, infiltrative form in 7 cases, in 5 cases superficial form and in 5 cases BCC with metaplasia. Investigating skin tumor dermatoscopically in 2 cases was diagnosed BCC that evolved on the actinic keratosis and histologically interpreted as BCC with metaplasia. Dermatoscopic analysis is made by dermatoscope Dermlite DL3N with Pigment Boost function.

**Results.** According to the first results of the study, in 5 cases histologically was found BCC with squamous metaplasia, however, in dermatoscopical study there was no evidence of structures that would distinguish BCC with metaplasia from BCC without it, but we could expect aggressive BCC type in tumors which formed on the background of actinic keratosis and for patients with telangiectasia on the skin of the nose and cheeks. Examining the extent BCC histologically invasion in cases of aggressive tumors observed decreased expression of laminin and collagen type IV in the basal membrane, which is planned to verify for all major forms of BCC, as well as to correlate these parameters with the expression of tissue-remodeling enzymes – metalloproteinases.

**Conclusions.** Superficial BCC often misdiagnosed as dry skin, eczema or actinic keratosis. The greatest prognostic value in dermatoscopical study of BCC are vascular structures. For infiltrative type of positive predictive value are arborizing blood vessels and short thin telangiectasia. Availability of the telangiectasia in perifocal tissue with infiltrative form can be regarded as a prognostic test that indicates the propensity for aggressive and recurrent course of BCC. The study of vascular structures, based on the use of instrumental methods in combination with the study of tissue changes, including tissue and barrier properties is a rationale.

#### 4. THE PATTERN OF TIBIAL ARTERY RUN-OFF IN PATIENTS WITH LONG SEGMENT POPLITEAL ARTERY STENTING

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**Background.** Endovascular therapy for popliteal lesions has gained the increase in procedure amounts since the appearance of the dedicated popliteal stents. Nevertheless, there is still a debate on whether postprocedural tibial vessel run-off pattern has an impact on popliteal stent patency rates.

**Purpose.** The aim of this study was to gather data about postprocedural tibial run-off pattern in patients with stented popliteal artery to create basis for further patency studies.

**Materials and methods.** We analyzed 29 patients with long segment stenting of popliteal artery in year 2015–2016 in our tertiary care hospital. The number of postprocedurally patent tibial run-off arteries below the stent level was evaluated.

**Results.** In 12 (41%) patients there was patent only one tibial artery: in 50% of cases – anterior tibial artery, 42% – peroneal artery, 8% – posterior tibial artery. In 13 (45%) patients there were patent two tibial arteries: 54% – anterior tibial artery, 85% – peroneal artery, 62% – posterior tibial artery. In 4 patients, all three major tibial arteries were patent.

**Conclusion.** In patients with long segment popliteal artery stenting there is a tendency for poor – one or two tibial arteries – run-off. Further studies have to be conducted to evaluate the influence of this finding on popliteal stent patency rate.

## 5. URETHRAL PRESSURE PROFILOMETRY DATA CORRELATION IN WOMEN WITH DIFFERENT TYPES OF URINARY INCONTINENCE

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**Background.** Urinary incontinence (UI) is a pathological condition found on average in 25–45% of women of any age. The selection of UI treatment and its effectiveness mostly depends on the pathophysiological mechanism, i.e., the type of UI. The type of UI can be identified by taking the history, filling out questionnaires and performing objective diagnostic procedures, known as urodynamic studies (UDS). UDS is viewed as the gold standard for objective diagnostics and interpretation of lower urinary tract dysfunction, especially when there are ambiguous complaints and before planning surgical treatment for UI. Urethral pressure profilometry (UPP) remains among the least investigated and somewhat controversial urodynamic tests. There are still no clearly defined measurable criteria for the characterisation of urethral function.

**Purpose.** The aim of the study was to analyse the correlation of subjective complaints and UPP data in women with different types of UI: stress urinary incontinence (SUI), urge urinary incontinence (UUI), and mixed urinary incontinence (MixUI) and establish whether UPP data may help to distinguish between different types of UI, which is necessary for effective treatment of UI.

**Materials and methods.** A study group of 405 women with complaints about UI were surveyed (UDI-6; ICIQ-UI), to determine the subjectively dominant type of urinary incontinence, and UPP was performed for all these women. The variables analysed by UPP were: the maximum urethral closure pressure at rest (MUCPrest), maximum urethral closure pressure at cough stress (MUCPstress), functional urethral length at rest (FULrest), functional urethral length during cough stress test (FULstress), pressure transmission ratio (PTR). The statistical variation between different groups of UI patients was calculated for all the analysed variables.

**Results.** The value of PTR was statistically significantly higher in the group of patients with isolated UUI, compared to the SUI and MixUI groups. The MUCPrest and MUCPstress values were consistently lower in women with isolated SUI, compared to isolated UUI. The FULrest and FULstress values showed no statistically significant difference between the groups with different types of UI.

**Conclusions.** The PTR value is a result of UPP test that allows to distinguish objectively between UUI, SUI, and MixUI. The PTR value can be used to characterise the hypermobility of urethra. The MUCPrest and MUCPstress values are consistently lower in women with isolated SUI, compared to those with isolated UUI. MUCP can be used as an objective criterion for differentiation of these two groups of patients.

## 6. NEUROLOGICAL OUTCOMES IN PATIENTS WITH OUT-OF-HOSPITAL CARDIAC ARREST ACHIEVING RETURN OF SPONTANEOUS CIRCULATION

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**Introduction.** Despite rapid development of technologies in emergency medicine and reanimatology, the prognosis of patients suffering from sudden cardiac arrest still is doubtful.

**Purpose.** The objective of the study was to assess the mortality and survival rates of patients suffering from out-of-hospital sudden cardiac arrest with achieved return of spontaneous circulation (ROSC) and to evaluate the neurological outcome of patients at the time of discharge from hospital.

**Materials and methods.** 206 patients undergoing cardiopulmonary resuscitation (CPR) according to Advanced Life Support algorithms with achieved ROSC at pre-hospital settings and who were admitted either in Pauls Stradiņš Clinical University Hospital or Rīga Eastern Clinical University Hospital "Gaiļezers" were included in this study. The medical documentation of patients was analysed retrospectively (electronic medical records of State Emergency Medical Service of Latvia and hospital medical histories). The neurological outcomes of patients who survived until discharge from hospital were evaluated according to Cerebral Performance Category (CPC) scale based on records in patient medical histories. Statistical analysis of data was performed by using *Microsoft Excel* and *IBM SPSS 20.0* software.

**Results.** The average age of patients was  $63,94 \pm 15,67$  SD years. In 64,6% the main diagnosis was cardiovascular disease, 8,2%- neurological or neurosurgical disease, 2,9% – sepsis or septic shock, 14,6%- conditions after influence of external factors, 9,7% – other diseases. The average duration of CPR performed in pre-hospital settings was 16,16 minutes. In 59,2% there was recurrent cardiac arrest at the hospital. 33,3% of patients survived less than 24 hours after admission to hospital, 23,2% survived more than 24 hours, but did not survive until discharge. 42,5% of patients were discharged from hospital, of which 44,3% of cases the neurological state was ranked with CPC – 1, 30,6% – CPC-2, 18,1% – CPC-3 and 6,8% – CPC-4. There were found no statistically significant correlation between the cause of cardiac arrest, initially detected rhythm or duration of CPR in pre-hospital settings and neurological outcome ( $p= 0,124; 0.098$  and  $0.097$ , respectively).

**Conclusions.** The rates of survival in patients with achieved ROSC in pre-hospital settings are relatively low. The most part of patients who survived until discharge of hospital had satisfactory neurological outcomes with none or mild to moderate consequences (CPC – 1, CPC-2). Although no statistically significant correlations were found, it was observed that neurological outcome tends to be better, if initially detected rhythm is shockable (ventricular fibrillation and pulseless ventricular tachycardia) and if the duration of CPR is shorter.

## 7. TREATMENT OF BENIGN SKIN TUMORS USING THE PLASMA GENERATING DEVICE *PLEXR*<sup>®</sup>

*Ingrīda Rītiņa*<sup>1</sup>, *Silvestrs Rubins*<sup>2</sup>, *Andris Rubins*<sup>2</sup>

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**Background.** For dermatologists and aesthetic medicine specialists choosing the treatment method of benign skin tumors (B.S.T.) is an important matter. Benign skin tumors are papilloma, dermatofibroma, xanthelasma, dermal nevus, milia. They are not threatening human health, but present aesthetic discomfort by unsightly appearance of the skin. Patients see experts for their removal on medical or aesthetic grounds. For doctors and patients is important to choose safe and effective procedure for following the rehabilitation period would be shorter, not remain after healing scars and pigmentation disorders.

**Purpose.** To assess the efficiency and convenience of the method of destruction B.S.T. using the plasma generating device *Plexr*<sup>®</sup>.

**Materials and methods.** The group of 363 patients was selected wishing to remove B.S.T. Each of them was examined visually and using a dermatoscopy. The procedure of destruction of 373 B.S.T. made using the device *Plexr*<sup>®</sup> by point interrupted exposure combined with continuous “spray” technique.

**Results.** 2 years had made 373 B.S.T. tissue sublimation procedures, of which 156 were papillomas, 36 dermatofibromas, 8 milliums, 8 sebaceous cysts, 23 seborrheic keratosis, 49 dermal nevus, 13 syringomas and 24 xanthelasmas on the eyelids and around the eyes, 56 warts on the extremities. After manipulation, the healing process was 7 to 10 days. After 2 months of tissue sublimation sites, it had no visible scars and pigmentation disorders. Repeated procedures were performed only in 2 (0,54%) cases.

**Conclusions.** The results convincingly demonstrate the new treatment methods of benign skin tumors by using the device *Plexr*<sup>®</sup> is effective, the maximum controllable and safe handling even making eye area and on the eyelids. The advantages are fewer pain sensations, fast healing process, not traumatized surrounding tissue and prognostic fewer repeat treatments.

## 8. LAPAROSCOPIC TRANS ABDOMINAL PRE-PERITONEAL (TAPP) REPAIR OF INGUINAL HERNIA USING SELF-GRIPPING MESHES

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**Background.** TAPP is one of the recommended methods for inguinal herniorrhaphy. It is known that mesh mechanical fixation is associated with pain; moreover, fixation devices increase operation costs. Using self-gripping meshes without fixation is a good alternative.

**Methods.** 77 patients with were operated with TAPP method. The self-gripping mesh with multiple resorbable polylactic acid microgrips on one side was used. Follow-up was done by phone and by visit. Complications, hospital stay, discomfort, pain (VAS-visual analogue scale), foreign body feeling, recurrence and satisfaction with procedure were assessed.

**Results.** Median patients' age was 53 (IQR=63-43) years. None of patients had postoperative complications. Mean follow-up was 19 months with maximum 53 months. There were no recurrences. Most patients were highly satisfied with operation (10 points of 10 possible) and all (77) patients would recommend this operation to others. 56 patients had follow-up 1 year and more. After 1 year, only 2 (3.5%) had mild inguinal pain (1-3 VAS), 2 (3,5%) had mild or moderate discomfort during physical activities and 1 (1,8%) had non-constant foreign body feeling. None of patients had discomfort in rest, severe or moderate pain and skin sensitivity problems.

**Conclusions.** Our study demonstrates that TAPP inguinal hernia repair using self-gripping mesh is a safe technique with low chronic pain and recurrence rates. This method is cost-effective because of non-expensive mesh and no requirement of mechanical fixation.

# POSTER PRESENTATIONS

## BASIC MEDICAL SCIENCES, PHARMACOLOGY, PATHOLOGY AND REGENERATIVE MEDICINE

### 1. PROGNOSTIC SIGNIFICANCE OF SELECTED MORPHOLOGICAL AND CLINICAL CHARACTERISTICS IN GLIAL TUMOURS

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**Background.** Glial tumours are the most common primary intracranial neoplasms, which represented up to 50–60% of all tumors. Gliomas are classified, according to their histologic features into three major types: astrocytomas, oligodendrogliomas, and mixed oligoastrocytomas based on similarities to mature glial cells. These tumors are notoriously refractory to conventional radiotherapy and chemotherapy, and the prognostic outlook for patients with high-grade gliomas is usually dismal. In addition, many patients present initially with a low-grade glioma that, in the majority of cases, progresses with time to high-grade.

**Purpose.** The purpose of the study was to compare prognostic significance of different morphological and clinical characteristics of glial cell tumors.

**Materials and methods.** Altogether 93 patients who underwent surgical treatment at Riga East University hospital during 2012–2014 were retrospectively enrolled in the study. The study was approved by a local ethical committee. The tissue samples were investigated by histological and immunohistochemical staining methods. The clinical data and morphological imaging were evaluated. The statistical analysis (including correlative and survival analysis) was performed.

**Results.** 93 patients were enrolled in the study. 50 patients were females and 43 patients were males. The average age of patients was  $47 \pm 27$  years. The most common tumour types were glioblastoma (WHO Grade IV), anaplastic astrocytoma (WHO Grade III) and anaplastic oligoastrocytoma (WHO Grade III).

Glioblastoma, anaplastic oligodendroglioma, anaplastic astrocytoma predominantly had multinodular growth pattern. At contrast, oligodendroglioma, oligoastrocytoma and gliosarcoma had solitary growth pattern. The positive correlation between patient age and tumour multinodular growth pattern was demonstrated ( $Rho = \pm 0.21$ ;  $p=0.04$ ). High-grade tumours, increased mitotic index, increased cellularity and increased Ki-67 index had an unfavourable influence on overall, five years survival and disease free survival ( $p<0.01$ ). Other histological parameters such as nuclear atypia, necrosis and microvascular proliferation did not alter the overall, five years survival and disease free survival.

**Conclusions.** The selected morphological and immunohistochemical characteristics correlated with tumour clinical and imaging characteristics and represented prognostic features of glial tumours



## 2. INFLUENCE OF METABOLIC PROCESSES ON TUMOR PROLIFERATION *IN VITRO*

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**Background.** Most cancer cells produce energy by increasing aerobic glycolysis even in the presence of oxygen. This phenomenon is often referred as the Warburg effect. Dichloroacetate (DCA), a well-established drug used in the treatment of lactic acidosis, was observed to reverse the Warburg effect by inhibiting pyruvate dehydrogenase kinase (PDK) and indirectly activating the gate keeping enzyme pyruvate dehydrogenase (PDH). Briefly, DCA shifts aerobic glycolysis towards mitochondrial glucose oxidation in cancer cells thus forcing them to attain apoptosis. Metformin., a widely used oral anti-diabetic agent, has been shown to have a strong anti-proliferative effect in many breast cancer cell lines by targeting complex I of the electron transport chain and leading to an accumulation of reactive oxygen species (ROS).

**Purpose.** The aim of this study was to investigate the anticancer effect of DCA and metformin. in breast cancer in vitro. We hypothesized that these two agents could synergistically potentiate cytotoxic effect and induce cancer cell apoptosis.

**Materials and methods.** MCF-7, MDA-MB-231, MDA-MB-468 breast cancer cells were treated with increasing DCA, metformin. and DCA-metformin. concentrations. The growth inhibitory effect of DCA, metformin. and DCA-metformin. was assessed by MTT assay. Apoptosis was analyzed using flow cytometry and metabolism of cells was analyzed using lactate assays.

**Results.** The inhibition of cell proliferation were dependent on drugs concentrations and were different comparing three breast cancer cell lines. We showed that DCA and metformin. combination potentiated apoptotic effect.

**Conclusions.** Novel therapeutic combinations such as DCA and metformin. give a good ground for expanding further investigations in breast tumors.

### 3. ULTRASOUND AND MECHANICAL SHOCK INDUCED VASCULAR RELAXATION

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**Background.** In 2015, the world's population of 60 years and older has reached 900 million. By 2050, population aged 60 years and older is expected to reach 2 billion. In the people group aged 65 and older cardiovascular dysfunction will take a place in more than 40% of all deaths and triple the cost of treatment. Thus focusing on the treatment of cardiovascular disease is a top priority. Ultrasound (US) based technologies have been successfully used in medicine, usually as a diagnostic tool. Attempts have been made to apply US as a therapeutic modality (e.g. intracoronary ultrasound plaque ablation). By establishing the vasomodulatory effects of ultrasound and mechanical waves, we provide the physiological basis for the development of therapeutic and rehabilitation devices exhibiting therapeutic effects via the aforementioned methods.

**Purpose.** The objective of the current study was to quantify the vasomodulatory effects of ultrasound and mechanical shock.

**Materials and methods.** 2 mm segments of rat (WISTAR) superior and small mesenteric arteries were dissected, isolated, and transferred into 4 °C physiological saline solution and mounted in myographs (model – 420A; DMT, Aarhus, Denmark) for functional studies. The arterial segments were stretched to their optimal lumen diameters for active tension development. Ultrasound waves and mechanical shock were applied on the vessels, precontracted with noradrenalin (NA). Acetylcholine-induced (10 μM ACh) relaxation was used as control and as proof of intact endothelial function. The changes in isometric tension were recorded. Vascular relaxation is presented as isometric tension and percentage change in mN from plateau of vascular contraction with NA. Data are expressed as median and interquartile range Mdn (IQR). Changes from baseline were evaluated using Wilcoxon Signed Ranks Test.

**Results.** 12 vessel segments were obtained from 4 Wistar male rats. The isometric tension (mN) decreased significantly in comparison to plateau (defined as peak isometric tension after contraction with NA) in the vessel segments exposed to: ultrasound waves – from 8.07 (1.74) mN to 6.44 (2.55) mN, 35.03 (32.55)%,  $p=0.001$ , to mechanical shock – from 10.94 (5.14) to 6.92 (3.39), 38.32 (21.95)%,  $p=0.002$  and in control from 17.55 (14.78) to 5.37 (13.29), 48.28 (58.09)%,  $p=0.043$ .

**Conclusions.** Ultrasound waves and mechanical shock induce vascular relaxation in rat mesenteric arteries and may have therapeutic applications.

**Acknowledgements/Funding.** *This work has been funded by a grant No. SEN-10/15 from the Research Council of Lithuania. Project acronym: “CaSpine”.*

#### 4. INFLUENCE OF CYCLOSPORINE AND EVEROLIMUS ON THE MAIN MYCOPHENOLATE MOFETIL PHARMACOKINETIC PARAMETERS. CROSS SECTIONAL STUDY

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**Background.** Patients, who have undergone kidney transplant surgery, are usually treated with more than one drug. Basic treatment strategy for these patients includes glucocorticoids, calcineurin inhibitors, immunosuppressive anti-metabolites (mycophenolate mofetil) and proliferation signal inhibitors. Controversy remains about the interaction between mycophenolate mofetil (MMF) and the calcineurin inhibitors cyclosporin (CsA). The need to double the dose of MMF in case of CsA co-administration to achieve the same mycophenolic acid (MPA) levels has been attributed [1].

**Purpose.** The Objective of the present study was to assess the effect of a cyclosporine (CsA) on the active mycophenolate mofetil (MMF) metabolite mycophenolic acid (MPA) pharmacokinetic parameters and to compare with effect of everolimus.

**Materials and methods.** History records of 404 anonymised kidney recipients were reviewed. The main pharmacokinetic parameters ( $AUC_{(0-12)}$  and  $C_{max}$ ) of the MPA were evaluated.

**Results.** The higher mean dose of CsA displayed higher MPA  $AUC_{(0-12)}$  exposure, accordingly  $40.50 \pm 10.97$  hmg/L versus  $28.08 \pm 11.03$  hmg/L, ( $r_s$ )= .497 ( $p < 0.05$ ) in low MMF dose group (1000 mg/day);  $43.00 \pm 6.27$  hmg/L versus  $28.85 \pm 11.08$  hmg/L, ( $r_s$ )=0.437 ( $p < 0.01$ ) in medium MMF dose group (2000 mg/day) and  $56.75 \pm 16.78$  hmg/L versus  $36.20 \pm 3.70$  hmg/L, ( $r_s$ )=0.608 ( $p < 0.05$ ) in high MMF dose group (3000 mg/day). Positive correlation was also observed between the higher mean dose of CsA and MPA  $C_{max}$ , accordingly  $C_{max}$   $22.83 \pm 10.82$  mg/L versus  $12.08 \pm 5.59$  mg/L, ( $r_s$ )=0.507 ( $p < 0.05$ ) in low MMF dose group and  $22.77 \pm 8.86$  mg/L versus  $13.00 \pm 6.82$  mg/L, ( $r_s$ )=0.414 ( $p < 0.01$ ) in medium MMF dose group.

The comparative analysis between two study lines (MMF + CsA and MMF + everolimus) showed that MPA  $AUC_{(0-12)}$  exposure was 43% higher in patients treated by medium dose MMF and everolimus than in patients treated by medium dose MMF and CsA.

**Conclusions.** Study results showed that co-administration of CsA has an impact on the main MPA pharmacokinetic parameters in a CsA dose-related manner. The use of a low CsA dose (<180 mg/d) reduces MPA  $AUC_{(0-12)}$  exposure under the therapeutic window and may lead to ineffective therapy, while the use of a high CsA dose (>240 mg/d) is related to greater than 10 mg/L MPA  $C_{max}$  and increases the likelihood of adverse events.

**References.** Cremers S, Schoemaker R, Scholten E, den Hartigh J, König-Quartel J, van Kan E, *et al.* Characterizing the role of enterohepatic recycling in the interactions between mycophenolate mofetil and calcineurin inhibitors in renal transplant patients by pharmacokinetic modelling. *Br J Clin Pharmacol.* 2005 Sep; 60(3):249-56.

## 5. CORRELATION STUDY BETWEEN LIFESTYLE, HABITS AND SALIVARY NITRITE LEVEL IN THE LATVIAN POPULATION

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**Background.** Nitrite is main nitric oxide (NO) metabolite as well one of the most important NO storage molecule in human tissues. It can be produced by oxidation of nitric oxide synthase synthesized NO or taken up by organic and inorganic compounds with food. Both nitrite metabolic ways are involved in nitrosation, nitrosylation, nitration of different protein and lipids. Thereby nitrite has significant impact on important signal transduction pathways, enzymatic processes, physiological functions and diseases.

**Purpose.** The objective of the current study was to find correlation between nitrite concentration in healthy people saliva and diet, oral hygiene, smoking, blood pressure, body mass index and common diseases.

**Materials and methods.** Altogether 67 healthy participants were enrolled to the study. 5 mL saliva was collected, as well volunteers were asked to fill form with questions about their lifestyle: diet, mouthwashes using, smoking, habits, common diseases and taking medicine. Blood pressure, pulse and weight also were measured. Using nitric oxide analyser NOA™ 280i, were measured nitrite concentration in saliva.

Used statistic methods IBM SPSS Statistics version 23.0

**Results.** It was discovered that there is significant correlation between gastritis and average nitrite concentration in saliva ( $p=0.04$  or  $p= 4.66 \times 10^{-2}$ ), unfortunately there was not found significant correlation between mouthwashes using and average nitrite concentration in saliva ( $p=0.52$ ).

**Conclusions.** The results show that there is no significant correlation between salivary nitrite and healthy human diet, mouthwashes using, lifestyle. But we see that salivary nitrite can work as indicator for some diseases, for example, gastritis and in future gastric ulcer indicator.

**Acknowledgements/Funding.** *The study was funded from the University of Latvia project “Proteasome genes structure, expression and pharmacogenomics study”.*

## 6. THE ROLE OF OXYGEN AVAILABILITY IN EMBRYONIC SKIN DEVELOPMENT

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**Background.** Oxygen transport is an important prerequisite for avascular epidermis development. Low levels of oxygen occur naturally during embryogenesis.

**Purpose.** The relationship between vasculogenesis in the dermis, hematopoietic ontogeny and development of the epidermis and its derivatives was examined.

**Materials and methods.** 6 embryos and 10 fetuses from 5 to 23 developmental weeks from embryological collection of the Department of Anatomy and Histology were studied. Tissue sections were stained with hematoxylin-eosin and S-100 protein antibody.

**Results.** By the end of the second month, hematopoiesis has switched from the extraembryonic yolk sac to the liver and bone marrow. Simultaneously the two-layered epidermis develops, consisting of basal layer and periderm. Until the 6<sup>th</sup> and 7<sup>th</sup> weeks of gestation, all embryonic erythrocytes are nucleated and located in a poorly developed dermal vascular framework. By the 12<sup>th</sup> week of gestation, nucleated red blood cell count decline and epidermis consists of three layers. During the 5<sup>th</sup> month of development the epidermis becomes more stratified. By the end of the 12<sup>th</sup> week, the major vascular organization of the fetal dermis is established and dermal arterioles and venules are able to be distinguished. Likewise, placental maturation begins and from this time to the end of the 5<sup>th</sup> month the remodelling of the endometrial blood vessels occurs, thus allowing for an expansion of vessels and as much as a 20-fold increase in the flow of blood into the intervillous space.

Around the 13–14<sup>th</sup> week, eccrine sweat gland anlagen are seen along the apices of the primary epidermal ridges (PER) on the palms. Merckel cells are seen in the PER around 16 weeks. S-100 positive myoepithelial cells and clear cells in the secretory portion of an eccrine sweat glands and S-100 positive Langerhans cells in the outer root sheath of the hair follicles and epidermis can be detected by 22 weeks. The first identifiable primordial hair follicles appear at about 9 weeks of age. The nail field becomes keratinized at 13 weeks and the nail plate completely covers the nail bed during the 5<sup>th</sup> month.

**Conclusion.** Our histological study showed that at the 5<sup>th</sup> month of gestation epidermis increases to five layers and is ready for keratinization, which begins after 20 weeks. Likewise, much of the derivatives of the epidermis were developed concurrently. These events closely correlate with significant improvement of fetal blood oxygen saturation in the placenta, erythroid maturation and final differentiation of dermal blood vessels.

## 7. CORNEAL TOPOGRAPHY AND VISUAL ACUITY CHANGES IN PATIENTS WITH KERATOCONUS AFTER CORNEAL SEGMENT IMPLANTATION

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**Introduction.** Keratoconus (KCN) is a progressive degenerative disease of the cornea, which results in the corneal tissue structural changes – the cornea becomes thin and conical. The process is usually bilateral, but asymmetric. This pathology usually affects young patients, and symptoms at an early age is prognostic unfavorable factor, which indicates the need for corneal transplantation in the future. There is a variety of therapeutic options in the treatment of keratoconus. One of the available techniques in Latvia is intrastromal corneal segment implantation.

**Purpose.** In a retrospective analysis of data, study visual acuity and corneal topographic changes after corneal segment implantation at keratoconus case.

**Materials and methods.** The study was conducted by Dr. Solomatin Eye rehabilitation and vision correction center in 2016. The study included 34 patients (42 eyes) (88% men, 12% women). The average age of the patients were  $29.6 \pm 3, 5$ . Patients with keratoconus were implanted with one or two segments in corneal stroma, which changes the front irregular corneal surface.

Patients been kept under strict control the next day after surgery and for 6 following months. Corneal surveyor "Pentacam" and "Atlas" were used to assess corneal topography changes in dynamics, as well as an objective evaluation of uncorrected and corrected distance visual activity remoteness.

**Results.** Compared corrected near visual acuity before surgery and 6 months after surgery, the average visual activity improved by 0.22 units (95% CI 0.17 to 0.27;  $p < 0.001$ ), as well as before surgery and 6 months after surgery corrected distance visual acuity average value is improved by 0.12 units (95% CI 0.07 to 0.17;  $p < 0.001$ ). Compared corneal topography examination before surgery and 6 months after surgery can be concluded that K1 (flattest curvature powers) decreased by 2,06 D (95% CI -2.97 – -1.15;  $p < 0.001$ ) K2 (steepest curvature powers) decreased by 1,65 D (95% CI -2.34 – -0.97;  $p < 0.001$ ) and Km ( $(K1 + K2) / 2$ ) by 1,88 D (95% CI -2.49 – -1.26  $p < 0.001$ ).

**Conclusions.** Corneal segment implantation for patients with keratoconus statistically significantly improves patient's uncorrected and corrected visual acuity, as well as significant changes in corneal topography, corneal curvature decreases.

## 8. THE EFFECTIVENESS OF HEPATIC STEATOSIS INDICES FOR PREDICTION OF NON-ALCOHOLIC FATTY LIVER DISEASE IN TYPE 1 DIABETES MELLITUS PATIENTS

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**Background.** Non-alcoholic fatty liver disease in type 1 diabetic are associated with cardiovascular events and complications. Markers of hepatic steatosis: fatty liver index – FLI and hepatic steatosis index – HSI have demonstrated reasonable efficacy in several patient groups, are cheap and easy to use.

**Purpose.** To screen the effectiveness of FLI and HSI for prediction of non-alcoholic hepatic steatosis in type 1 diabetic patients.

**Materials and methods.** 252 patients from prospective diabetic complications study “LatDiane” were analyzed. Patients with diabetes duration less than 5 years and with high-risk alcohol consumption were excluded. For remaining 201 patients, FLI and HSI indices were calculated. 40 patients with the highest and the lowest FLI/HSI values were invited for magnetic resonance study (MRI). A decrease in signal intensity in MRI was converted to numeric value corresponding to microscopic liver fat content. Accuracy of FLI/HSI was assessed from the area under the receiver operating characteristic curve (AUROC).

**Results.** 12 (30.0%) patients had liver steatosis confirmed by MRI. For FLI, sensitivity was 90%, specificity was 74%, positive likelihood ratio was 3.46, negative likelihood ratio – 0.14, PPV – 0.64; NPV – 0.93. For HSI, sensitivity was 86%, specificity was 66%, positive likelihood ratio was 1.95, negative likelihood ratio – 0.21, PPV – 0.50; NPV – 0.92. AUROC for FLI was 0.86 (95% confidence interval [0.72;0.99]); for HSI – 0.75 [0.58;0.91]. In multiple regression model, only CRP (p=0.038), GGT (p=0.047) and waist circumference (p=0.01) were independent determinants of microscopic fat content and together explained 45% of its variation (p=0.001). FLI values correlated with CRP, serum total cholesterol, ALT, AST, alkaline phosphatase, systolic and diastolic blood pressure. HSI values correlated with waist circumference and CRP. Parameters of insulin sensitivity were associated neither with indices, nor liver microscopic fat content. FLI ≥ 60 and HSI ≥ 36 were significantly associated with metabolic syndrome and nephropathy.

**Conclusions.** The tested indices can serve as surrogate markers for liver fat content and metabolic syndrome in type 1 diabetic patients, however broader studies are needed. CRP might be considered for development of novel biomarkers for liver steatosis assessment in type 1 diabetes.

**Acknowledgements/Funding.** *This project was elaborated in the Laboratory for Personalized Medicine at the Department of Internal Medicine, Faculty of Medicine, University of Latvia with support of the project “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”, Scientific Council of Roche Academy, and the Student Council of Faculty of Medicine, University of Latvia.*

## 9. GLYCEMIC CONTROL, FREQUENCY OF CHRONIC COMPLICATIONS AND HYPOGLYCEMIC EPISODES IN TYPE 1 DIABETES MELLITUS AND DEPRESSION GROUP

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**Background:** Depression is one of risk factors, triggering unsatisfactory *diabetes mellitus* (DM) control and causing development of DM complications, poor health-related quality of life and increased mortality.

**Purpose:** The aim of the study is to describe depression influence on glycemic control, as well as its association with DM complications and a number of hypoglycemic events. The tasks of the study are to reveal the relationship between depression and HbA1c, DM complications, hypoglycemic events, quality of life and bad habits.

**Materials and methods:** Cross sectional study on data from 254 patients with type 1 diabetes. Data were received from LatDiane: “Latvian diabetic nephropathy study”.

**Results:** Depression occurs in 17,1% of the participants. Compared to men, women are twice as likely to develop depression (24% vs. 11%;  $p=0,008$ ). 58% of the participants had 1-4 hypoglycemic episodes last 4 weeks. 40% of the participants in depression group had 5-8 hypoglycemic episodes last month ( $p=0,002$ ). The study found the biggest amount of the hypoglycemic episodes (>8 during last month) was associated with depression group (13,3% vs. 9,7%;  $p=0,002$ ). Fear of hypoglycemia commonly occurs in depression group (71,1% vs. 50,2%;  $p=0,008$ ).

Depression is associated with an increased risk of clinically significant microvascular and macrovascular complications: diabetic proliferative retinopathy (42,2% vs. 25,1%;  $p=0,043$ ), diabetic polyneuropathy (57,8% vs. 39,6%;  $p=0,031$ ), end-stage kidney disease (11,4% vs. 1,5%;  $p=0,007$ ).

**Conclusions:** Depression impairs DM compensation and cause development of DM complications. Depression is associated with more frequent hypoglycemic events and cause a fear of hypoglycemia. Depression impairs patients’ quality of life and contributes to every bad habit.

**Acknowledgements:** “LatDiane: Latvian diabetic nephropathy study” is supported by State Genome data base project and Latvian Association of Endocrinology. This project was elaborated in the Laboratory for Personalized Medicine at the Department of Internal Medicine, Faculty of Medicine, University of Latvia with support of the project “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”.



## 10. THE IMPACT OF OVERWEIGHT AND OBESITY ON THE DISEASE ACTIVITY IN PATIENTS WITH AUTOIMMUNE AND CHRONIC INFLAMMATORY ARTHRITIS TREATED BY ANTI-TNF DRUGS

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**Introduction.** It has been suggested that adipose tissue take role in the pathophysiology of chronic inflammatory arthritis (IA) induced by immune system and also can affect pharmacokinetic properties of drugs. The impact of overweight and obesity (usually characterized by body mass index (BMI)) during the antiTNF drug treatment of autoimmune and chronic IA such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA) still remains a challenge.

**Objectives.** We aimed to determine whether overweight and obesity affects disease activity in patients with IA treated by antiTNF drugs such etanercept (ETN) and adalimumab (ADA).

**Material and methods.** 53 patients (23 males, 30 females) with IA were included in cross-sectional study conducted in Pauls Stradins Clinical University Hospital from November 2016 to January 2017. The following parameters were chosen for the analysis: BMI, *disease activity score 28 used c-reactive protein* (DAS28crp) and the *Bath ankylosing spondylitis disease activity score* (BASDAI). Patients were split to two groups depending on BMI – normal (18.5-25 kg/m<sup>2</sup>), overweight and obese (≥25 kg/m<sup>2</sup>). Active disease was defined by DAS28crp≥2.6, BASDAI≥4. The link between overweight or obesity and disease activity was evaluated by using IBM SPSS 21.0.

**Results:** The spectrum of IA was: 23(43%) RA, 6(11%) adults with JIA, 6(11%) PsA and 19(34%) AS patients (mean age 49.6 years(±14.4)). 37(69%) patients were treated by ETN and 16(31%) by ADA. The mean value of BMI was 28.0 kg/m<sup>2</sup> (SD 5.7), DAS28crp-3.4(SD 1.35), BASDAI-3.2(SD 2.3). 37(69%) patients were included in the group with increased BMI. The mean value of DAS28crp and BASDAI in this group was accordingly 3.6(SD 1.2) and 3.4(SD 2.4). In the group with normal BMI the mean DAS28crp was 3.2(SD 1.4) and BASDAI 2.5(SD 1.9). The values of the disease activity were not statistically different between the groups. Although there was tendency to be more patients with active disease in group with increased BMI – 48%(n=16) and only 40%(n=8) in group with normal BMI (p=0.38). There was no statistically significant correlation between BMI and BASDAI (r=0.3, p=0.15) also BMI and DAS28crp (r=0.27, p=0.14).

**Conclusions.** These results showed that disease activity measurements such as DAS28crp and BASDAI are not affected by BMI for IA patients treated with TNF inhibitors in the study. Further prospective studies, including larger disease-specific population group, are needed to answer whether body weight could represent a modifiable factor to achieve remission and significantly influence immunogenicity of antiTNF drugs.

## 11. FACTORS INFLUENCING PROGRESSION OF SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS

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**Background.** Multiple sclerosis is one of the most common chronic neurodegenerative conditions, which progresses, leading the patient to work disability and causes a significant impact on patient's quality of life.

**Purpose.** To clarify the speed of progression of disability in patients with secondary progressive multiple sclerosis, depending on the progression of disease, disease of age, disease duration, and sex therapy.

**Materials and methods.** Retrospective study of patients was carried out, viewing outpatient cards of patients with secondary progressive multiple sclerosis at the Latvian Maritime Medical Centre, Latvian Multiple Sclerosis Centre. Overall, 80 patients' outpatient cards were examined regarding the disease to the last entry in the outpatient card. It was analyzed by the age, sex, EDSS, therapy and MRI findings diagnosis of the approval.

**Results.** Confirmation of disease at the time of the mean EDSS  $2.99 \pm 1.17$  for both sexes. The average age of disease for both sexes is  $39.59 \pm 11.75$  years (95% CI 36.93 ...42.08 years) with an interval of 14 to 61 years. A decrease in the time between the first symptoms and diagnosis confirmation, decreasing EDSS level of the first examination. Increasing age, reduce the period for which is reached EDSS 6.0. With the increase in EDSS level of the first inspection, reduce the period for which is reached EDSS 6.0. EDSS 3 the medium need to  $3.50 \pm 4.31$  years, and then to reach EDSS 6 to  $8.23 \pm 3.74$  years. In order to achieve a certain level of EDSS, women take longer than that for men. 98% at the time of MRI diagnosis confirmation deposit has multiple CNS demyelinating foci.

**Conclusions.** The study concluded that secondary progressive multiple sclerosis progression is affected by the patient's age at the time of illness, sex, EDSS during the first visit and the time between the first symptoms and diagnosis confirmation. The older the patient is at the time of illness, the more rapid progression of the disease, and the disease progresses more rapidly in men. The results were obtained that the disease is diagnosed to have a neurological deficit and if the first visit is higher in EDSS, the disease progresses more rapidly. EDSS 3.0 rashness not affect the achievement of reaching EDSS 6.0 speed. The larger the time between the first symptoms and diagnosis approval of accelerates the progression of the disease. Field MRI diagnosis of the approval bears no relation to neurological deficits.

## 12. CHRONIC C HEPATITIS TREATMENT EFFECTIVENESS USING DIRECT-ACTING ANTIVIRALS: REAL LIFE DATA

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**Introduction.** Chronic hepatitis C primarily affects liver. In early stages of disease in most cases there is no symptoms. However after some time develops cirrhosis and occasionally hepatocellular carcinoma. So far chronic hepatitis C treatment with *peginterferon alfa-2a* or *2b* and *ribavirin* was heavy for patients, lasted 48 weeks and caused many side effects. In some cases treatment failed because of the medication side effects. Since 2016 in Latvia chronic hepatitis C is treated with direct acting antiviral medications, course of treatment is shorter, better tolerated and 100% effective.

**Purpose.** To evaluate direct acting antiviral medication treatment efficiency and benefits in Latvia.

**Materials and methods.** Overall, the study includes 164 patients (79 women and 85 men). Age range from 24 to 71. Patients are divided into 5 groups. Each group presents data on a specific medication scheme, the HCV RNA after treatment at week 24. Data are obtained retrospectively from patients' medical records, Latvian Infectology Center archives. Statistical data processing method *SPSS 20.0.* and *MS Excel.*

**Results.** *Ombitasvirum/Paritaprevirum/Ritonavirum, Dasabuvirum* received 59,1% (n=97). HCV RNS after treatment week 24 not found 100% (n=97).

*Ombitasvirum/Paritaprevirum/Ritonavirum, Dasabuvirum + Ribavirin* received 25,6% (n=42). HCV RNS after treatment week 24 not found 98% (n=41), therapy interrupted 2% (n=1).

*Daclatasvir, Sofosbuvir* received 9,8% (n=16). HCV RNS after treatment week 24 not found 100% (n=16).

*Ledispavir, Sofosbuvir* received 4,9% (n=8). HCV RNS after treatment week 24 not found 75% (n=6), relapse 12,5% (n=1), ineffective 12,5% (n=1).

*Daclatasvir, Sofosbuvir + Ribavirin* 0,6% (n=1). HCV RNS after treatment week 24 not found 100% (n=1).

**Conclusions.** The obtained results show that in 3 of 5 medication groups treatment effect is 100%. In treatment with *Ledispavir, Sofosbuvir* effectiveness is 75% (n=6), relapse 12,5% (n=1), ineffective 12,5% (n=1). In other group: *Ombitasvirum/Paritaprevirum/Ritonavirum, Dasabuvirum + Ribavirin* effectiveness is 98% (n=41), therapy interrupted due to side effects 2% (n=1). These 3 cases need to be analysed individually.

### 13. DISEASE-RELATED CONCERNS OF PATIENTS WITH EPILEPSY IN LATVIA

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**Background.** Epilepsy is one of the most common neurological diseases, affecting about 70 million people globally. Disease-related concerns influence quality of life in epilepsy patients in different ways among cultures and age groups.

**Purpose.** The goal of this study was to examine the most important concerns of living with epilepsy as expressed by randomly-selected adult patients.

**Materials and methods.** A cross-sectional, descriptive study design was used. Adult epilepsy patients were randomly recruited at Outpatient Clinic and the 7<sup>th</sup> Neurology Department of Riga East Clinical University Hospital "Gaiļezers" in Riga, Latvia between April, 2016 and January, 2017 to participate in the survey. The inclusion criteria were as follows: being 18 years of age or older at the time of recruitment, having a secure diagnosis of epilepsy, being able to give informed consent and willing to participate in the study. Participants were asked to complete 7-point survey questionnaire which included previously reported concerns of epilepsy patients. Data were statistically analyzed using the IBM SPSS (Version 22) software package (IBM Corporation, New York, USA). The study was approved by the Medical and Biomedical research Ethics Committee of the Riga East Clinical University Hospital.

**Results.** The study involved 56 epilepsy patients, 23 females and 33 males, with ages ranging from 20 to 87 years (mean = 44.9 ± 15.5). Only 4 patients (7.1%) reported having no concerns caused by their disease. The most frequent concerns reported by respondents were: fear of seizures in 33 (58.9%) patients, necessity of medication use in 23 (41.1%), side effects of medications in 22 (39.3%), work restrictions in 20 (35.7%), lifestyle restrictions in 19 patients (33.9%), driving restrictions in 18 (32.1%), sudden unexpected death in epilepsy syndrome in 12 (21.4%) and social stigma in 11 (19.4%) patients.

**Conclusions.** The vast majority of patients with epilepsy diagnosis have disease-related concerns, amongst which fear of seizures is the most common. The results are consistent with findings from other studies. We report relatively low level of epilepsy stigma experienced by our patients, which is at least twice as low as reported in other European studies.

## 14. THE ASSOCIATION BETWEEN *PORPHYROMONAS GINGIVALIS* PEPTIDYLARGININE DEIMINASE AND THE DEVELOPMENT OF RHEUMATOID ARTHRITIS: A REVIEW

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**Background.** During the last two decades interest has increased in finding the possible cause and understanding the pathogenesis of rheumatoid arthritis. Accumulating evidence supports its connection with infectious periodontal diseases, most notably periodontitis. *Porphyromonas gingivalis*, a major pathogen causing periodontitis, has received special attention, because of its ability to citrullinate peptides with its enzyme peptidylarginine deiminase (PPAD). Citrullination is shown to be a part in pathogenesis of rheumatoid arthritis and several other diseases. Research on these issues has started to develop recently in several institutions abroad, while no studies on this topic were published in Latvia.

**Purpose.** The aim of the review is to evaluate, whether the current scientific data support the hypothesis that bacteria *P. gingivalis* is involved in the development of rheumatoid arthritis *via* the mechanism of its enzyme PPAD.

**Materials and methods.** Keywords “*Porphyromonas gingivalis*, peptidylarginine deiminase, rheumatoid arthritis” were used for searching articles in *PubMed* and *Google Scholar* linking PPAD and rheumatoid arthritis. Relevant articles were selected manually. The application *Mendeley* was used for managing and selecting the articles useful for the qualitative analysis to review the current scientific hypotheses, objective evidence and discussions concerning the chosen topic.

**Results.** After filtering the articles, 143 were considered to be relevant to the topic, which included clinical and preclinical research reports as well as review articles. First articles associating *Porphyromonas gingivalis* and rheumatoid arthritis appeared in the 1990's, however, increase in amount of publications can be seen in the last decade and 108 out of 143 articles were published during the last 5 years.

**Conclusions.** After analysing the literature, it has become clear that there is strong evidence supporting the association of PPAD *ex P. gingivalis* with pathogenesis of rheumatoid arthritis including elevated titers of anti-*P. gingivalis* in ACPA-positive rheumatoid arthritis patients. Activity of rheumatoid arthritis and its severity seems to be correlating with the status of periodontitis. State funded oral healthcare has fundamental role in the health of the population, not only in masticatory physiology, but also as a *prophylaxis* against severe chronically developing dystrophic conditions. It is important to introduce the accumulated knowledge about a potential pathogen involved in the development of rheumatoid arthritis and neurological proteinopathies, and to discuss the implications of these findings.

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## 15. EVALUATION OF COGNITIVE FUNCTION IN PATIENTS WITH ATRIAL FIBRILLATION

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**Background.** As it is known, atrial fibrillation (AF) is an important and independent risk factor for cerebrovascular disease at any age. Its prevalence progresses with age and reaches 17,8% in Europe aged 85 and older. Those AF patients who develop cerebral infarction (CI) as a result usually have worse outcomes (higher mortality, more disability) than patients without AF. Increasing evidence also suggests that AF is associated with “silent” or asymptomatic CI, thus promoting cognitive decline. As the risk for “silent” CI remains underestimated, patients may not be receiving optimal anticoagulant treatment.

**Purpose.** To compare the cognitive function in patients with and without AF, as well as to identify other influencing factors and the role of anticoagulants.

**Methods.** Prospective study was performed in Latvian Cardiology center of Pauls Stradins Clinical University Hospital. Data of 85 patients older than 60 years of age without any previous cerebrovascular events was obtained – 45 of them had AF, 40 had sinus rhythm (SR). Patients were asked to do a mini-mental state examination (MMSE).

**Results.** Overall, a mean score of  $23,1 \pm 3,8$  (out of 30) was obtained. Half of all the patients (50,6%) were classified as having dementia. MMSE score was progressively decreasing with age, and the prevalence of dementia increased almost 2 fold after age 75. Patients with AF had more statistically significant cognitive decline as compared to patients with SR. Higher education had a protective effect on risk acquiring dementia, decreasing the cognitive impairment.

There was also a statistically non-significant difference in cognitive decline between patients who received anticoagulation treatment and those who did not. But further studies with more individuals need to be performed to conclude about positive anticoagulant effect on cognitive function. A disturbing trend was observed during the study – the majority of all AF patients (75,6%) did not use anticoagulants, although they had absolute indications to use them.

### **Conclusions.**

1. The prevalence of dementia in this study was half (50,6%) of all the patients included.
2. Patients with atrial fibrillation have bigger cognitive impairment compared to patients with SR.
3. Age is the main risk factor for dementia. Higher education had a protective effect on the risk to acquire dementia.
4. A trend in lesser cognitive impairment in patients with oral anticoagulation was observed, but it was non-significant.
5. The majority (75,6%) of all patients with AF did not receive anticoagulation treatment.

# GASTROENTEROLOGY AND GASTROINTESTINAL ONCOLOGY

## 16. SHORT TERM OUTCOMES IN TREATMENT OF RECURRENT GASTRIC CANCER IN SURGICAL ONCOLOGY CLINIC OF RIGA EAST UNIVERSITY HOSPITAL

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**Background.** Recurrence of gastric cancer is severe health condition that is associated with poor prognosis and limited treatment possibilities. Many physicians consider that recurrent gastric cancer is incurable disease, and all patients should receive symptomatic or palliative therapy, without distinguishing exact health condition and considering curative or potentially curative treatment.

**Methods.** Retrospective study. 195 patients, who underwent surgical treatment due to gastric cancer in LOC (Riga, Latvia) (2007–2013). IBM SPSS 20 used for statistical analysis. Patients with recurrent gastric cancer were selected and divided in three groups according to received treatment: I group – 9(12,3%) only palliative chemotherapy or chemoradiation; II group – 14(19,2%) curative or potentially curative resection of recurrent disease; III group – 50(68,5%) only symptomatic treatment.

**Results.** Recurrence location: Multiple organs 24(32,8%). Peritoneum 9(12,3%). Liver 7(9,5%). Ovaries 5(6,8%). Locoregional l/n 5(6,8%). Gastric stump 5(6,8%). Hepatoduodenal ligament 3(4,1%). Lungs 2(2,7%). Bones 1(1,4%). Brain 1(1,4%). Gastrojejunal anastomosis 1(1,4%)

**I group.** Hematogenous recurrence – 5 patients. Peritoneal recurrence – 3 patients. Locoregional lymphatic recurrence – 1 patient. Treatment: Systemic chemotherapy – 7 patients. P/o 5 fluoracils – 1 patient. Combination of systemic chemotherapy and 46 gy radiation therapy – 1 patient. Survival: Mean overall survival 36,2 month. Mean disease free survival 26,5 month. Mean survival after recurrence 9,6 months.

**II group.** Local recurrence – 8 patients; Peritoneal recurrence – 5 patients; Hematogenous recurrence – 1 patients; Treatment: Gastric stump excision – 7 patients (1 patient also received systemic chemotherapy). Hysterectomy + adnexectomy – 3 patients (1 also received systemic chemotherapy). Adnexectomy – 2 patients (1 patient also received systemic chemotherapy). Hemihepatectomy – 1 patient. 1 – patient peritonectomy and systemic chemotherapy. Survival: Mean overall survival 58,6 months. Mean disease free survival 27,9 months. Mean survival after recurrence 30,5 months.

**III group.** Hematogenous recurrence – 26 patients. Peritoneal recurrence – 6 patients. Locoregional lymphatic recurrence – 8 patients. No data – 10 patients. Treatment: All patients received symptomatic treatment. Diagnostic operation – 3 patients. Palliative operation or stenting 8 patients. Survival: Mean overall survival 19,2 months. Mean disease free survival 15,4 months. Mean survival after recurrence 5,2 months.

**Conclusions.** Patients with resectable local, hematogenous (solitary) or peritoneal recurrence (20% of all patients with recurrence) will benefit from aggressive surgical treatment and have a chance of full recovery.

## 17. THE HISTOPATHOLOGICAL AND CLINICAL CHARACTERISTICS OF GASTRIC CANCER

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**Background.** Gastric cancer is one of the most common cancer worldwide with high morbidity and mortality.

**Purpose.** The purpose of the study was to compare histopathological and clinical characteristics of gastric cancer.

**Materials and methods.** Altogether 162 patients were enrolled in the study, who underwent surgical treatment in Riga East University hospital during 2010-2014. The study was approved by local ethical committee. The histopathological and clinical information was evaluated. The comparative analysis of histopathological and clinical data was performed.

**Results.** 108 men and 54 women with gastric cancer were enrolled in the study. The average age of patients was  $67 \pm 11$  years. Obtained results showed that 114 patients had tubular adenocarcinoma, 27 patients had signet ring cell carcinoma and 21 patients had mixed carcinoma.

Obtained results demonstrated the significant positive correlation between tumor grade and Lauren classification ( $Rho = +0.367$ ;  $p = 0.0001$ ), histological type and tumor grade ( $Rho = +0.297$ ;  $p = 0.0001$ ) and histological type and Lauren classification ( $Rho = +0.611$ ;  $p = 0.0001$ ). In addition, significant correlation between intestinal metaplasia and dysplasia in peritumoral tissue was observed ( $Rho = +0.205$ ;  $p = 0.009$ ). Furthermore, a positive correlation between histological type and Borrmann classification and between Lauren and Borrmann classification was found, and between tumour stage and Borrmann classification. In addition, a positive correlation between gastritis grade and the extent of intestinal metaplasia was revealed.

**Conclusions.** The significant correlation between clinical and histopathological characteristics of gastric cancer was demonstrated in particular between histological type and Lauren classification and tumor grade and Lauren classification.



## 18. COLORECTAL CANCER STAGE II AND III: IMPACT ON PATIENT'S DISEASE PROGNOSIS AND OUTCOME

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**Background.** Colorectal cancer is one of the most common cancers in Latvia. 1089 new cases of colorectal cancer were diagnosed in the year 2015. To stage the cancer TNM classification is used. It categorizes colorectal cancer based on the size of the lesion, affected regional lymph nodes and the presence of metastasis. There were 288 new cases of stage II colorectal cancer and 249 new cases of stage III colorectal cancer in the year 2015. Overall there were 6536 colorectal cancer patients by the end of the year 2015 and 3539 of these patients have been in the records for more than 5 years. Another measurement that is used is colorectal cancer grading system. The grade describes how closely the cancer looks like normal tissue in histological examination.

**Purpose.** The objective of the study is to determine how treatment of stage II and III cancer affects disease-free survival and overall survival rates in patients with colorectal cancer. During the study, the author will analyse the treatment associated factors that affect the outcome of colorectal cancer. Some of the treatment associated factors that will be analysed in the study include surgical treatment, adjuvant chemotherapy and other treatment factors. In addition to the aforementioned, the study will include an assessment of the histological findings of the colorectal cancer affected areas of gastrointestinal tract and lymph nodes and overview of colorectal cancer grades. The study will also include demographic analysis of colorectal cancer patients as well as will determine the share of recurrent colorectal cancer cases and newly diagnosed ones.

**Materials and methods.** A retrospective study that enrolled 200 patients with stage II and III colorectal cancer who received treatment in Oncology Centre of Latvia of Riga East Clinical University Hospital during the year 2011. The information about patients and the progress of their disease was taken from patients medical cards.

**Results.** Medical data of 200 patients were analysed. 114 of them have stage II colorectal cancer and 86 of them have stage III colorectal cancer. 104 of the patients are women and 96 are men. Data analyses continues. The final results will be presented at the conference.

## 19. MANIFESTATION OF CROHN'S DISEASE IN THE ELDERLY – CASE REPORT

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**Introduction.** *Crohn's* disease (CD) is a chronic inflammatory bowel disease and most commonly appears between second and third decade of life. CD can occur in people of any age. Complains in older patients are quite similar to younger patients, but more common characterized by diagnostic delay, because of problems with comorbidities, frequent extra intestinal manifestation and rarely appreciated the possibility of late onset CD.

**Objective.** To present a case report of late onset *Crohn's* disease.

**Materials and methods.** Case presentation.

**Case presentation.** A 75-year-old female presented with a 2-week history of pain in the right lower abdominal quadrant, bloody diarrhoea four times a day, fever and jaundice. She described a 10 years history of bilateral knee and ankle pains. Physical examination showed moderately tenderness in the right side of her abdomen. No joint effusion or skin lesions were noted. Stool samples were negative for infections. The laboratory workup showed a mild microcytic anemia (Hgb 11, 1 g/L), leukocytosis with a left shift ( $16, 5 \times 10^9/l$ ), elevated levels of *C-reactive protein* (345,1 mg/L) conjugated *hyperbilirubinemia* (139 mkmol/l) and mild *cholestasis* (*alkaline phosphatase* 262 U/L). Ultrasonography examination presented right elbow tendinitis. CT angiography scans revealed inflammatory changes basically on the *ileocaecal* area – distal *ileum*, *caecum* and *colon ascendens*. Colonoscopy identified deep ulceration extending from the terminal ileum to the ascending colon. Histology showed inflammatory changes which contains granulomas. In hospital she received antibacterial therapy and intravenous rehydration. On day 5 she started therapy with oral mesalazine (2400 mg/daily) and intravenous methylprednisolone (125 mg/daily), with dose tapering *per os*. Long term treatment was effective (CDAI decrease from 192 to 137), patient's complains disappeared. Level of *C-reactive protein* decreased till 8,7 mg/l. One month after the initial treatment, follow up colonoscopy revealed superficial inflammation of the terminal ileum mucous, no other pathology was found.

**Conclusions.** Case report demonstrates manifestation of luminal CD in old age patient (very late onset) with typical symptoms of CD, with extraintestinal manifestation and uncomplicated course. Treatment was effective as combination of steroid and mesalazine. Elderly patients represent a rare proportion of the CD population.

## 20. PHARMACOLOGICAL TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE USED IN GENERAL PRACTICE

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**Background.** Treatment of gastroesophageal reflux disease (GERD) is based on medication and also on dietary and lifestyle interventions. Commonly used drugs are proton pump inhibitors (PPI), antacids and prokinetic agents who are prescribed as monotherapy or in combination with PPIs.

**Purpose.** To evaluate pharmacological treatment recommendations for patients with GERD prescribed by general practitioners from different territorial areas of Latvia. Determine the first line treatment used in GERD therapy.

**Materials and methods.** General practitioners (GP) registered in The National Health Service filled quantitative survey questionnaire; 201 completed replies were received. The data were analyzed using Excel and SPSS 24.0.

**Results.** 201 GPs (average age – 49 years, average work experience – 24 years) from five territorial regions of Latvia 32% (n=65) from Riga region, 20% (n=41) from Zemgale region, 19% (n=38) from Kurzeme region 16% (n=32) from Vidzeme region, 13% (n=25) from Latgale region. 65% (n=131) of respondents choose proton pump inhibitors (PPI) as the first line (p=0.0000) of treatment.

Our data showed, that for most GPs from Riga 29% (n=45), Kurzeme 30% (n=27) regions first line choice is *esomeprazole* (p=0.0000). GPs in Vidzeme 34% (n=28), (p=0.0001) and Zemgale 33% (n=31), (p=0.0000) regions choose *pantoprazole*, but in Latgale 37% (n=20), (p=0.0063) *omeprazole*.

First choice antacids in all Latvian regions were aluminium and magnesium based; in Riga 42% (n=44), Vidzeme 35% (n=19), Zemgale 40% (n=26), Kurzeme 32% (n=19), Latgale 34% (n=14), p=0.0000 for all groups.

Most popular prokinetic in Riga 39% (n=35) and Kurzeme 34% (n=21) regions was *domperidone* (p=0.0000), but in Zemgale 39% (n=22), Vidzeme 42% (n=19) and Latgale 36% (n=12) was *metoclopramide* (p=0.0000).

GPs with work experience less that 20 years (n=76) choose *esomeprazole* 31% (n=56), aluminium and magnesium based antacids 37% (n=44) and *domperidone* 41% (n=44); p=0.0000, but GPs with work experience more than 20 years (n=125) choose *pantoprazole* 31% (n=92), aluminium and magnesium based antacids 38% (n=78) and *metoclopramide* 36% (n=64); p=0.0000.

**Conclusions.** Our data showed that first line treatment in GERD therapy were proton pump inhibitors, and decision making varies between *esomeprazole*, *pantoprazole* and *omeprazole*, depending on the area of GP practice and work experience. Use of H<sub>2</sub> antagonists was low in all groups. The most used antacids were aluminium and magnesium based, and the most used prokinetics were *metoclopramide* and *domperidone*. Decision making in the treatment of GERD is related to GPs' work experience and area of practice.

## 21. NON-PHARMACOLOGICAL APPROACHES OF GASTROESOPHAGEAL EFLUX DISEASE TREATMENT IN GENERAL PRACTICE

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**Background.** Treatment of gastroesophageal reflux disease (GERD) is based on combination of diet, lifestyle recommendations and effective medicine. If any of the components are missing, the effectiveness of treatment drops. Diet recommendations are known as a part of treatment success.

**Purpose.** To evaluate the treatment recommendations for patients with GERD prescribed by general practitioners from different territorial areas of Latvia. Determine diet and lifestyle recommendations in the complex of therapy.

**Materials and methods.** General practitioners (GP) registered in The National Health Service filled quantitative survey questionnaire; 201 completed replies were received. The data were analyzed using Excel and SPSS 24.0.

**Results.** 201 GPs (average age 49 years) from five regions of Latvia; 32% (n=65) from Riga region, 20% (n=41) from Zemgale regions, 19% (n=38) from Kurzeme region, 16% (n=32) from Vidzeme region, 13% (n=25) from Latgale region. Data analysis was made according the most popular diet recommendations in all regions. Majority recommended to avoid spicy foods (Riga-27% (n=52); Zemgale-25% (n=29); Kurzeme-28% (n=31); Vidzeme-24% (n=22), Latgale 29% (n=20), avoid sweets (Riga-14% (n=27); Zemgale-18% (n=21); Kurzeme-22% (n=25), Vidzeme-16% (n=15); Latgale-16% (n=11) and to avoid citrus fruits (Riga-20% (n=38); Zemgale-18% (n=21); Kurzeme-12% (n=13); Vidzeme-14% (n=13); Latgale-14% (n=10)).

*Table 1.* Lifestyle recommendations for GERD patients recommended by general practitioners

Lifestyle recommendations for GERD patients	Latgale	Riga	Zemgale	Kurzeme	Vidzeme
Stop smoking	14% (n=19)	16% (n=59)	15% (n=36)	15% (n=33)	13% (n=22)
Reduce weight, if overweight	16% (n=21)	14% (n=52)	13% (n=30)	14% (n=31)	13% (n=22)
Avoid eating before lying down	14% (n=19)	15% (n=56)	14% (n=33)	13% (n=29)	15% (n=26)
Avoid overeating	16% (n=21)	14% (n=53)	15% (n=35)	14% (n=32)	17% (n=29)
<i>P</i>	0.0000	0.0000	0.0000	0.0000	0.0000

**Conclusions.** Our data showed existing differences in the diet and lifestyle recommendations for GERD patients in different regions of Latvia. The most popular lifestyle recommendations were to avoid smoking and overeating, eating before sleep and to reduce weight. Avoid spicy foods, sweets and citrus are the most popular diet recommendations in all areas (Riga, Zemgale, Kurzeme (p=0.0000), Latgale (p=0.0003) and Vidzeme (p=0.0196)).

## 22. YIELD OF PEPSINOGEN TESTING IN A GENERAL POPULATION SAMPLE OF CAUCASIAN ORIGIN

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**Introduction.** Pepsinogen testing has been suggested to be the best available non-invasive screening tool for atrophy as the precursor of gastric cancer by several international guidelines, including by Kyoto international consensus and Maastricht V. However, studies addressing the yield of this type of screening are originating predominantly from Asia; little evidence is available from general population studies in Caucasians.

**Purpose and methods.** Individuals from a cross-sectional population-based study in Latvia with decreased pepsinogen levels during the recruitment were invited to undergo upper endoscopy with a proper biopsy work up. The results of the initial tests have been described elsewhere<sup>1</sup>. Blood samples were obtained prior to the endoscopy. Pepsinogen I and II was measured in plasma simultaneously from either in the initial or the follow-up sample by a latex-agglutination test system (from Eiken Chemical Co., Tokyo, Japan). Moderately decreased pepsinogen results were considered if  $\text{Pgl} \leq 70$  ng/ml and  $\text{Pgl/PgII} \leq 3$ , but severely decreased if  $\text{Pgl} \leq 30$  ng/ml and  $\text{Pgl/PgII} \leq 2$ ; the remaining cases were considered to have normal pepsinogen levels. The presence/absence of the gastric mucosal lesions was scored according to the OLGA and OLGIM staging systems. The presence of *H.pylori* IgG was assessed serologically (Mikrogen Diagnostik, Neuried, Germany).

**Results.** Results from 259 individuals (31.7% men; median age 58 years, range 22-88) were available for the analysis. The median follow-up interval was 3.5 years (range 3-6 years). Two gastric cancer cases (0.8%) and 21 cases with dysplasia (8.1%) were identified. Moderately decreased pepsinogens according to the results from the initial sample collected during the recruitment process was found in 133 subjects (51.4%), severely decreased – in 57 cases (22.1%). The distribution of the precancerous lesions between the groups is given in the Table. No significant further decrease in the pepsinogen values was observed between the initial and follow-up samples.

**Conclusions.** Pepsinogen detection could be a useful tool for identification of subjects at increased risk for developing gastric cancer in general Caucasian population; however only the minority of individuals with decreased pepsinogen levels are presenting with advanced gastric mucosal lesions.

## 23. COMPARATIVE EVALUATION OF TWO SEROLOGICAL TESTS FOR DETECTION OF *H. PYLORI* INFECTION IN LATVIAN POPULATION

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**Background.** Although tests for serological diagnosis of *H.pylori* are widely available, the performance could vary among different populations. The recent study showed excellent results some of 29 commercial kits (17 enzyme – linked immunosorbent assay (ELISA)), with performance parameters as sensitivity, specificity and three others more than 90% (*Burucoa et al., 2013*).

**Purpose.** To find out the accuracy of two serological tests in Latvian population.

**Materials and methods.** Healthy individuals, aged from 39 to 64 years, from country population register (within GISTAR study) were randomly chosen and asked to answer to questionnaire. Further patients were offered a pepsinogen test. If the test was positive, patients were asked to come to an endoscopy. Patients were asked not to use proton pump inhibitors and antibacterial medications one month before investigations.

Accuracy of two tests (latex-agglutination test – Test 1; ELISA test – Test 2) was analysed. *H.pylori* seropositivity was determined according to manufacturers' recommendations:  $\geq 10\text{g/L}$  for Test 1 and  $\geq 30\text{g/L}$  for Test 2. The accuracy of both tests was analysed in relation to histology as a gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy were calculated using *MedCalc/16.4.1* program.

**Results.** The final patient sample for analysis of *Test 1* contained data of 789 patients (the mean age  $52.06 \pm 6.70$  years, male:female ratio – 385 (48.8%): 404 (51.2%)), for analysis of *Test 2* – 1014 patients (the mean age  $51.97 \pm 6.68$  years, male:female ratio 458 (45.2%): 556 (54.8%)).

Accuracy of both tests in relation to histology is shown in the *Table*.

Test	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
<b>Test 1</b> (Accuracy 84.16)	86.06% (82.55–89.09)	81.52% (76.90–85.56)	86.62% (83.15–89.61)	80.78% (76.13–84.87)
<b>Test 2</b> (Accuracy 86.09%)	96.76% (94.99–98.04)	71.43% (66.89–75.67)	82.32% (79.26–85.09)	94.14% (90.99–96.43)

**Conclusions.** Test 2 showed higher accuracy. Whereas one of the tests showed higher specificity while the other – higher sensitivity, which should be noted, when interpreting the results and using the tests for scientific, clinical or screening purposes.

## 24. NEUROENDOCRINE TUMOR OF LARYNX – A RARE CASE IN GASTROENTEROLOGY PRACTICE

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**Background.** A carcinoid tumor is a type of neuroendocrine tumor, which most commonly arises in the gastrointestinal system (esophagus, stomach, intestines) and about 10% arise in the lungs. Neuroendocrine neoplasms of the larynx are rare but are the most common nonsquamous tumors of this organ and represent <1% of all primary laryngeal tumors.

**Purpose.** We present a rare case of neuroendocrine tumor localized in larynx.

**Materials and methods.** A 34-year-old male patient was admitted to the hospital in December 13, 2016 with signs of a jaundice. He had a history of hoarseness, dyspnea since July 2016. Computed tomography detected mass in the right side of the larynx, glottic stenosis and metastatic lesions in the liver. On October 30, 2016, tracheostomia inferior with biopsy from *plicae vocalis* dextra were performed (no signs of malignancy). On 24.11.2016. repeated biopsy from *larynx* was performed which showed high malignancy low differentiated neuroendocrine carcinoma (Ki67- 95%, CD20-negative, CD3-positive in some cells, CD56-positive, synaptophysin – positive, chromogranin and cytokeratin – positive in plaques). On admission to the hospital, patient had moderate pain in the left side of thorax where was a palpable solid mass. Magnetic resonance imaging revealed multiple metastasis in spine, the left side of thorax and liver with compression of the common bile duct. Endoscopic retrograde cholangiopancreatography (ERCP) showed common bile duct stricture and 8,5 Fr plastic stent was inserted in common bile duct to ensure the flow of bile. Mild post-ERCP pancreatitis was reduced with symptomatic treatment. Palliative chemotherapy was started on the 20<sup>th</sup> day of admission when bilirubin level dropped down from 127mkmo/L to 39mkmol/L.

**Results.** Patient was transferred to oncology unit to start palliative chemotherapy.

**Conclusions.** Our case report showed rare location of low differentiated neuroendocrine carcinoma with aggressive growth (Ki67- 95%, CD20-negative, CD3-positive in some cells, CD56-positive, synaptophysin – positive, chromogranin and cytokeratin – positive in plaques) and wide metastatic spreading. Liver metastasis with compression of common bile duct was indication for ERCP and plastic stent insertion. An important step of treatment was reduction of jaundice before the start of chemotherapy.

## 25. FAECAL CALPROTECTIN COMPARISON BETWEEN ULCERATIVE COLITIS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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**Background.** Calprotectin is a relatively new biomarker of inflammation, which can be found in all human secretions. Nowadays faecal calprotectin is used to monitor inflammatory bowel diseases activity and effectiveness of treatment. This test is mainly used for the detection of intestinal inflammation and to assess its severity. It seemed interesting for us to find out faecal calprotectin and its affecting factors' changes comparing ulcerative colitis (UC) and chronic obstructive pulmonary disease (COPD) patients.

**Purpose.** Calprotectin levels and its extraction laboratory methods were analyzed between the two patient's groups UC and COPD.

**Materials and methods.** A prospective study included 45 patients with moderate and severe activity UC (25) and COPD (20). At the first work stage all patients' data were analyzed compared between the two patient groups: group I – UC patients, group II – COPD patients. At the second work stage two calprotectin detection methods of Pauls Stradins Clinical University Hospital (PSCUH) Immunology laboratory were analyzed. The first method was enzyme-link immunoassay (ELISA) automated method (*Alegria*), the second – immunochromatography assay (*CalFast*).

**Results.** 25 (55.6%) patients had a diagnosis of UC and 20 (44.4%) patients with a diagnosis of COPD. The average age in group I,  $39 \pm 11$  years, group II,  $66 \pm 10$  years. We compared full blood count test and C-reactive protein (CRP) between group I and II. Comparing calprotectin levels between the two groups, there was a statistically significant difference,  $p = 0.01$ . Calprotectin was positive in 21 (84%) of ulcerative colitis and 6 (30%) COPD patients.

**Conclusions.** The results statistically proved that higher values of calprotectin are more characteristic of UC patients. Among calprotectin and laboratory parameters have not been observed any correlations. In one part of COPD patients elevated levels of calprotectin were found. In most cases it can be explained by COPD and factors affecting it, but others require further clinical examinations. In PSCUH applied calprotectin detection methods ELISA *Alegria* and *CalFast* are comparable, but need a more detailed study of the reference interval.



## 26. VOLATILE ORGANIC COMPOUND EMISSION COMPARISON IN GASTRIC CANCER AND NON-CANCEROUS TISSUE – PRELIMINARY RESULTS

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**Background.** Volatile organic compound (VOC) detection in the exhaled air has a potential for gastric cancer screening. Questions of the VOC origin and their biological relevance still require to be answered.

**Purpose.** We aimed to identify substances being expressed in different concentrations between gastric cancer and non-cancerous tissue.

**Methodology.** Head space needle trap extraction gas chromatography mass spectrometry (HS-NTD-GC-MS) was applied to identify and quantify VOCs released by healthy and cancer tissue obtained from surgery material of 15 patients. Samples (approx. 100mg) were located in sealed glass vials and the VOCs emitted into the head-space gas were transferred using a constant flow of ultra-pure air into the needle trap devices for extraction. Next, the extracted analytes were desorbed into the GC-MS system (7890A/5974C, Agilent, USA).

**Results.** After excluding for hospital environment related contaminants, altogether 25 VOCs were found to be produced by either types of samples. Emission of six of them (CS<sub>2</sub>, pyridine, methanethiol, pyrrole, 2-pentanone, 2-propenenitrile, NN-dimethylacetamid) was found to be significantly higher from cancer tissue when compared to the non-cancerous tissue.

**Conclusions.** Different VOCs are emitted by gastric cancer tissue when compared to the non-cancerous tissue. Five of the VOCs identified in the study have been found in exhaled breath in previously published studies and suggested to be potential gastric cancer markers. Therefore, the study is providing proof that the origin of VOCs in breath is from the stomach tissue.

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## 27. VAGINAL BIRTH AFTER CAESAREAN DELIVERY

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**Background.** The number of caesarean sections performed in a group of women with a history of is increasing, while the number of vaginal births in this group decreases. Thus, it is worth examining the risks associated with vaginal birth after caesarean section history.

**Purpose.** The aims of this study are to examine the most common risk factors, concluding which of them affect vaginal birth after caesarean sections history, to find out the most common acute caesarean section indication and to investigate the probability of safe vaginal birth after caesarean section.

**Materials and methods.** Data included in outpatient cards were analysed in a descriptive study, the acquisition of cards was based on a special data registration form. The study took place in “Jelgavas Pilsētas slimnīca” regional hospital and the data were collected during the period 01/2013-01/2016. The study analysed data of 74 women who tried to give birth vaginally after caesarean section history. The obtained data were analysed with MS Excel and IBM SPSS programmes.

**Results.** Out of 74 vaginal birth after caesarean section history, 67 of which ended in vaginal birth and 7 in acute caesarean section. Uterine dysfunction – most frequent acute caesarean section indication (n = 3; 43%). Most respondents had one caesarean section (n = 70; 94.59%) and two caesarean sections (n = 4; 5.41%). Average age –  $30.13 \pm 4.8$  years. Average Body mass index –  $24.05 \pm 4.35$  kg/m<sup>2</sup>. Average newborn birth weight –  $3479.05 \pm 360.84$  (g). Average thickness of the uterine scar – 3.93 (mm). The most used induction method was with oxytocin (n = 32/55; 43.24%).

**Conclusions.** Women with a history of caesarean section are safe to have vaginal birth 90.55%. Acute caesarean section indication in 43% cases – primary uterine dysfunction. The most common risk factor was not found due to small sample size, but it is known that certain risk factors have a certain risk associated with them, which as a result may adversely affect vaginal birth outcome.

## 28. CHARACTERISTICS OF PATIENTS WITH HIGH-GRADE MALIGNANT GLIOMA DURING 2009–2015 IN PAULS STRADINS CLINICAL UNIVERSITY HOSPITAL

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**Background.** Gliomas from approximately 30% of all brain and central nervous system tumors. The incidence of primary brain tumors has been increasing over the last 30 years, especially in elderly persons. WHO grade III tumors comprise anaplastic astrocytoma, mixed anaplastic oligoastrocytoma and anaplastic oligodendroglioma, while glioblastoma represents grade IV.

**Purpose.** To characterize patients with high-grade malignant gliomas.

**Materials and methods.** A retrospective study was performed. The data of histologically confirmed grade III and grade IV malignant gliomas were obtained from Pauls Stradins Clinical University Hospital from 2009 until 2015. Histological type, age, gender, tumor localization, received treatment, recurrence and transformation status was analyzed.

**Results.** In total we identified 176 confirmed cases of high-grade malignant gliomas. 5% (n=8) of patients had anaplastic oligodendroglioma, 13% (n=23) – anaplastic astrocytoma and 82% (n=145) – glioblastoma (p<0.00).

Mean age in patients with anaplastic astrocytoma was 47 ± 10.5 years. 57% (n=13) were men, 44% (n=10) – women (p=0.532). 44% (n=10) of patients tumor was localized in frontal lobe, 26% (n=6) temporal lobe, 13% (n=3) parietal lobe and other localization less often (p=0.001). 35% (n=8) received surgery and consequent radiotherapy plus temozolomide or surgery with consequent radiotherapy, 17% (n=4) only radiotherapy, 9% (n=2) only surgery and 4% (n=1) radiotherapy plus temozolomide (p=0.052).

Mean age in patients with anaplastic oligodendrogliomas was 47 ± 17 years. 50% (n=4) were men, 50% (n=4) – women (p=0.987). 50% (n=4) of patients tumor was localized in frontal lobe, 25% (n=2) temporal lobe, 12.5% (n=1) parietal lobe and 12.5% (n=1) occipital lobe (p=0.392). 50% (n=4) received surgery and consequent radiotherapy plus temozolomide and 50% (n=4) – surgery with consequent radiotherapy (p=0.971).

Mean age in patients with glioblastoma was 58 ± 11.6 years. 52% (n=75) were men, 48% (n=70) – women (p=0.678). 30% (n=43) of patients tumor was localized in frontal lobe, 37% (n=53) temporal lobe, 17% (n=24) parietal lobe and other localization less often (p<0.00). 50% (n=73) received surgery and consequent radiotherapy plus temozolomide, 40% (n=57) – surgery with consequent radiotherapy, 6% (n=9) only radiotherapy, 4% (n=6) radiotherapy plus temozolomide (p<0.00).

### Conclusions:

1. Glioblastoma is the most common high-grade malignant glioma.
2. Mean age of anaplastic astrocytoma and oligodendroglioma patients was 47 years, but of glioblastoma patients – 58 years.
3. No statistically significant difference was found between genders.
4. High-grade gliomas more often occurred in frontal or temporal lobes.
5. The most common treatment combination was surgery with consequent radiotherapy plus temozolomide.

## 29. COEXISTENCE OF PANCREATIC ADENOCARCINOMA IN COMBINATION WITH NON-FUNCTIONING PANCREATIC NEUROENDOCRINE TUMOR IN A PATIENT WITH TYPE 2 DIABETES – CASE REPORT

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**Background.** In clinical practice adenocarcinoma is the most common cancer of the pancreas that is characterized by poor long term survival. Pancreatic neuroendocrine tumors (pNET) are rare, usually sporadic and account for 1–2% of all pancreatic neoplasms. Comparing to adenocarcinoma pNET patients have relatively good prognosis. According to the PubMed database, coexistence of pancreatic adenocarcinoma and NET are uncommon. Moreover, this is so far the first reported case in Latvia.

**Materials and methods.** Analysis of the patient's medical history and a review of PubMed publications on the subject.

**Results.** A 76-year-old asymptomatic female with a suspicious mass of the distal pancreas found on abdominal ultrasound examination was referred to the hospital on November 2015. Physical examination and laboratory findings were unremarkable. Her BMI was 32.19 kg/m<sup>2</sup>. Past history included conventional appendectomy in 1956, right knee replacement surgery in 2000, thyroidectomy in 2008, ischemic left middle cerebral artery stroke in 2014 and a history of type 2 well metabolically controlled insulin dependent diabetes mellitus for 10-years, comprising to ASA III. No data on pancreatitis nor family pancreatic tumors was found. Computed tomography (CT) revealed a mass located in the body of the pancreas that was in close contact with the confluence of the superior mesenteric and the splenic vein. Distal pancreatectomy with splenectomy and lymph node dissection was performed. Histopatological examination of the specimen confirmed a 2.0 cm well-differentiated ductal adenocarcinoma pT<sub>1</sub>N<sub>1</sub>M<sub>0</sub>G<sub>1</sub>R<sub>0</sub> and 3 mm neuroendocrine microadenoma, proved by immunohistochemical expression of synaptophysin, chromogranin A, pan-cytokeratin AE1/AE3. The Ki-67 proliferation index was less than 2% comprising to G<sub>1</sub> pNET. Postoperative period was uneventful. She was discharged on postoperative day 9. No adjuvant treatment was administered. During one year of follow-up, the patient has remained in good health with completely controlled diabetes mellitus. CT scans 6 and 12 months after operation revealed no recurrent disease.

**Discussion.** The coexistence of both pancreatic adenocarcinoma and pNET is very rare and it is difficult to draw any conclusions regarding overall prognosis and long term survival. There are some publications speculating that pNET have genetic potential in transforming to neuroendocrine carcinoma and finally adenocarcinoma, however it is still a matter of debate and definite follow up guidelines are still lacking. Finally, we hope that this case report could help to describe the spectrum of pancreatic malignancies, paying attention to the importance of deeper understanding of genetic complexity of pancreatic tumors.

### 30. PROGNOSTIC FACTORS FOR MEDIAN SURVIVAL IN PATIENTS WITH GLIOBLASTOMA DURING 2009–2015 IN PAULS STRADINS CLINICAL UNIVERSITY HOSPITAL

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**Background.** Glioblastoma is the most common and most aggressive cancer of the brain, representing 15% of brain tumors. Typically, treatment involves surgery followed by chemotherapy and radiation therapy. Temozolomide is frequently used as a part of chemotherapy. Despite maximum treatment, the cancer usually recurs. The most common length of survival following diagnosis is 12–15 months. Without treatment survival is usually 3 months.

**Purpose.** To determine factors affecting median survival time in patients with glioblastoma.

**Materials and methods.** A retrospective study was performed. The data of histologically confirmed glioblastoma was obtained from Pauls Stradins Clinical University Hospital during the period of 2009 until 2015. Age, gender, tumor localization was analyzed. Median survival time, progression-free survival and impact of the treatment was evaluated.

**Results.** In total we identified 145 confirmed cases of glioblastoma. 52% (n=75) were men and 48% (n=70) – women. Mean age was  $59 \pm 11.6$  years. 93% (n=135) of patients were dead at the moment of the study.

The median survival time in patients with glioblastoma was  $11.7 \pm 0.9$  months. In age group up to 40 years median survival was 15.9 months, age 41 to 70 years – 12 months, but in age group  $\geq 71$  years – 8.1 months ( $p=0.01$ ). The median survival was 11.7 months for males and 11.5 months for females ( $p=0.38$ ). The median survival time was 3.5 months for glioblastomas localized in mesencephalon or diencephalon and 12 months if localized in any of the lobes ( $p<0.00$ ). 12% (n=18) didn't finish radiotherapy. In unfinished radiotherapy group median survival was 5 months, in finished radiotherapy group – 12.2 months ( $p<0.00$ ). 28% (n=41) had radiological confirmation of disease progression. Progression-free survival was 11.1 months for those who received surgery and consequent radiotherapy plus temozolomide, 8.1 months – radiotherapy plus temozolomide, 5.9 months – surgery and consequent radiotherapy ( $p=0.182$ ). The median survival time in patients who received treatment in case of progression was 18 months ( $p<0.00$ ).

**Conclusions.**

1. The median survival time of elderly patients was significantly lower compared to that of younger patients.
2. Glioblastomas localized in mesencephalon or diencephalon had significantly worse prognosis.
3. Patients who completed radiotherapy had longer median survival.
4. The longest progression-free survival was in surgery and consequent radiotherapy plus temozolomide group but it was not statistically significant.
5. The median survival time was longer in patients who received treatment in case of progression of the disease.

### 31. A RARE TYPE OF CYSTIC DUCT ANATOMICAL ANOMALY AND ITS LAPAROSCOPIC MANAGEMENT: CASE REPORT

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**Introduction.** The cystic duct belongs to the external biliary duct and typically connects the gallbladder with the common bile duct. There are many anomalies of biliary tree described in literature, some of them are rare. We report a very rare anomaly of extrahepatic biliary ducts which is not yet published.

In our case, the patient has one *ductus hepaticus sinister* and two *ductus hepaticus dexter* (lateral and medial) and *ductus cysticus* connected with lateral *ductus hepaticus dexter* above the bifurcation.

**Purpose.** The goal is to present a very rare case of biliary tree anatomical anomaly and its successful laparoscopic management.

**Materials and methods.** 75-year-old female with acute abdominal pain and mild jaundice was hospitalised with acute calculous cholecystitis and suspected choledocholytiasis. Abdominal ultrasound was done, which proved acute cholecystitis with perivesical inflammation. Because of suspected choledocholytiasis magnetic resonance imaging (MRI) was performed and no stones were found in common bile duct. The laparoscopic cholecystectomy was scheduled and performed.

Laparoscopic cholecystectomy was technically demanding, because of perivesical inflammation, it was done in reverse technique – from the *fundus*. During cholecystectomy the atypical biliary duct, connected to the gall bladder was visualised in the region of the *portae hepatis*. To clarify biliary anatomy, intraoperative cholangiography was performed. It showed atypical localisation of cystic duct and atypical anatomy of biliary tree: there were two *ductus hepaticus dexter* and cystic duct was connected with *ductus hepaticus dexter lateralis* close to bifurcation. The choledochostoma was left in the cystic duct, cholecystectomy was performed and operation was finished with subhepatic drainage. Postoperative course was uneventful. The repeated cholangiography postoperatively proved the anatomical anomaly. Thorough investigation of MRI images also confirmed rare atypical anatomy. Patient was discharged from the hospital and on day 14 choledochostoma was removed without any complication.

**Conclusions.** Patients with rare atypical biliary tract anomaly could be successfully managed by laparoscopy and intraoperative cholangiography.

## 32. URETERIC STENTING: ANALYSIS OF ANTEGRADE AND RETROGRADE PROCEDURES

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**Background.** In the UK, approximately 12,000 patients are admitted yearly due to nephrolithiasis and associated complications, with stones having a prevalence of 2–3% across the population. Though the typical presentation is one of acute pain, urethra obstruction compounded by urosepsis is the true emergency and ureteric stenting the forerunner as the therapy of choice<sup>1</sup>.

**Purpose.** The objective of the study was to test the correlation between treatment options provided by Surgery or Interventional Radiology and demographic status and sagittal anatomical preference of ureteral impeding<sup>2</sup>.

**Materials and methods.** A sample 76 patients were enrolled into this retrospective study at Basildon & Thurrock University Hospital during the year 2016. Data analysis programme IBM SPSS 22.0 was used.

**Results.** A ratio of 2.04 males:females with mean ages of 53.24 ( $\pm$  14.09) and 54.08 ( $\pm$ 18.79) respectively was in keeping with literature<sup>3</sup>. Females however tended to present younger with a modal age of 33 compared to 47 in males, and similarly had a lower value for the range of age presentation at 18 versus 23 in males. 40% of females had radiological therapy by antegrade procedures compared to 13.3% in males. Evaluation of imaging described a predominance of urethral tract obstruction to develop on the left in both males (31/49 cases) and in females (14/24 cases).

Chi-Square calculations were performed. P (0.04558) was significant ( $<$  0.5) when testing antegrade and retrograde procedures to gender. No further statistical significance was obtained for procedure and ureter position, or gender and ureter position.

**Conclusions.** In this study, antegrade stenting was more appropriate for females, and conversely retrograde for males. This remains an area of development and should be targeted to each individual and clinical presentation. A potential for future consideration is monitoring the timescales of stent removal with aims of assessing if this in keeping with guideline suggestions<sup>4</sup>.

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<sup>1</sup> Borofsky MS, Walter D, Shah O, Goldfarb DS, Mues AC, Makarov DV. Surgical decompression is associated with decreased mortality in patients with sepsis and ureteral calculi. *J Urol.* 2013;189(3):946

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<sup>3</sup> EAU/AUA Nephrolithiasis Guideline Panel. 2007 Guideline for the Management of Ureteral Calculi.

<sup>4</sup> Türk, C., Petřík, A., Sarica, K., Seitz, C., Skolarikos, A., Straub, M. and Knoll, T., 2016. EAU guidelines on interventional treatment for urolithiasis. *European urology*, 69(3), pp. 475-482.

### 33. FACTORS THAT IMPACT MEDIAN SURVIVAL IN PATIENTS WITH NON-RESECTABLE NON-SMALL-CELL LUNG CARCINOMA DURING 2015 IN PAULS STRADINS CLINICAL UNIVERSITY HOSPITAL

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**Background.** Lung cancer is the most commonly diagnosed cancer worldwide and its incidence continues to grow. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancers. Histologically, NSCLC is divided into adenocarcinoma and squamous cell carcinoma (SCC). Lung cancer is more common in men than in women. Most lung carcinomas are diagnosed at an advanced stage, conferring a poor prognosis. Lung cancer is highly lethal. If the cancer is non-resectable, the prognosis is poor, with a mean survival rate of 8–14 months.

**Purpose.** To evaluate the median survival and to analyze impact on median survival in patients with non-small-cell lung carcinoma.

**Materials and methods.** A retrospective study was performed. The data of histologically or cytologically confirmed non-resectable NSCLC were obtained from Pauls Stradins Clinical University Hospital in the year 2015. We evaluated the median survival and analyzed gender, histological type and treatment impact on median survival.

**Results.** In total we identified 82 confirmed cases of non-small-cell lung carcinoma. 46% (n=38) of patients had squamous cell carcinoma, 34% (n=28) – adenocarcinoma and 20% (n=16) – not otherwise specified non-small-cell lung carcinoma. 80% (n=66) were men and 20% (n=16) – women. 52% (n=43) had stage III lung cancer, 38% (n=31) – stage IV, 9% (n=7) – stage II and one patient had stage I. Only 40% (n=33) patients received palliative chemotherapy.

Median survival in women was  $5.1 \pm 2.4$  months, in men –  $5.5 \pm 1.7$  months ( $p=0.396$ ). Median survival in patients with adenocarcinoma  $4.3 \pm 1$  months, SCC –  $7.8 \pm 2.8$  months and not otherwise specified NSCLC –  $8.9 \pm 6$  months ( $p=0.158$ ). Median survival in patients with stage III lung cancer who received chemotherapy was  $9.1 \pm 1.8$  months compared to  $3.5 \pm 0.8$  months in patients with best supportive care ( $p=0.157$ ). Median survival in patients with stage IV cancer who received chemotherapy was  $8.4 \pm 0.5$  months compared to  $1.7 \pm 0.4$  months in patients with best supportive care ( $p=0.007$ ).

#### **Conclusions.**

1. Gender does not affect the median survival of lung cancer.
2. The least estimated median survival is in patients with adenocarcinoma but it is not statistically significant.
3. Patients with stage III lung cancer who receive chemotherapy have greater median survival compared to patients with the best supportive care but it is not statistically significant.
4. Patients with stage IV lung cancer who receive chemotherapy have statistically significantly greater median survival compared to patients with the best supportive care.



### 34. CASE REPORT: MANAGEMENT OF ELECTIVE CESAREAN DELIVERY IN THE PRESENCE OF *PLACENTA PREVIA* AND *PLACENTA INCRETA*

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**Background.** *Placenta accreta* is a placenta implantation that results in an abnormal firm adherence to the uterine wall. There are 3 types of placental pathology – *accreta* - partial or complete absence of decidua with adherence of placenta directly to the superficial myometrium. *Placenta increta* extends in the myometrium (invade into whole myometrium) but not through the uterine musculature. The most severe form of *accreta* is *percreta*. In *placenta percreta* penetration of the trophoblast through the myometrium possibly occurs into the peritoneum and invades adjunct organs and can cause uterine rupture.

**Purpose.** To present a clinical case in which affordable radiological methods are helping to diagnose serious pathology of the uterus during pregnancy requiring hysterectomy.

**Case presentation.** A 31-year-old woman (gravida VI, para III) with no concomitant diseases and a history of prior cesarean section due to placenta previa. During pregnancy was made regular 1<sup>st</sup> and 2<sup>nd</sup> trimester ultrasonography to rule out a low-lying or adherent placenta, but the scan did not show any signs of an abnormal placenta. On admission 13.06.2016 at 3:15am, the patient presented frequent voiding of urine and pulling abdominal and spinal pain. A day before hospitalization was referred to hospital due to abnormal placentation diagnosed during a routine sonographic examination at 35/36 weeks of gestation. An urgent abdominal ultrasound examination in hospital showed a viable fetus with appropriate biometrical parameters and normal amniotic fluid, while Eco-Doppler images suggested the diagnosis of placenta *increta* suspecta. Careful evaluation of the placenta with pelvic noncontrast magnetic resonance imaging confirmed the ultrasound diagnosis. The patient was made aware of the potential obstetric complications. An elective cesarean delivery was planned at 36+2 weeks of gestation. Because she had received spinal anesthesia for her previous cesarean sections, this surgery was also planned with spinal anesthesia. A healthy female baby, with weight 2,540 g was delivered. In connection with the diagnosis was made hysterectomy, the resulting material was sent to histological examination. Finally in pelvic floor was left drain and the abdomen was closed using a regular technique. During the surgery, the patient lost 2000 ml of blood and developed severe hemodynamic instability, with a 10%–20% decrease in systolic blood pressure. A transfusion protocol was initiated. Intraoperative allogeneic red blood cells (556 ml) and free-frozen plasma (988 ml) were transfused. The patient was cared for in the intensive care for one day. The postoperative course was uneventful, and the patient was discharged on day 7 in good conditions.

**Conclusions.** Placental pathology is associated with high morbidity and the risk of maternal death, even despite advances in ultrasonographic diagnostics, well-established surgical treatment and multi-disciplinary medical care. A rise in the rates of *Cesarean section* and intrauterine surgical procedure is considered to be the main factor responsible for the growing incidence of placenta *accreta*. A Cesarean section combined with hysterectomy and application of various techniques to limit massive bleeding is usually performed between 34 to 36 weeks of pregnancy before the onset of labor.

## 35. CORRELATION BETWEEN MATERNAL WEIGHT GAIN AND BIRTHWEIGHT OF A NEWBORN

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**Background.** Over the last five years in Latvia several trends have been observed: increase in age at which women plan to become pregnant, increase in birth weight of a newborn and increase in weight gain during pregnancy (The Centre for Disease Prevention and Control of Latvia: Statistical Yearbook of Health Care in Latvia 2015).

**Purpose.** The objective of the study was to investigate the correlation between the changes in the body mass index of women during pregnancy and birth weight of a newborn.

**Materials and methods.** In the study medical case records of 136 pregnant women in the period from January 1 to November 15, 2016 were analyzed including their age, body mass index as well as the birth weight of a newborn. The correlation between maternal weight gain and birth weight of a newborn was analysed in six BMI groups, three maternal weight gain (calculated from pre-pregnancy weight and weight at the last prenatal visit) groups and three birth weight groups. The weight gain during pregnancy was categorised by the Institute of Medicine guidelines; BMI groups were created according to World Health Organization Regional Office for Europe BMI categories.

**Results.** The mean age was 29.65 years (SD  $\pm$  4.53). 77% (n=105) of analysed cases were normal-weight women (BMI 18.5–24.9 kg/m<sup>2</sup>). In this BMI group a significant (p<0.01) weak positive linear correlation (correlation coefficient,  $r_p = 0.292$ ) between maternal weight gain and birth weight was found. In BMI groups with a body mass index below 18.5 kg/m<sup>2</sup>, 25.0–29.9 kg/m<sup>2</sup> and greater than 30.0 kg/m<sup>2</sup> no significant relationship between maternal weight gain and birth weight was found.

With birth weight 2500–4000 g (n=111) we found a significant (p<0.01) weak ( $r_s=0.260$ ) positive non-linear correlation between maternal weight gain and birth weight. In other analysed groups no significant relationship between maternal weight gain and birth weight was found.

**Conclusions.** Weight gain during pregnancy of normal-weight women is associated and positively correlates with the birth weight of a newborn.

## 36. SURGICAL MANAGEMENT OPTIONS OF PTERYGIUM (LITERATURE REVIEW)

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**Background.** Pterygium is a superficial, elevated, fibrovascular growth of degenerative conjunctiva into the cornea and usually seen on nasal side. This invasion of the corneal surface can lead to significant visual morbidity caused by irritation of the ocular surface, irregular astigmatism, obstruction of the visual axis, and loss of corneal transparency. It has reported prevalence of 2% to 7% worldwide mostly in tropical, subtropical areas. The incidence of this condition vary among different populations and are influenced by a variety of factors including age, sex, and geographic location

The etiology of pterygium is unclear but is associated with variety of risk factors like outdoor work, UV light exposure, occupational exposure to irritants, ocular inflammation and dryness. Current management options for pterygium include excision, conjunctival autografting, and the use of adjuvant therapies.

**Purpose.** The aim of this study is to summarize and analyse the most recent literature about surgical options of pterygium treatment, as well as to compare alternative treatment possibilities.

**Materials and methods.** A literature search was conducted electronically in databases PubMed and EBSCO using keywords “pterygium”, “pterygium surgery”, “pterygium treatment”. The search was limited to articles published in the English language between 2010–2016.

**Results.** In all 75 articles were found, 26 of which met the aforementioned requirements and thus were included and analysed in the study. 49 scientific papers could not be included in the literature review.

**Conclusions.** Surgical techniques for the management of pterygium vary, but high recurrence rates after successful excision remain a challenge. The aim of pterygium surgery is to excise the pterygium and prevent its recurrence. The variety of techniques, range from the bare scleraprocedure to more complex approaches, such as amniotic membrane transplantation and lamellar keratoplasty, including conjunctival autograft, and limbalconjunctival transplant, conjunctival flap, conjunctival rotation autograft surgery, cultivated conjunctival transplant and the use of fibrin glue.

Pterygium excision with limbal conjunctival autograft, has been reported to be more effective with low recurrence rate but it may compromise the corneal stem cell population. Additionally, adjunctive use of amniotic membrane graft results in low recurrence rate. Analysis of the literature made it clear that sutureless and glueless conjunctival limbal autograft following primary pterygium excision is safe, easy and effective in primary pterygium surgery.

### 37. A VEGETARIAN DIET'S IMPACT ON THE FEMALE REPRODUCTIVE SYSTEM

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**Introduction.** Healthy lifestyle is becoming more and more popular in the modern society which provides the opportunity to think about the importance of a healthy diet. The increasing tendency to commit to a vegetarian lifestyle raises a question – does it affect female reproductive system. The current necessity of this research was based on the lack of studies about a particular food type group in Latvia.

**Purpose.** To research if vegetarian food affects female reproductive system and health.

**Materials and methods.** Analysis of scientific literature. Quantitative research method – a 20-question survey was made in Latvian and Russian languages. Survey has been translated from Latvian to Russian and from Russian to Latvian language to prevent translation mistakes. The study was done through distribution of the questionnaire at different non-governmental organisations, social environment and internet. The obtained data was analysed via SPSS 22.0 computer software.

**Results.** The study included 76 women respondents living in different regions of Latvia, aged 14–56, who follow the vegetarian diet daily (76 lacto-ovo vegetarians). 13.1% (n=10) respondents had irregular menstrual cycle. 3.9% (n=3) of them had amenorrhea more frequent than 2 times a year. 81.3% (n=61) women, who use vegetarian food daily responded that they had felt pain in lower part of their stomach, increased sensitivity of breasts and PMS symptoms in their menstrual cycle. 39.2% (n=29) respondents had noticed changes in their menstrual cycle since they started consuming vegetarian food.

**Conclusion.** The research confirms the hypothesis that “A vegetarian diet affects the female reproductive system”. Vegetarian lifestyle affects reproductive system objectively by irregular menstrual cycle and subjectively – makes women experience discomfort during their menstrual cycle and menstruation. The majority of respondents, who started vegetarian diet noticed changes in their menstrual cycle.

## 38. WOMAN'S QUALITY OF LIFE IN THE AGE OF TRANSITION

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**Introduction.** 85% of all women experience some symptoms of menopause. The analysis of the quality of life has always been closely related to priorities of a certain period of life. The term "quality of life" entails both objective indicators and subjective satisfaction, as well as individual's ability to build their lives according to their goals. The current necessity of this research was based on the lack of studies concentrated on a particular age group in Latvia.

**Purpose.** To research the impact of physiological changes of women's transitional period on their quality of life.

**Materials and methods.** Analysis of scientific literature. A 26-question survey in Latvian was created. The North American Menopause Society's Menopause Health Questionnaire was used as a foundation which is appropriate for the particular group of respondents studied. The study was done through distribution of the questionnaire at different health care facilities.

The obtained data was analysed via SPSS 22.0 computer software.

**Results.** The study included 85 women respondents living in different regions of Latvia, aged 45 to 55. Analysis of objective indicators:

1. Heat wave presence noted in 57.6% of women, 24.7% of which noted they form often ( $p = 0.01$ ).
2. Night sweats noted in 51.8% of women, 8.2% of which claimed it gets frequent and troublesome, but gets frequent in 9.4% ( $p = 0.01$ ).
3. Flatulence felt by 62.4% of women, 2.4% of which felt it frequently and troublesome, and 14.1% claimed it happen frequently ( $p = 0.01$ ).
4. Mastodynia experienced by 47.1% of women, 5.9% of which claimed it gets frequent and troublesome, and 7.1% claimed it gets frequent ( $p = 0.01$ ).

Analysis of subjective indicators: Mood swings noted in 45.9% of women, 24% of which noted that it is frequent and troublesome, but just frequent – in 12.9% ( $p = 0.01$ ).

**Conclusions.** 54.4% of respondents experience the presence of objective symptoms during the transitional period, which affects their quality of life. The study confirms the hypothesis that "The physiological changes during the transitional age period have an impact on a woman's quality of life".

## DENTISTRY

### 39. THE EXPRESSION OF E-CADHERIN AND MMP-9 IN PATIENTS WITH ORAL SQUAMOUS CELL CARCINOMA

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**Background.** Oral squamous cell carcinoma (OSCC) is the most common oral malignancy. Specific biomarkers for tumour progression and prognosis are crucial for the risk stratification of premalignant lesions and oral carcinoma.

**Purpose.** The purpose of the study was to compare the expression of biomarkers E-cadherin and MMP-9 in patients with oral squamous cell carcinoma and in patients with premalignant lesions.

**Materials and methods.** Altogether 31 patients were enrolled in the study, who underwent biopsy or surgery at Riga East University hospital. 26 patients had oral squamous cell carcinoma, 5 patients had premalignant lesions. The tissue samples were investigated by histochemical and immunohistochemical staining methods.

**Results.** 22 men and 4 women with oral squamous cell carcinoma were enrolled in the study. The average age of the patients were  $56.7 \pm 6.5$  years. In addition, 5 patients with premalignant oral lesions were enrolled in the study. The average age of the patients were  $55.6 \pm 4.8$  years. Our results showed that the expression of MMP-9 was increased in patients with oral squamous cell carcinoma ( $25.9 \pm 16.5$  cells/mm<sup>2</sup>) compared to patients with premalignant lesions ( $10.4 \pm 3.3$  cells/mm<sup>2</sup>). Furthermore, the expression of E-cadherin was increased in OSCC patients ( $56.3 \pm 29.4$  cells/mm<sup>2</sup>) compared to patients with premalignant lesions ( $25.4 \pm 7.7$  cells/mm<sup>2</sup>).

**Conclusions.** E-cadherin and MMP-9 were significantly increased in oral squamous cell carcinoma compared to premalignant lesions. MMP-9 and E-cadherin could be potentially relevant biomarkers for risk stratification of oral premalignant lesions and squamous cell carcinoma.

## 40. CORRELATION BETWEEN PERIODONTITIS AND TYPE II DIABETES MELLITUS: STUDY DESIGN

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**Background.** Diabetes mellitus (DM) is one of the major healthcare problems in modern society according to the last World Health Organization reports. Late diagnosis is one of the challenges of type 2 DM, as it is almost symptomless in its early stages and may remain undiagnosed for years. DM is considered as a risk factor for oral disease including periodontitis and dental caries. Susceptibility to periodontitis is increased approximately three-fold in people with diabetes. There is compelling evidence for the bi-directional relationship between DM and periodontitis – DM increase the risk for periodontitis and periodontitis is associated with compromised glycemic control. There is a role for dental practitioners in early DM diagnosis and further monitoring of its control.

**Purpose.** The objective of this study will be to identify individuals with undiagnosed DM or prediabetes. The correlations between glycated hemoglobin (HbA1c), presence or absence of the history of diabetes, and severity of periodontitis will be evaluated.

**Materials and methods.** The study is planned to be performed on individuals of NAF Air Base Lielvarde. Study will be approved by Ethical committee of the University of Latvia. Participants  $\geq 40$  years old will receive a periodontal examination and glycated hemoglobin (HbA1c) level will be recorded. Additionally they will complete questionnaires concerning general health, including family history of DM, body mass index and waist circumference. The correlations between the HbA1c, presence or absence of the history DM, and severity of periodontitis will be evaluated using SPSS software.

**Expected results.** We expect to obtain the following results of this study:

1. To find association between periodontitis and HbA1c.
2. To recognize patients with undiagnosed DM in this study group.
3. To develop recommendation for healthcare practitioners for managing patients suffering from poorly controlled DM and periodontitis.

**Conclusions.** Results of the current study will be relevant to public health in Latvia and will open the discussion about possible role of oral health providers in the identification of undiagnosed and poorly managed DM. The overall goal is to facilitate the cooperation between physicians and dentists for improved care of patients suffering from these conditions.

## 41. IMPROVEMENT OF DENTAL SITUATION IN PRESCHOOL AND SCHOOL CHILDREN: DESIGN OF INTERVENTIONAL STUDY

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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: availability of dental services are more around major cities of the country rather than rural areas due to density of dental praxes and considerable gap between living standards of mentioned areas. Unfortunately, it is a lack of precise information about parent knowledge on children oral health, and as a result of it there is a lack of concrete guidelines for parents and physicians on this issue.

**Purpose.** The objective of the current study is:

1. To investigate the association between parents knowledge on children oral health and an existing dental situation in preschool and school children;
2. To perform the interventional study to improve a dental situation in Latvian regions;

**Materials and methods.** 1. The study will be performed in five schools: one in Riga and four regional schools in Vidzeme, Zemgale, Latgale, Kurzeme. Study will be approved by Ethical committee of the University of Latvia. Children from 5 till 15 years of age in baseline examination will be enrolled into the study. Parents will sign an informed concern for both parts of the study – baseline and interventional. Children oral situation will be examined concerning caries and gingivitis problems. Parallel, parents will be interviewed to obtain the information on socio-demographic factors, eating habits and hygiene knowledge. Multiple logistic regressions for associations between factors obtained in parents' interviews and children' caries and gingivitis, adjusted for socio-economic parameters, will be built. Additionally, differences between Riga and regional school situation will be analyzed. 2. Interventional study with case-crossover design will be performed. Pairs "parent-child" will pass the explanatory exercise on oral hygiene and oral health-related factors. Follow-up examinations of participants of interventional study will be performed every six months during two years after the intervention.

**Results.** We expect positive association between parents' knowledge and children's oral health that will be improved at first six months after intervention for gingivitis, and during a follow-up for intervention.

**Conclusions.** Knowledge on dentistry situation in different regions of Latvia is extremely important for public health in Latvia. Based on obtained knowledge, oral health guidelines for parents and physicians will be developed.



## 42. MIO-FUNCTIONAL CHANGES IN PRESCHOOL AND SCHOOL CHILDREN IN LATVIA: STUDY DESIGN

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**Background.** It is known that dental situation in children in Eastern Europe is different from that in Western Europe. Insufficient knowledge of parents concerning oral health-related factors that need special attention during child's development (for instance, breast feeding, nourishing with hard food) can lead to different mio-functional problems in preschool and school children, such as incorrect tongue position, hyper/hypo tonus of *Musculus mentalis* and *Musculus masseter*, and bite problems. Untimely or inappropriate treatment of these problems can future lead, for example, to incorrect speech development. Investigations of contemporary situation with mio-functional changes in children in Latvia were not performed until now. This fact delays a performance of relevant changes for improvement of mio-functional situation in children in Latvia.

**Purpose.** The objective of the current study will be to investigate different kinds of factors associated with mio-functional changes in preschool and school children in different regions of Latvia.

**Materials and methods.** The study is planned to be performed in five schools: one in Riga and four in each region of Latvia (Vidzeme, Zemgale, Latgale, Kurzeme). Study will be approved by Ethical committee of the University of Latvia. Children from 5 to 7 years of age will be enrolled into the study. Parents of children will sign an informed concern. During a cross-sectional investigation, mio-functional situation in children will be examined. Parallel, parents will be interviewed about their socio-demographic factors and teeth-related problems in early years of children life (breast feeding, surgical interventions). Associations between factors obtained in parents' interviews and children' mio-functional parameters will be analyzed using SPSS software. Additionally, differences between mio-functional changes of children in Riga and regional schools will be analyzed.

**Expected results.** We expect to obtain the following results of this study:

1. To describe a contemporary mio-functional situation in children of Latvia – it has not been done before;
2. To observe differences between children in Riga and children from four regions of Latvia, and perhaps differences between regions themselves;
3. To find associations between teeth-related problems in early years of children life and mio-functional problems of children;
4. To be able at the end of the study to prepare guidelines for elimination of mio-functional problems in children and to propose guideline to relevant state authorities.

**Conclusions.** Disclosure of contemporary situation with mio-functional problems in preschool and school children in Latvia will have a great relevance for public health and policies related to children's dentistry and dental education.

## PEDIATRICS

### 43. PHYSIOLOGICAL WEIGHT LOSS AMONG LATVIAN NEONATES: ASSOCIATED FACTORS AND COMPLIANCE WITH PUBLISHED CHARTS

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**Background.** Healthy neonates typically have a physiological weight loss (PWL) during the first week of life. Although different opinions about factors influencing PWL exist, changes in PWL might indicate health disturbances in neonates, thus helping doctors to identify high risk neonates. During the previous years, several studies about PWL have taken place resulting in attempts to create a chart resembling normal ranges for PWL. However, so far there is no study about PWL in Latvian neonates.

**Purpose:**

- to evaluate PWL in healthy and sick Latvian neonates and to analyse factors affecting PWL;
- to evaluate the possibility to use American PWL charts for Latvian neonates as well as to evaluate the possibility to create a PWL chart for Latvian neonates.

**Materials and methods.** The retrospective study included data about all neonates treated in the neonatal department, Children Clinical Hospital "Gaiļezers" from January 1 till December 31, 2015 and all children from an out-patient praxis in Riga during 2014 and 2015. The following data were gathered: gender, type of delivery, type of feeding, week of delivery and health status. The final sample for analysis included 220 newborns (118 data from the hospital; 102 data from the praxis). Statistical analysis: ANOVA, Chi-squared test, multiple regression.

**Results.** The mean PWL of Latvian neonates in the studied sample was 6,4%(SD±2,31). The maximal PWL for all neonates occurred on the third or fourth day. Overall the birth weight was regained by the 10th day postpartum (except for 15 neonates).

PWL was lower among sick neonates compared to healthy neonates (5,9%(SD±2,71) vs. 6,9%(SD±1,96), respectively, p=0,01) and among formula fed neonates compared to breast fed neonates (5,8%(SD±2,83) vs. 6,5%(SD±2,21), respectively, p=0,06). The other studied factors showed no significant influence on the PWL.

In multiple regression analysis PWL was significantly associated with health status of the neonate.

After plotting Latvian neonates' data on the American charts the mean PWL among breast fed infants was below 50<sup>th</sup> percentile.

**Conclusions.** PWL in the studied patient sample was significantly lower among sick neonates, thus showing that newborns with health problems did not follow the normal PWL pattern possibly due to formula feeding and/or intravenous therapy received.

Although the mean PWL of Latvian neonates generally comply to American charts, PWL in Latvian breast fed neonates was below 50<sup>th</sup> percentile, possibly resembling different feeding patterns or breast milk contents in our population, suggesting a need for development of regional PWL chart.

#### 44. *H. PYLORI* PREVALENCE TREND AND TREATMENT PECULIARITIES IN SYMPTOMATIC CHILDREN

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**Background.** *Helicobacter pylori* (*H. Pylori*) infection is associated with an increased risk of development of duodenal and gastric ulcer, gastric adenocarcinoma and MALT lymphoma. *H.pylori* prevalence in Latvia is higher than in Western Europe and is often diagnosed in children during esophagogastroduodenoscopy.

**Purpose.** The aim of the study was to detect prevalence of *H.pylori* infection among symptomatic children and to compare the prevalence with data obtained in 2000/2001. Further, management of *H.pylori* infection was analyzed among *H. pylori* positive patients.

**Materials and methods.** A retrospective study was performed analyzing data about all patients at Children Clinical University Hospital in Riga, who were coming for esophagogastroduodenoscopy during January 1, 2014 and December 31, 2014. *H.pylori* positivity was detected with rapid urease tests and compared to data from patient sample gathered in 2000/2001. Diagnosis, eradication therapy and endoscopy data were analyzed in *H.pylori* positive patients.

**Results.** Oesopahogastroduodenoscopy was performed in 2235 patients between January 1, 2014 and December 31, 2014. In the total patient sample *H.pylori* positivity was 15.5% (362/2235). *H.pylori* positivity among symptomatic patients was significantly lower in 2014 compared to 2000/2001: 15.5% (362/2235) vs. 54% (70/130);  $p < 0,001$ . Detailed analysis of *H.pylori* infection was performed in 199 patients. Ulcer was present in 4% (8/199), erosions – in 6% (12/199) of *H.pylori* positive patients. In total, *triplex* therapy was prescribed in 42% (84/199) of patients and regimen with metronidazole was used most often. Eradication treatment control with non-invasive test was not prescribed.

**Conclusions.** *H.pylori* positivity among symptomatic children in Latvia was higher than in Western European countries but lower compared to data 15 years ago. Ulcer prevalence of duodenal ulcer in children was close to that in Western European countries. Although eradication treatment among *H.pylori* positive patients was prescribed according to ESPGHAN/NASPGHAN guidelines, eradication control should be performed with a non-invasive test.

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## 45. PRIMARY CILIARY DYSKINESIA, KARTAGENER'S SYNDROME

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**Background.** Kartagener's syndrome (KS) is a rare, congenital ciliary motility disorder that involves clinical triad: chronic sinusitis, *situs inversus* and bronchiectasis. KS incidence is about 1 in 30.000 live births. Primary ciliary dyskinesia manifests from early life with recurrent chest infections, ear/nose/throat symptoms and later infertility. Early diagnosis is important, because it allows to prevent many of the complications of the disease.

**Clinical case.** Eight-month-old girl came to department with complaints about continuous nasal discharge and cough since birth. She has been admitted three times to the hospital with diagnosis of acute bronchitis. She was treated as an outpatient by inhalation of *Salbutamol/Budesonide/Tyloxapol* without improvement. She was born in full term, weighed 3 kilos and was 57 cm long. She was exclusively breastfed till 4 months of age, then proceeded with formula feeding. Vaccination was made. On examination, the vital parameters were within the normal limits. She weighed 10 kg and was 74 cm tall. She had watery discharge from nose. On auscultation, bilateral crackles were audible, with heart sounds being best heard on the right side of the chest. Previous echocardiography revealed dextrocardia with normal cardiac function. There were no pathological changes on chest x-ray, except dextrocardia. Sweat probe was 28 mmol/l. Laboratory tests, including specific IgE, were unchanged. The serology against *Cl.pneumoniae*, *M.pneumoniae*, adeno-, rhino-, RSV, parainfluenza, influenza type A and B viruses was negative. We made some additional examinations. Electrocardiogram showed evidence of dextrocardia. The ultrasonography revealed *situs inversus*. No anatomical abnormalities were observed during bronchoscopy, except mild inflammation of mucosa. Histologic evaluation of nasal epithelium showed no movements or cilia, that confirmed diagnosis of primary ciliary dyskinesia, Kartagener's syndrome. Genetic consultation reveal, there is unnecessary to do genetic tests to confirm the diagnosis. We may not find the appropriate gene, that cause the mutation. However, that does not exclude the diagnosis.

**Results.** The median age at diagnosis primary ciliary dyskinesia is 5 years. In our case, the disease was diagnosed in the first year of life. Early diagnosis is important for the preservation of pulmonary function and quality of life. Children who have nasal discharge, recurrent chest infection, ear/nose/throat symptoms since birth should be checked for primary ciliary dyskinesia diagnosis. Especially in cases of internal organ position anomaly.

## 46. NON-NEURONOPATHIC GAUCHER DISEASE IN A CHILD

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**Background.** Gaucher disease is a rare sphingolipid storage disorder which is inherited as an autosomal recessive trait. It is caused by glucocerebrosidase deficiency which disrupts the breakdown of sphingolipids to variable extents (*Barranger et al., 1989*); (*Niederau et al., 2000*). The estimated prevalence in Europe is 1 in 40,000 live births, but only about 1% of affected individuals have been diagnosed with the disease. (*Niederau et al., 2000*). Although non-neuronopathic Gaucher disease can cause various complications, early diagnosed and with specific treatment patients have a lifespan similar to general population. The most important disease complications arise from bone involvement (e.g. osteonecrosis, osteoporosis, fractures) (*Perez-Lopez et al., 2016*).

**Case report description.** A 3-year-old boy was first admitted to hospital in May, 2007 with unexplained hepatosplenomegaly. There were no other complaints and no abnormalities found on physical examination. All laboratory tests were normal and screening for virus hepatitis was negative. Abdominal ultrasound revealed enlarged liver 1,5 cm below the costal margin and spleen 6,7 cm below the costal margin. There were no radiographic evidence of a bone disease.

After consulting a specialist in the Clinic of Medical Genetics and Prenatal Diagnostics, it was decided to send a patient's blood sample to the Institute of Psychiatry and Neurology, Warsawa in order to do the lysosomal enzymes tests. On June 14, 2007, Gaucher disease was confirmed – chitotrioididase level was 21460 nmol/mh/h (normal range <150).

The therapy with imiglucerase 60U/kg was initiated and continued every two weeks according to the dosing schema.

Currently boy is admitted to hospital every two weeks in order to receive the treatment. There are no complaints and no pathologies seen on physical examination. Laboratory tests show no signs of pancitopenia. Most recent abdominal ultrasound reveals mild splenomegaly and no hepatomegaly. There is no evidence of bone involvement.

**Conclusions.** After 9 years of enzyme-replacement therapy, the patient has not developed any symptoms or complications characteristic to Gaucher disease.

As literature reveals, the outcome of non-neuronopathic Gaucher disease is considerably variable from severely affected till asymptomatic individuals. Variability is not explained by beta-glucerebrosidase allelic heterogeneity and remains unsolved. (*Goldblatt et al., 2016*).

**Acknowledgements.** *I would like to thank Dr. Ieva Saulīte, Prof. Ingrīda Rumba-Rozenfelde and Children's Clinical University Hospital for the support in this research.*

### 47. KNOWLEDGE AND ATTITUDE TOWARDS ANTIBIOTIC USE AND ANTIMICROBIAL RESISTANCE IN ONE GENERAL PRACTICE: MYTHS AND REALITY

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**Background.** Nowadays, antimicrobial resistance (AMR) has become a major health problem. Antibiotics being available over the counter and inappropriate use of antibiotics by the public are contributing to emergence of resistance. The lack of new antibiotics on the market also is a big concern. Primary care specialists working directly with patients often encounter cases of AMR and can play an important role in finding the solution to the problem.

**Purpose.** The objective of this study was to determine patient awareness of AMR problem; evaluate their knowledge and attitude towards antibiotic use in primary care; and determine possible reasons of irrational antimicrobial therapy in general population.

**Materials and methods.** The study is based on the analysis of patient surveys on antibiotics, their use with or without doctor's prescription and experience with antimicrobial resistance. 109 patients aged 18–84 participated in the surveys from December 2016 to January 15, 2017.

**Results.** 75 patients were females and 34 – males. The average age was  $34,8 \pm 16,3$  years. A considerable number of patients – 40,3% thought that antibiotics help against viruses and 29,4% that common cold or flu should be treated with antibiotics. Only 40,4% of patients knew that penicillin was discovered in the 20<sup>th</sup> century, surprisingly, 54,2% of healthcare workers were also wrong. On average, patients reported using antibiotics 1 time per year and 21,1% of patients admitted buying antibiotics in local pharmacies without doctor's prescription. The majority of patients followed the recommendations about antibiotics use, but 8,3% used prescribed antibiotics only for a few days until they got clinically better. 53,2% of patients did not have a correct knowledge of the concept of AMR and associated mechanisms. A considerable number of patients (34,9%) had experience with adverse effects.

**Conclusions.** Overall, in this study it was found that misconceptions exist about the use and indications of antibiotics. Lack of knowledge regarding AMR was prevalent. Patients, even healthcare professionals, believe that resistance is due to human organisms getting used to drugs, and not because bacterias are no longer susceptible to the common medicines used to treat them in the past. The survey shows that sales of antibiotics are partially uncontrolled and not strictly monitored. Self-treatment, inappropriate antibiotic use and early discontinuation of the antibiotic course have major influence on resistance problem. Interaction between patients and primary care professionals can help to improve the situation.

**Acknowledgements.** *Authors would like to express a special gratitude to our colleagues from VCA "Aura".*

## 48. CURRENT SMOKING TRENDS OF PATIENTS IN ONE GP PRACTICE

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**Background.** Smoking has been practiced in one form or another since ancient times, but only in the 20<sup>th</sup> century it became a health concern. Despite social awareness campaigns and restrictions smoking is spread worldwide and remains one of the major health problems. Moreover, the smoking trends are changing, tobacco cigarettes are replaced by hookahs or electronic smoking devices. The influence of electronic cigarettes and other smoking devices on human health is not researched enough and potentially harmful effects are largely unknown. Addressing smoking problem can be helped by understanding current smoking tendencies and using this information in educational work with patients in primary health care.

**Purpose.** The objective of the study was to determine the prevalence of tobacco and other smoking device use in one general practice; to evaluate patients' attitude and preferences in smoking and their awareness of the global smoking problem.

**Materials and methods.** The study is based on the analysis of patient surveys on smoking behaviour and habits. 102 patients aged 18–84 participated in the surveys from December 2016 to January 15, 2017. Statistical analysis was performed with *IBM SPSS Statistics 22.0*.

**Results.** 43 patients were males and 59 – females. The average age was  $34,39 \pm 15,15$  (*SD*). 48% have tried smoking, 36,7% of them are smoking every day. Smoking with friends was mentioned as a main reason to start. 67,3% started smoking under the age of 18, but 61,2% admitted at least one of their parents was smoking. 80,4% have seen pregnant woman smoking. 28,4% consider hookah use less harmful than tobacco cigarettes, but 39,2% think that electronic cigarettes are less dangerous. In opinion of 33,3% patients, electronic smoking devices can be used to facilitate quitting smoking. A reasonable number of patients (14,7%) show less trust in doctors that are smoking.

**Conclusions.** While tobacco cigarette smoking prevalence is rather high, there has been a rise in popularity of new electronic devices among all age groups surveyed. The majority of respondents started smoking under the age of 18 and were passive smokers at home or work. There is lack of information about the effects of hookah and electronic cigarette smoking, but they are considered less dangerous and sometimes even beneficial. Undoubtedly, society needs stricter smoking limitations and more intense educational work of healthcare specialists to find a solution for this global matter.

**Acknowledgements.** *Authors would like to express a special gratitude to our colleagues from VCA "Aura".*

## 49. STEREOTYPES OF AGE AND AGING, AND WORKING ABILITY: LATVIAN PART OF INTERNATIONAL PROJECT

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**Background.** Aging population in modern societies require new knowledge concerning aging processes. Better physical and cognitive conditions, development of technologies and medicine permit elderly to prolong their professional career. On the other hand, stereotypes of age and aging (SAA) may lag fast technological changes, affecting activity of older workers. 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 and tends to leave the work force prematurely, thus leading to a shortage of health care workers. Negative SAA of older workers with respect to their personality, their abilities and their role at work may contribute to a decrease in motivation, performance and perceived work ability (WA), to more work stressors (WS), and eventually to premature retirement. Additionally, it is very likely that SAA concerning older workers differ between people with different background, mentality and nationality. Studies investigating different aspects and consequences of SAA of older workers seem to be necessary to understand aging process and their effect on working ability.

**Purpose.** The objective of the current study is to investigate associations between SAA of working medical personal in Latvia and their WA.

### **Materials and methods.**

A cross-sectional study on 250 nurses and medical doctors will be performed between January, 2017 and December, 2018 in two major hospitals in Riga, Latvia – 1<sup>st</sup> Riga Hospital and “Gaiļezers” Hospital. Following measures will be used: 1. For socio-demographic situation and WC – German socio-economic panel study questionnaires; 2. For WC – KFZA (*Kurz Fragebogen zur Arbeitsanalyse*) questionnaire translated from German; 3. For WA – Workability Index; 4. For SAA: National Character Survey, and *Beliefs about older worker's* questionnaire. Linear models adjusted for socio-demographic factors will be built using SPSS software.

**Expected Results.** We expect to obtain the following results for this study:

1. Negative association between SAA and WA;
2. Negative association between WS (physical and psychological) and WA;
3. WC have moderating/mediating effect on the association between SAA and WA;
4. Differences between Latvian-speaking and Russian-speaking workers concerning their SAA.

**Conclusions.** Disclosure of SAA and their consequences have great relevance for public health and occupational policies.

**Funding.** *Latvian part of the study is funded by University of Latvia (A73-AL/800 ) and by Baltic-German Liaison Office.*



## 50. COGNITIVE FUNCTION AND ITS CONSEQUENCES ON WORKING ABILITIES IN LATVIAN AND ISRAELI POPULATIONS: STUDY DESIGN

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**Background.** Accumulation of changes that accompany advancing age is associated with progressive decrease in functioning including workability (WA). One of such changes can be cognitive function (CF). Functional capacities show a declining trend after the age of 30 years, and the trend can become critical after the next 15–20 years. On the other hand, workers' perceptions of their WA indicate that some of them reach their peak before the age of 50 years, and five years later about 15–25% report that they have a poor WA, mainly those in some mentally demanding positions. CF as a part of mental function capacity can affect WA. Age-related cognitive decline can be a part of normal aging processing, and in this case some Selection, Optimization and Compensation (SOC) mechanisms can be developed to compensate this decline. Up to date there is a lack of information on the association between CF and WA especially with respect to age-related SOC mechanisms.

**Purpose.** The objective of the current study is to investigate and to compare between the association of CF with WA in Latvian and Israeli workers.

**Materials and methods.** A cross-sectional study on 250 nurses and medical doctors will be performed between January, 2017 and December, 2018 in two major hospitals in Riga, Latvia – 1<sup>st</sup> Riga Hospital and “Gaiļezers”. During personal interviews medical personal will fulfil a Workability Index for WA assessment, German socio-economic panel study questionnaires for personal data, and validated SOC questionnaire. Four cognitive tests – word fluency, immediate and delayed word tests, and labyrinth test – will be performed and z-transformed for future linear regressions. SOC as a mediation factor in the association between CF and WA will be additionally investigated. The same study will be conducted in two hospitals in Beer Sheba, Israel: Assuta and Soroka, and results of Latvian and Israeli parts of the study will be compared.

**Expected Results.** We expect to observe independent positive associations of age and of CF with WA. We expect for the mediational effect of SOC on the association of CF, but not of age, with WA. Stronger effect is expected between age and WA, but not between CF and WA for Israeli participants in comparison with Latvian medical personal.

**Conclusions.** Despite the complexity of situation with aging workers, it can be partly controlled through SOC that can have relevance in development of working strategies regarding old workers.

## 51. EVALUATION OF EMPLOYMENT STATUS AND EDUCATION LEVEL IN RANDOMLY SELECTED EPILEPSY PATIENTS

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**Background.** Financial security and being employed are among the most important aspects for patients with epilepsy. Apart from being a source of financial income, employment provides self-esteem, belonging to a certain social group, self-realization, affecting quality of life and social functioning. Not only finding employment but also staying employed are among major concerns for patients suffering from epilepsy.

**Purpose.** The aim of this study was to assess employment status and education level of patients with epilepsy in comparison to general population in Latvia.

**Materials and methods.** 56 randomly selected adult epilepsy patients treated in Riga East Clinical University Hospital "Gaiļezers" in Latvia between April 2016 and January 2017 were invited to participate in a survey to ascertain their education level and employment status. Data were statistically analyzed using the IBM SPSS (Version 22). The study was approved by the Ethics Committee of the Riga East Clinical University Hospital.

**Results.** The study involved 56 epilepsy patients – 23 female and 33 male patients, with ages ranging from 20 to 87 (mean =  $44.86 \pm 15.46$ ). Primary school education was reported in 17.9% (n=10), secondary school education in 41.1% (n=23), professional secondary school education in 21.4% (n=12) and university education in 19.6% (n=11) patients. The majority of respondents 60.7% (n=34) were without permanent employment – 7.14% (n=4) were retired, and 53.60% (n=30) were unemployed. Unemployment rate was 65.2% (n=15) in women in contrast to 54.5% (n=18) in men ( $p=0.302$ ). These data suggest high unemployment level among epilepsy patients in comparison to the general population – Central Statistical Bureau data in 2015 shows that general unemployment rate in Latvian population aged between 15 to 74 years are 9.9% (8.6% in women and 11.1% in men). In patients with primary school education compared to respondents with university degree unemployment status was 80% (n=8) and 27.3% (n=3), accordingly,  $p=0.08$  (tendency).

**Conclusions.** More than a half of patients with epilepsy in Latvia are unemployed, the unemployment rate is much higher than the one in general population. Unemployment significantly affects social functioning and quality of life for any person. Education level may significantly affect employment status, which was not demonstrated by our study due to insufficient number of patients.

## 52. CASE STUDY – REIMBURSEMENT FOR MEDICINAL MARIHUANA IN GERMANY, THORSTEN HETFELD V. AOK BAYERN

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**Background.** The use of cannabinoids in modern medical practice in most western countries is handled restrictive, as they are classified as controlled substances in many countries. Due to their potential benefit in various diseases, patients and patient rights groups have long been trying to facilitate access to medicinal cannabinoids, with legislation differing between countries. The presented case about a 47-year old IT-engineer from Bavaria who is suffering from Fibrous Dysplasia is exemplary for the difficulties that patients face in the process of acquisition of medicinal marihuana and related products. The patient is suing his insurance provider AOK Bayern for reimbursement of his therapy costs. In Germany, there are several ongoing court cases and multiple rulings in similar and related cases, which reveal the administrative and financial effort that patients currently have to face.

**Purpose.** Research was conducted on the background of current national laws of Germany regarding handling of cannabinoid based drugs. Public pressure on policy makers to change legislation has led to a re-evaluation process at the German Ministry of Health, with passing of a new law to be expected on January 19, 2017 in the German Parliament. While the original presentation in the setting of the LU course “Medical Law” is focused on patients’ rights on the aspect of Human Rights and thus advocates the medicinal use of marihuana from the physician’s side of view as a tool to benefit patients, the Author would like to help raise awareness among health care personnel and policy makers about the topic, in order to lead a science-based discussion rather than confounding recreational use of marihuana with its medicinal potential.

**Materials.** Analysis of scientific research and relevant international and national laws.

**Results.** At the present time cannabis therapy cannot be prescribed at the expense of the general health insurance, but have to be paid for by the patients. Physicians in Germany are allowed to prescribe a few comparatively expensive synthetic cannabinoid derivatives and cannabis-based medicinal extract products, but are forbidden to prescribe cannabis. However, selected patients can apply for a permission to obtain cannabis through a complicated system with physician’s support.

**Conclusions.** The complexity, ambiguity and inconsistency of this German system are outlined in this study and an outlook on possible future solutions is given.

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### 53. RIGHTS OF THE CHILD ENDANGERED BY ILLEGAL HOSPITAL FEES FOR PARENTAL STAY: A CASE STUDY OF THE CHILDREN'S CLINICAL UNIVERSITY HOSPITAL

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**Background.** International and national law provides an obligation towards the state and its institutions, services and facilities responsible for the care of children to safeguard and protect the rights of the child. The same obligation requires hospitals and health care practitioners, to establish a proper children protection plan and to eliminate practices violating or diminishing rights and wellbeing of the child. The practise of the Children's Clinical University Hospital (Children's hospital), requiring payment for parental stay in the hospital should be analyzed in the light of the rights of the child. It has to be questioned whether such payments might endanger realization of children's rights and therefore might be illegal.

**Purpose.** This research should potentially determine if the specific case indeed can be considered as malpractice, with the aim then to stimulate elimination of such practices, that might endanger implementation of rights.

**Materials and methods.** The evidence of existing practices in the Children's hospital, in respect to fees for parental stay in hospital, was collected during two years. Facts revealed were analyzed in the light of national and international children's rights law. Legal theory, guidelines of children protection in hospital, data of scientific research projects on the psychological, legal and organizational issues in respect to the parental role for a child in hospital have been collected and analyzed. The research allowed to draw conclusions and to prepare suggestions regarding the chosen research topic.

**Results.** There is an obligation established by the board of the Children's hospital to pay for parental overnight stay with the child in the hospital. The fee is EUR 6 per night for the first 7 days and EUR 3 per night starting from the 8<sup>th</sup> day. There are exceptions revoking the obligation to pay if the child is below the age of 5 or a treating doctor approved the necessity of parental stay. All parents, except breastfeeding mothers, if the child is younger than 1 year, are required to provide catering on their own. The Children's hospital is requiring a parent to sign a contract to enforce payments. Otherwise a parent has to leave child alone in Children's hospital at 9 pm.

**Conclusions.** The board of the Children's hospital has been approving the policy and a price list requiring hospital personnel to act contrary to the best interest of the child, especially putting burden on families living in poverty. Payments for parental stay in a hospital are endangering wellbeing of the child and might lead to psychological harm for the child. Parents are requested to pay for fulfilling their legal obligations. Therefore such payments should be eliminated and proper organization of parental stay with a child in hospital should be granted.

## 54. ALCOHOL, ITS ROLE OF FREQUENT VIOLENT DEATHS IN LATVIA

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**Introduction and purpose.** The aim of this study is to find out how often alcohol consumption is related to violent death in Latvia or more precisely in region of Riga. In this research we reviewed death from mechanical asphyxia – hanging, drowning, choking with foreign body, death after falls from height, death in traffic accidents – drivers, pedestrians and train accidents, death related to hypothermia and death caused by high temperatures.

**Materials and methods.** This is retrospective, descriptive research. Study population is made by people who died from mechanical asphyxia, falls from height, road accidents, hypothermia, effect from high temperatures and whom autopsy were made in State Centre for Forensic Medical Examination of the Republic of Latvia, in Riga. Period of research was from year 2010 till 2014. Total number of cases included in this study is 1468. Data for this research was obtained from criminal case materials. Data was summarized and analyzed using programs MS Excel and SPSS 22.

**Results.** The total number of cases from hanging in the loop was 515, of which 257 were committed under the influence of alcohol. Number of drowning cases in five years (2010–2014) was 229, of which 150 were under the influence of alcohol. From 2010 to 2014 thirty cases were found to be caused by suffocation with foreign body and ethanol was detected in 22 of those cases. The total number of cases caused by falling from height was 142, of which 58 were under the influence of alcohol. Speaking of road accidents related to pedestrian death, there were 157 of such cases and 73 were associated with alcohol intoxication. However, the number of road accidents related to driver death was 52, 11 of which were associated with alcohol intoxication. From 2010 to 2014 57 cases were detected related to railway accidents and 23 of those cases were associated with alcohol intoxication. Within five years, 192 hypothermia cases were registered, of which 98 were under the influence of alcohol. Registered deaths associated with exposure to high temperature were 104, of which 30 were related to alcohol intoxication.

**Conclusion.** Evaluating previously enumerated death occasions, we found that alcohol has a certain influence on violent death in the region of Riga.

## INTEGRATIVE MEDICINE

### 55. ORIGINS OF AYURVEDA AND THE ROOTS OF DIABETES MELLITUS IN THE HISTORY OF INDIAN MEDICINE

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**Background.** *Madhu meha* (MM) or *Diabetes Mellitus* (DM) has been well known and documented in *ayurvedic* classical literature since antiquity.

**Purpose.** The aim of the current study is to illustrate the depth of ancient *ayurvedic* knowledge on etiology, prevention, role of diet and lifestyle, knowledge of symptoms, diagnostic and treatment options of MM.

**Materials and methods.** Analysis of medical history books using library resources of AVCRI, internet search of PubMed, ScienceDirect, DHĀRĀ (Digital Helpline for Ayurveda Research Articles), Google Scholar publications, to analyze the historical sequence of medical texts on Ayurveda.

**Results.** The first mention of a disease, which manifests with sweet urine and polyuria is already in *Kaushika sutra* of *Atharva Veda* (1500–1200 BC). Detailed description is given in major texts of *Susruta* (surgical textbook, 500 BC,) and *Charaka* (internal medicine textbook, 400 BC) *samhitas*. MM was define as illness when patient's urine becomes sweet like honey, thus attracting ants, along with complains of polyuria and polydipsia. Different subtypes of MM where recognized that correlate to Type 1 and Type 2 Diabetes (T2D), also aspects of hereditary and acquired disease are mentioned. In etiology of T2D genotype of *Kapha prakriti* with higher BMI, demographic aspects of older age and family history of T2D, lifestyle aspects of low physical activity, sleeping during the day, altered circadian rhythm, and dietary habits of foodstuff with high glycemic index where recognized. In prevention opposite activities where recommended. Detailed description of symptoms and complications has been given – correlating to autonomic and peripheral neuropathy, diabetes foot ulcers, coronary heart disease, hyperglycemia induced glycosuria and infections, obesity induced laziness, looseness of the body, excessive thirst, sweating and foul smell, symptoms of electrolyte disorders, like dryness in the mouth, palate, throat, giddiness, signs of diabetic nephropathy. There is also a detailed explanation of symptoms and treatment recommendations individualized according to the stage of the MM, as well as patient's somatotype in *tridosha* system and also comorbidities of each individual are addressed.

**Conclusions.** There are strong similarities in etiology, pathogenesis and prevention aspects of MM in ancient *ayurvedic* texts and DM in modern biomedicine. *Ayurvedic* textbooks greatly emphasized individualized approach to each patient and also the role of psychosomatic aspects in MM, thus *ayurvedic* system approach can be seen and used as complementary tool in personalizing the modern treatment of T2D.

## 56. REVIEW STUDY TO CORRELATE PHYSIOLOGY AND ANATOMY OF PLEXUS COELIACUS AND MANIPURA CHAKRA

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**Background.** Integrative medicine provides system understanding of human anatomy and physiology, thus helps in preventive health care and the treatment of chronic gastrointestinal disorders, especially of psychosomatic multifactorial origin.

**Purpose.** To comprehensively evaluate the physiological and anatomical correlation of modern anatomy and physiology of *plexus coeliacus* (PC) to the ancient Indian science of *ayurveda* and *yoga* in respect to *manipura chakra* (MC).

**Materials and methods.** The group of experts in field compared the PC functions to the classical texts on *ayurveda* and *yoga* describing MC – the main regulatory center in the gastrointestinal area, responsible for correct metabolic activities, food substance transformation, absorption and distribution to the cells. Two reference sources for modern anatomy were used – the older classification from Gray's anatomy (GA) and the newer from *Terminologia Anatomica* (TA).

Research articles from PubMed and Science Direct databases were analyzed on the effects of *yoga* in the treatment of gastrointestinal disorders.

**Results.** In preclinical analysis a strong correlation between *ayurvedic tridosha* concept of physiology and the GA classification was established.

According to the GA classification, secondary plexuses from PC are the phrenic, splenic, hepatic, left gastric, inter-mesenteric, suprarenal, renal, testicular or ovarian, superior mesenteric and inferior mesenteric. Same organ involvement is found in MC physiologically controlled area. Whereas TA offered more narrow area of influence – PC secondary plexuses: hepatic, splenic, gastric, pancreatic, suprarenal, which does not reflect fully physiologic functions of MC described in *ayurveda*.

In clinical analysis strong evidence of improvement in Irritable Bowel Syndrome (IBS) Symptom Severity Scales and IBS Quality of Life was found in patients practicing *yoga* postures, breathing, meditation and relaxing techniques. *Yoga* practices improved functional ability, decreased pain and anxiety in IBS, also improved regulation of autonomic nervous system and blood supply to the gastrointestinal area.

**Conclusions.** There is a growing international research evidence testifying that practices of Integrative medicine added on to the modern treatment improve the quality of life in patients struggling with symptoms of functional gastrointestinal disorders.

## 57. ANTIMICROBIAL ACITIVITY OF *JATHYADI THAYLAM* AND ITS HERBAL FRACTIONS

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**Background.** *Jathyadi Thailam* is polyherbomineral formulation known in Ayurveda since ancient times for chronic wound and diabetic foot healing. There is an obvious need to do a systematic research on existing formulation to prove its antibacterial effect, especially on drug resistant bacteria.

**Purpose.** The aim of this study was to do antibacterial testing *in vitro*, with methods modification for *J. Thailam*. Different herbs and their combination should be tested in order to find most effective antibacterial combination. The modified version of *J. Thailam* such as lamellar gel phase was also studied.

**Materials and methods.** The antibacterial efficacy was tested by well diffusion method and by microdilution methods for most common isolates from diabetic wounds. As reference strains we used drug susceptible strains: *Staphylococcus aureus* ATCC 2848, *Pseudomonas aeruginosa* ATCC 2843, *Klebsiella pneumoniae* ATCC 2558, *Proteus mirabilis* ATCC 432 351, *Echerichia coli* ATCC 25 922 and drug resistant strains: MRAB – *Acinetobacter baumannii*, ESBL – *Klebsiella pneumoniae* and MRSA.

**Results.** Initially, the inhibitory effect was shown by crude herbal extract (Kalka-nopolar) for susceptible *Staphylococcus aureus* 2848 reference strain.

Fraction	Microorganism, zone of inhibition, mm					10% DMSO
	<i>Staph aureus</i> , ATCC 2848	<i>Escherichia coli</i> , ATCC 25922	<i>Pseudomonas aeruginosa</i> , ATCC 2843	<i>Klebsiella Pneumoniae</i> , ATCC 2558	<i>Proteus Mirabilis</i> , ATCC 432 351	
AVP-kalka-NP (1g/ml)	27-30mm	No ZOI	No ZOI	No ZOI	No ZOI	No ZOI
AVP-kalka-P (100mg/ml)	9-10mm	No ZOI	-	-	-	No ZOI
CAFL – NP (50mg/ml)	14-15mm	No ZOI	No ZOI	No ZOI	No ZOI	No ZOI
Gentamycin (4ug/ml)	25mm	28mm	25mm	27mm	23mm	No ZOI

ZOI – zone of inhibition

**Conclusions.** Further research is necessary to establish antimicrobial activity of *J. Thailam*.

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## 58. A CASE STUDY OF INTEGRATIVE TREATMENT OF DIABETIC FOOT

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**Background.** Over half of diabetic patients develop symptoms of sensory neuropathy caused by several molecular mechanisms, including accumulation of advanced glycation end products, activation of polyol pathway, protein kinase C, inflammation, etc. Serious complication of diabetic peripheral neuropathy is the diabetic foot syndrome. There is no unified concept of treatment of diabetic neuropathy, different drugs can be applied e.g. antioxidants (alpha-lipoic acid). In many cases results from conventional therapy do not provide expected outcomes hence integrative approach combining a modern biomedicine with a complimentary whole system medicine like *Ayurveda* can provide better outcomes clinically and improved quality of life.

**Purpose.** The aim of the study is to present a clinical case of a patient who refused a surgical intervention and was treated by integrative approach using per oral and topic *ayurvedic* medicines.

**Materials and methods.** A case report of 66 years old non-obese male with no known family history of Type 2 Diabetes (T2D) who presented with complaints of multiple non-healing ulcers in the right foot, the largest lesion involving the first toe and the plantar surface below it. The associated symptoms were extreme pain, burning and tingling sensation, low grade fever and a foul smelling pale yellow pus discharge. A year ago patient had developed similar complaints in the second toe of the same foot because of which he approached a general physician and was confirmed to have T2D. After intensive oral hypoglycemic therapy and wound management his glycemic index improved but ulceration continued for which he had to amputate his second toe. Due to the reoccurrence of symptoms in his first toe after six months patient visited outpatient department of AVCRI outpatient clinic, at that point he was on pioglitazone and repaglinide.

After *ayurvedic* clinical examination and diagnosis the therapy was implemented involving internal medication including herbs such as *Curcuma longa*, *Tinospora cordifolia*, *Rubia cordifolia*, *Cassia fistula*, *Azadirachta indica*, *Strychnos potatorum*, *Pichoriza kurroa*, *Raphanus sativus*.

Daily external wound care treatment was done by washing and herbal fumigation using *Curcuma longa*, *Emblica officinalis*, *Terminalia bellirica*, *Terminalia chebula*, *Cassia fistula* and *Commiphora wightii*.

**Results.** Within two months of active treatment, all the above symptoms were resolved, healthy granulation achieved and epithelization resumed.

**Conclusions.** This case gives an insight into successful integration of *ayurvedic* intervention along with conventional anti-diabetic therapy in the treatment of neurological and vascular T2D complications leading to diabetic foot syndrome.

## NURSING

### 59. PATIENTS' PHANTOM PAIN TREATMENTS AFTER LIMB AMPUTATION

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**Background.** Phantom pain affects quality of life and creates psychological stress. Phantom pain requires care and treatment.

**Purpose.** The main objective of the study was to analyze care for phantom pain patients after limb amputation.

**Materials and methods.** This research paper used a qualitative research method. Research tool: semi-structured interviews. Four men and one woman (23 to 43 years old) were interviewed, all with a traumatic amputation at different levels, and 100% consciousness over the amputated limb prior to the amputation. Four respondents suffered in various accidents, and one respondent suffered in a gas explosion. One respondent had both lower limb amputations at various levels. Two respondents had prostheses. All the respondents were patients of the same hospital, and were given the same curing and treatment.

**Results.** During the study it was found that there are four main factors that cause phantom pain for patients after limb amputation. The factors include posture, temperature, psychological factors and weather conditions. All respondents noted that after the operation they had problems with sleep, difficulty to find a comfortable position and turn in the bed, they also felt pain at night. The study showed that the feeling of internal psychological comfort is critical for elimination of phantom pain. Physical activity reduces phantom pain. Urination and defecation process provokes and reinforces the phantom pain. Nutrition and fluid intake does not affect the phantom pain, as well as the choice of clothing and dressing.

**Conclusions.** Active involvement in social life, participation in cultural and social events, learning and hobbies might eliminate phantom pain.

## 60. FACTORS AFFECTING WORKING ENVIRONMENT OF SURGICAL NURSES IN HOSPITAL

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**Background.** The problem is very important, since environmental factors play a major role in nursing work.

**Purpose.** The main objective of the study was to explore working environment and factors which influence surgical care nurses.

**Materials and methods** This research paper based on non-experimental quantitative method. The research was done in one hospital in Latvia where one hundred (100) surgical care nurses were evaluated.

**Results.** The results affirm that most of surgical nurses are discontented with working conditions which are harmful work environment influencing factors, psychological stress and lack of staff.

1. The majority (92%) of respondents consider that night work worsen nurses' health while (8%) says that there is no influence.
2. Both day shift (64.3%) and night shift (68.3%) nurses consider that the main reason for large amount of duties is the lack of medical stuff.
3. Night shift effect on the psychology is much higher (55.6%) than day work (10.7%) ( $p < 0.001$ ).

### **Conclusions.**

1. Night shift nurses experienced more psychological and skeletal – muscular system problems.
2. Night shift respondents have significantly more allergic reactions than day shift respondents;
3. Night shift respondents confirm that night work has negative impact on health.

## 61. PREPAREDNESS OF THE STAFF OF THE EMERGENCY CLINIC IN EMERGENCY MEDICAL SITUATIONS

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**Background.** Growing amounts of natural and human caused disasters worldwide is a global problem. Medical consequences of these disasters are called Emergency Medical Situations. Proof based medicine notes that readiness of hospitals to Emergency Medical Situations and various catastrophes is the most important factor in dealing with them. Hospital readiness to Emergency Medical situation is determined not only by available logistics but also by the readiness of its personnel.

**Purpose.** The aim of the study is to assess and to describe the way emergency unit's staff evaluate their preparedness of the emergency medical staff for emergencies.

**Materials and methods.** Study method: a quantitative study. Study tool: a questionnaire.

**Results.** Analysis of 100 respondents' (doctors, paramedics, nurses) self evaluation shows that practical experience in emergency situations determines a better understanding (preparedness) of management of emergency situations and individual duties related to them, compared to staff without prior experience in emergencies.

**Conclusions.** Data obtained during this research and the analysis of this data shows that personnel with prior practical experience in dealing with Emergency Medical situation shows increased readiness.