

Sveučilište u Zagrebu, Medicinski fakultet/University of Zagreb, School of Medicine  
**Doktorski studij Biomedicina i zdravstvo/PhD Programme Biomedicine and Health Sciences**  
**Dan doktorata 2013/PhD Day 2013**  
**Knjiga sažetaka/Abstract book**

---

Sveučilište u Zagrebu, Medicinski fakultet/University of Zagreb, School of Medicine  
**Doktorski studij Biomedicina i zdravstvo/PhD Programme Biomedicine and Health Sciences**  
**Dan doktorata 2013/PhD Day 2013**  
**Knjiga sažetaka/Abstract book**

---

A CIP catalogue record for this book is  
available from the National and University  
Library in Zagreb under ??????.  
**ISBN 978-953-176-???-?**

---

© Medicinska naklada, Zagreb, 2013.

All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means (electronic, mechanical, photocopying, recording or otherwise) without the prior permission of the publisher.

**Doktorski studij  
Biomedicina i zdravstvo  
PhD Programme  
Biomedicine and Health Sciences**

**Dan doktorata 2013  
PhD Day 2013**

Knjiga sažetaka  
Abstract book



MEDICINSKA NAKLADA  
ZAGREB, 2013.



# TABLE OF CONTENTS

Preface.....	VII
PhD Day 2013 Programme .....	IX
1. Research Abstracts.....	1
1.1. Research Abstracts - Basic Medical Sciences .....	1
1.2. Research Abstracts - Clinical Medical Sciences.....	19
1.3. Research Abstracts - Public Health and Health Care .....	51
2. Research Proposals .....	57
2.1. Research Proposals - Basic Medical Sciences .....	57
2.2. Research Proposals - Clinical Medical Sciences .....	71
2.3. Research Proposals - Public Health and Health Care.....	163



# PREFACE

Slowly becoming a traditional annual event, PhD Day 2013 is a day-long presentation of research results related to PhD theses through poster presentations and published abstracts being held on 24 May 2013. It is also a required part of the course load for PhD candidates in their 2nd and 3rd year of studies in the PhD programme Biomedicine and Health Sciences at the University of Zagreb, School of Medicine.

PhD Day is an excellent opportunity for PhD students to exchange research ideas amongst themselves, to share and learn from each other's positive and negative experiences and, most importantly, to promote and facilitate cooperation in research. Invited lectures of the world renowned scientists serve as additional motivation and encourage the PhD students to continue on their often arduous path of scientific research. Selected oral presentations of our candidates further strengthen the spirit of competitive cooperation as the main feature of interaction of scientists today. Likewise, the presence of mentors and guests encourages PhD students to engage in even more intense and inventive research. Comments of colleagues, teachers and guests serve as additional incentives, since organized scepticism is one of the essential features of science.

PhD Day shows individual scientific contributions of young scientists, but also paints a vivid and comprehensive picture of research activity of the PhD programme in Biomedicine and Health Sciences. It is meant to serve as a partial cross-section of the scientific activities of the School of Medicine as well as fellow domestic and foreign institutions. We are pleased to have an increasing number of PhD theses with two mentors, the so-called „Scandinavian style” theses, as well as theses in English.

Finally, PhD Day as a public display of our research activities is an excellent opportunity for the quality assessment of the PhD programme Biomedicine and Health Sciences, but also a great training ground for transferable skills useful even to students who will not be engaged in future research work. These skills include synthesis of a large amount of critical data, a critical attitude towards the research of others, communication skills and ability to summarize the results clearly in the form of posters or oral presentations. PhD Day is also a recognition and a reward to mentors and PhD candidates for their continuous efforts in scientific research, a major part of any PhD programme.

In conclusion, it is my hope that this PhD Day will be a day of celebrating science and research, a day of collaboration and a meeting of researchers, colleagues and friends.

Zdravko Lackovic  
PhD Programme Director





# PHD DAY 2013 PROGRAMME

09:00 - 09:45	<b>Students' Registration</b>
10:00 - 10:30	<b>PhD Day Opening:</b> Prof. Zdravko Lackovic, Prof. Melita Kovacevic (Chair EUA-CDE)
10:30 - 11:00	<b>Research Excellence Lecture</b> (Chair: Zdravko Lackovic) <ul style="list-style-type: none"><li>• Academician László Vécsei* (Szeged): <i>Kynurenines: role in the pathomechanism of neurological disorders and future therapeutic strategies</i></li></ul>
11:00 - 12:00	<b>Guest Students' Oral Presentations</b> (Chairs: Ana Borovecki and Robert Likic) <ul style="list-style-type: none"><li>• Moscow</li><li>• Ljubljana</li><li>• Pécs</li></ul>
12:00 - 13:30	<b>Organised Poster Session; Coffee and Lunch Break</b>
13:30 - 14:30	<b>Selected Oral Presentations</b> (Chair: Ante Tvrdeic and Marko Jakopovic) <ul style="list-style-type: none"><li>• Igor Erjavec: <i>Effect of blood serotonin levels on four months old rat skeleton</i></li><li>• Mario Blekic: <i>17q12-21 and asthma - interactions with early life environmental exposures</i></li><li>• Marko Kutlesa: <i>Efficacy of therapeutic hypothermia in patients with inflammatory diseases of the central nervous system</i></li><li>• Luka Vucemilo: <i>Are physician-patient communication practices slowly changing in Croatia? - A cross-sectional questionnaire study</i></li></ul>
14:30 - 16:00	<b>Organized Poster Sessions with Discussion</b>

*\* Prof. László Vécsei M.D., Ph.D., D.Sc., is a member of the Hungarian Academy of Sciences, Dean of the Faculty of Medicine, Director of Department of Neurology, Albert Szent-Györgyi Medical and Pharmaceutical Center, University of Szeged, Szeged, Hungary. His research interests include the kynurenine system, pathomechanisms of neurodegenerative disorders, headaches and multiple sclerosis, as well as novel therapeutic strategies aimed at these diseases. He is the author of more than 250 in extenso publications, numerous books and monographs.*



**1.**  
**RESEARCH  
ABSTRACTS**

**1.1.**  
**RESEARCH ABSTRACTS  
- BASIC MEDICAL SCIENCES**



## POSTER TITLE: DIFFERENTIATION OF CARDIOMYOCYTES FROM HUMAN INDUCED PLURIPOTENT STEM CELLS

**PhD candidate:** Ana Šepac, MD

**Part of the thesis:** Cardiomyocytes Differentiated from Human Pluripotent Stem Cells as an Experimental Model for Anesthetic-induced Preconditioning

**Mentor/s:** Professor Sven Seiwert, MD PhD and Professor Zeljko J. Bosnjak, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of Pathology

**Introduction:** Pluripotent stem cells can be differentiated into various cell types, including cardiomyocytes. Human induced pluripotent stem cells (hiPSCs) are generated by reprogramming human somatic cells, such as fibroblast, into pluripotent cell lines. Relative inaccessibility of human myocardium for research purposes hampers efficient translation of experimental data obtained in animal studies to human subjects. Cardiomyocytes derived from human pluripotent cell lines are considered a promising experimental model for studying human disease that bridges animal models and clinical trials.

**Materials and methods:** hiPSC lines C2a and C6a are obtained from the laboratory of Dr. S Duncan, MCW. The lines are generated from human skin fibroblasts that are treated with stemness factors Oct4, Sox2, Nanog and Lin28. Prior to differentiation into cardiomyocytes, pluripotent cells were cultured in hypoxic conditions on mouse embryonic fibroblasts. hiPSC colonies were passaged by microdissection. Cardiac differentiation was induced by treatment with activin-A and bone morphogenetic protein-4. Genetic labelling of viable cardiomyocytes was performed by transducing cells with a lentiviral vector carrying a coding sequence for reporter protein enhanced green fluorescent protein (eGFP) under transcriptional control of cardiac specific promoter myosin light chain-2v

(MLC-2v). Immunocytochemistry was performed by labelling cells with primary antibodies for titin, sarcomeric alpha actinin and cardiac troponin T.

**Results:** Following in vitro cardiac differentiation, C2a and C6a hiPSC lines formed spontaneously and rhythmically beating cell clusters that indicates the presence of functional cardiomyocytes. More than 60% (from three independent differentiations) of cells isolated from such beating clusters were positive for labelling with MLC-2v-eGFP, verifying extensive cardiomyocyte enrichment. Immunostaining showed a striated pattern of sarcomeric proteins in these cells, indicating presence of cardiomyocytes with organized sarcomeres.

**Discussion:** hiPSCs can be differentiated into contracting cardiomyocytes that exhibit highly organized contractile machinery. Such data encourage further research testing feasibility of using hiPSC-derived cardiomyocytes for in vitro drug testing and disease modelling.

**Acknowledgments:** I am grateful to my mentors, Drs. Seiwert and Bosnjak, lab members and the Graduate School.

**MeSH/Keywords:** human induced pluripotent stem cells, cardiomyocytes, differentiation

**Poster code:** A-3-148

## **POSTER TITLE: CORRELATION BETWEEN ASTROGLIAL CHANGES, COGNITIVE AND CHOLINERGIC DEFICIT IN A RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE: LONG-TERM FOLLOW UP**

**PhD candidate:** Ana Knezović, dipl.ing.

**Part of the thesis:** Cholinergic system in the brain of the streptozotocin-induced rat model of sporadic Alzheimer's disease

**Mentor/s:** Professor Melita Šalković-Petrišić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of Pharmacology

**Introduction:** Sporadic Alzheimer's disease (sAD) is associated with cognitive and cholinergic deficit and astrogliosis in addition to the amyloid and tau protein pathology, development of which is difficult to track in humans. Central administration of streptozotocin (STZ-icv) is shown to induce also these Alzheimer-like changes due to the STZ-icv rat model has been recently proposed as a non-transgenic sAD animal model. We aimed to characterize the STZ-icv dose- and post- treatment time-dependency of cognitive and cholinergic deficit and astrogliosis in the brain of the STZ-icv rat model.

**Materials and methods:** Adult Male Wistar rats were given STZ- (0.3, 1 and 3 mg/kg) or vehicle-icv (controls) and sacrificed one, three, six and nine months after the treatment. Cognitive functions were measured by Passive Avoidance Test (PA) before sacrifice. Acetylcholinesterase (AChE) activity was measured in hippocampus (HPC) by Ellman's method. Paraffin-embedded brain sections were immunohistochemically stained with glial fibrillary acidic protein (GFAP) and analysed with cellSense Dimension software. Data were analysed by Kruskal-Wallis and Mann-Whitney U test ( $p < 0.05$ ).

**Results:** STZ-icv rats exhibit significant dose- and time-dependent cognitive decline in PA test,

emphasized with higher doses (-45% to -90%). AChE activity in the STZ-icv (3 mg/kg) treated rats was significantly elevated in HPC after one (20%) and nine (32%) months. Higher STZ doses increased (35 to 45%) the expression of GFAP positive cells in HPC one and nine months following STZ administration compared to the controls. Six months after the STZ-icv treatment GFAP expression was found decreased in STZ animals.

**Discussion:** Results suggest that cognitive deficit induced by higher STZ-icv doses, tend to correlate with the appearance of hippocampal astrogliosis and cholinergic deficit in the STZ-icv rat model. Found changes follow similar biphasic pattern which starts with acute changes found 1 month after the treatment (acute response), followed by normalization and then progressive deterioration found 6-9 months after the treatment (chronic response).

**Acknowledgments:** Supported by UKF and MZOS (108-1080003-0020)

**MeSH/Keywords:** sporadic Alzheimer's disease, intracerebroventricular streptozotocin, memory, astrogliosis, cholinergic transmission

**Poster code:** A-4-14

## POSTER TITLE: THE EFFECT OF PENTADECAPEPTIDE BPC 157 AND HIGH DOSE DICLOFENAC ON INDUCED SHORT BOWEL SYNDROME

**PhD candidate:** Nermin Lojo, MD

**Part of the thesis:** THE EFFECT OF PENTADECAPEPTIDE BPC 157 AND HIGH DOSE DICLOFENAC ON INDUCED SHORT BOWEL SYNDROME

**Mentor/s:** Professor Predrag Sikirić, MD, PHD, Associate Professor Žarko Rašić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of Farmacology and Pathology

**Introduction:** Stable gastric pentadecapeptide BPC 157 (an anti-ulcer peptide effective in IBD trials, LD1 not achieved) counteracted short bowel syndrome (Sever et al Dig.Dis Sci 2009) and protected rats against diclofenac gastrointestinal injuries (Ilic et al. J Physiol. Pharmacol, 2009). In this study we tested the effect of pentadecapeptide 157 on induced short bowel syndrome rats aggravated with high dose of diclofenac.

**Materials and methods:** We used 80%-small intestine resection and then short bowel syndrome rats received diclofenac application (12.5 mg/kg i.p.). Medication (BPC 157 10 µg/kg or an equivolume of saline (5 ml/kg ip) was given immediately after diclofenac. Animals were sacrificed 24 h after the surgery. Assessment included bleeding period (sec), gastrointestinal lesions (sum of longest diameters of lesions stomach, small and large intestine), serum AST, ALT, bilirubine levels. Microscopic analysis was also performed.

**Results:** All BPC 157 treated animals had shorter bleeding period compared to control group animals (210 ± 37s vs. 480 ± 43s). Bilirubine levels were significantly increased in control group

animals compared to BPC 157 treated animals (192.3 ± 46.7 µmol/ L vs. 6.8 ± 3.1 µmol/L). AST, ALT, LDH were increased in both tested groups (AST 308 ± 14 u/L (BPC157) vs. 383 ± 27 u/L (con.) ALT 52 ± 4 u/L (BPC157) vs. 63 ± 6 u/L (con.)) Number of gastrointestinal lesions (gastric, duodenal, small and large intestinal ulcerations) was significantly larger in control animal group compared to BPC 157 treated animals (gastric 5.6 ± 2.7 lesions (con) vs. 0.5 ± 0.2 lesions (BPC) duodenal (1.3 ± 0.2 lesions(con) vs. 0 lesions (BPC) jejunum, ileum and rectum score (1- ulcerations, 2- erosions and erythema, 3- normal mucosal surface) Jejunum 1.6 ± 0,7(con) vs. 2.8 ± 0.2 (BPC) Ileum 1 ± 0,4 (con) vs. 2.8 ± 2 (BPC) Rectum 1 ± 0.3 (con) vs. 2.6 ± 0,4 (BPC)).

**Discussion:** According to our results we could conclude that BPC 157 improves small bowel and liver lesions healing in malnutrition conditions even during high dose diclofenac exposure.

**Acknowledgments:** Prof. Predrag Sikirić, Associate Professor Žarko Rašić

**MeSH/Keywords:** pentadecapeptide BPC 157, short bowel, diclofenac

**Poster code:** A-4-92

## **POSTER TITLE: PENTADECAPEPTIDE BPC 157 ANTIARRHYTHMIC EFFECT IN RATS TREATED WITH BUPIVACAINE TOXIC DOSES**

**PhD candidate:** Gordana Živanović Posilović MD, MSc

**Part of the thesis:** Pentadecapeptide BPC 157 Antiarrhythmic Effect In Rats Treated With Bupivacaine Toxic Doses

**Mentor/s:** Professor Predrag Sikirić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of Pharmacology

**Introduction:** Bupivacaine, still drug of choice in all the techniques of regional anesthesia, acts mainly through blockade of Na channels, K and Ca<sub>2</sub> channels as well, changing the way heart conduction system works with very serious and mostly lethal cardiac rhythm disturbances in a case of inadvertent i.v. application because we still don't have an antidote that could be applied. Pentadecapeptide BPC 157 antiarrhythmic effects were already established in previous studies of digoxin toxicity, hyper- and hypokalemia. These effects were realized through the interaction with NO-system. The aim of the study is to establish BPC 157 antiarrhythmic effect when cardiac rhythm disturbances are caused by bupivacaine toxic dose and to explore whether this effect is dose-dependent and related with NO-system.

**Materials and methods:** The study was conducted on female Wistar albino rats, divided into groups of 6. We had two protocols with 4 experimental groups each, treated with BPC 157 i.p. (50 µg/kg, 10 µg/kg, 10 ng/kg, 10 pg/kg) and the control group treated with saline 5ml/kg i.p. either 30 minutes before (preventive) or 1 minute after bupivacaine 100 mg/kg i.p (therapeutic). Three standard leads ECG was recorded for 90 minutes. The wave amplitudes P, R, S and T, the duration of waves and intervals P, PR,

QRS and RR, the presence of ventricular ectopies, tachycardia, AV block and asystolia were analyzed.

**Results:** Bupivacaine caused bradycardia, PQ prolongation, all degrees of AV block, QRS widening, ST-T wave changes, multiform ventricular ectopies (VES), ventricular tachycardia (VT) and asystolia. BPC 157 treated animals in both protocols had less prolongation of P wave, QT and RR intervals and of QRS complex. VT occurred later (8. min vs. 4. min) and lasted shorter than in the control group, while the number of VES/min was lower during the first 10 minutes, as critical time before extracardial bupivacaine effects occurred (respiratory arrest, neurotoxic effect). Mortality in all BPC 157 groups was also lower (16,7% vs. 50%).

**Discussion:** BPC 157 has shown cardio protective effect in both protocols and in all applied doses. Since prolongation of QT interval was lower in experimental groups, the predisposition to malignant arrhythmias was also lower, which could explain the lower mortality.

**Acknowledgments:**

**MeSH/Keywords:** cardiac arrhythmias, bupivacaine, pentadecapeptide BPC 157

**Poster code:** A-4-96



## POSTER TITLE: PENTADECAPEPTIDE BPC 157 AS A THERAPY FOR CORROSIVE MUCOSAL LESIONS IN RATS

**PhD candidate:** Tomislav Bečejac, MD.

**Part of the thesis:** The Effect Of Pentadecapeptide BPC 157 In The Therapy Of Caustic Lesions Of The Tongue, Esophagus, Stomach And Duodenum Induced By 96% Alcohol In Rats

**Mentor/s:** Professor Dinko Stančić-Rokotov, MD, PhD, FETCS.

**Affiliation:** University of Zagreb School of Medicine, Department of Pharmacology, Zagreb, Croatia, University Hospital Centre-Zagreb, Clinic for Thoracic Surgery „Jordanovac“, Zagreb, Croatia

**Introduction:** Corrosive mucosal lesions are very important medical and socioeconomical problem in general. It has usually been seen as an accidental intake of a corrosive substance (children) or in attempts of committing suicide (adults). Experimental researches of caustic injuries on animal models are rare and inconclusive. Ingestion of a chemical agent (absolute alcohol) was used for model of A. Robert's cytoprotection. A safe stable gastric pentadecapeptide BPC 157(GEPPPGKPADDAGLV, MW 1419, stable in human gastric juice, LD1 not achieved) may be the novel mediator of Robert's cytoprotection, and thereby, may counteract all corrosive mucosal injuries. Successful in inflammatory bowel disease trials, it counteracts esophagitis, sphincters failure, gastrointestinal ulcer, skin ulcer, and fistulas in rats.

**Materials and methods:** Corrosive mucosal injuries in rats were induced by applying 1ml of 96% alcohol at the tongue, whilst BPC 157 (10 µg, 10 ng/kg) or saline (5ml/kg) in combination with L-arginin (100mg/kg) or L-NAME (5mg/kg) were given intraperitoneally immediately after. Tongue, esophagus, stomach and duodenal mucosal defects, lower esophageal sphincter (LES) and pyloric sphincter (PS) pressure were evaluated at the time period of 30 sec, 1, 5, 15, 30, 60, 120 minutes, and 24 hours.

**Results:** PRELIMINARY RESULTS: Control. Mucosal defects after 30 sec: tongue (lesions

area, mm<sup>2</sup>, 52.0±2.8), esophagus (110.5±43.1), stomach (125.0±84.9) and duodenum (9.0±1.41). Mucosal defects after 24 h showed progression: 24.7±21.3 (tongue), 174.6±111.4 (esophagus), 271.3±76.9 (stomach), 30.9±48.7 (duodenum). Sphincters pressures remained continuously low i.e. 46.2±11.3 cm H<sub>2</sub>O (LES 24 h), 34.0±13.4 cm H<sub>2</sub>O (PS 24 h). L-arginin showed smaller and L-NAME larger corrosive lesions. BPC 157 ug-regimen initially exhibited smaller mucosal defects on tongue (18.5±9.2), esophagus (8.5±6.4), stomach (3.0±4.2) and duodenum (4.5±4.9) after 30 sec. Mucosal defects remained significantly lower than control during 24 hours (7.1±10.0 (tongue), 18.3±32.9 (esophagus), 61.3±65.5 (stomach), 4.7±3.9 (duodenum)). Sphincters pressures were restored i.e. 58.8±11.6 cm H<sub>2</sub>O (LES 24 h), 45.1±10.0 cm H<sub>2</sub>O (PS 24 h). L-arginin with BPC 157 and L-NAME with BPC 157 showed smaller corrosive lesions than control. BPC 157 ng-regimen shows the same effectiveness (vs. control p<0.05).

**Discussion:** BPC 157 could be used as a therapy for corrosive mucosal lesions.

**Acknowledgments:** I would like to thank my mentor for making this experiment possible

**MeSH/Keywords:** pentadecapeptide BPC 157, corrosive mucosal injuries

**Poster code:** A-4-133

## POSTER TITLE: EFFECT OF BLOOD SEROTONIN LEVELS ON FOUR MONTHS OLD RAT SKELETON

**PhD candidate:** Igor Erjavec

**Part of the thesis:** Blood serotonin levels effect on bone remodeling metabolism

**Mentor/s:** Associate Professor Lovorka Grgurević, MD, PhD

**Affiliation:** Laboratory for Mineralized Tissue, School of Medicine, University of Zagreb, Croatia

**Introduction:** Serotonin or 5-hydroxytryptamine (5HT) has a major role in vasoconstriction, peristaltic bowel movement, blood clotting and has an important role as a neurotransmitter in the central nervous system. Latest discoveries imply on serotonin's effect on bone.

**Materials and methods:** To examine serotonin effect on bone in this experiment we used well described animal model with altered blood serotonin levels. Four months old female Wistar-Zagreb 5HT (WZ-5HT) rats were used. Animals were developed by selective breeding to create two distinct animal sublines, high-5HT and low-5HT. Trabecular and cortical bone structure and quality were investigated in distal part of femur while only trabecular parameters were analyzed in the body of third lumbar vertebrae. Animals were weight on a digital scale and femur length was measured with a caliper. Bone structure was analyzed using SkyScan 1076 micro CT system while bone quality was assessed by biomechanical testing. Using a Texture analyzer TA.HD Plus femurs were subjected to three point bending test for cortical bone analysis and an indentation test for trabecular bone analysis.

**Results:** Animals with high serotonin level had increased weight, femur length and bone tissue volume. Analyzing cortical bone no difference in cortical bone volume and thickness was observed between the two sublines, while high-5HT animals had increased endosteal volume due to larger bones. Biomechanical testing confirmed results from micro CT analysis with no

difference in cortical bone strength between the high-5HT and low-5HT subline. No difference in trabecular bone parameters between high-5HT and low-5HT animals were observed on periphery, while in axial skeleton trabecular parameters were significantly better in animals with low serotonin level. Indentation test revealed no difference between the two sublines in force parameters of the trabecular bone in femur.

**Discussion:** In four months old female animals effect of serotonin on development and growth was evident due to difference in weight and bone length. 5HT had no effect on femur bone parameters while on axial skeleton negative effect of increased 5HT was observed. Our findings point out that serotonin has a distinct negative effect on trabecular bone properties in axial skeleton while we observed no effect on cortical or trabecular bone in peripheral skeleton in four months old females.

**Acknowledgments:** Special thanks to Lipa Čičin-Šain, from Institute „Ruder Bošković“, for collaboration and for providing the animals for this study and Damir Ježek from Faculty of Food Technology and Biotechnology for help with biomechanical testing. Also many thanks to Đurđica Car and Mirjana Marija Renić for help around handling the animals.

**MeSH/Keywords:** serotonin, 5-hydroxytryptamine, bone remodeling, micro CT, trabecular bone, cortical bone, biomechanical testing

**Poster code:** A-5-142

## POSTER TITLE: PPARG VARIABILITY IS AN IMPORTANT FACTOR IN THE DEVELOPMENT OF METABOLIC SYNDROME

**PhD candidate:** Tamara Božina, Master of Bioprocess Engineering

**Part of the thesis:** Effect of Gene Interactions and Environment Factors on the Incidence of Metabolic Syndrome

**Mentor/s:** Professor Jadranka Sertić, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** Peroxisome proliferator-activated receptor gamma (PPARG) is a nuclear transcription factor with a crucial role in the expression of key genes involved in adipogenesis, lipid and glucose metabolism, atherosclerosis, inflammation and immunity. Polymorphic variant of PPARG Pro12Ala modulates transcriptional activity and thus the stimulation of target genes LPL, IL-6, ACE and AT1R. Therefore PPARG function may represent a key role in the development of dyslipidemia, obesity, hyperglycemia and hypertension, major risk factors for the development of the metabolic syndrome (MetS). The aim of this study was to examine the role of PPARG Pro12Ala gene variant in the interaction with target genes.

**Materials and methods:** The study included 527 subjects (265 with MetS and 262 controls). Measurements included: triglycerides, total cholesterol, LDL-C, HDL-C, fasting glucose in blood, CRP, blood pressure (BP), waist circumferences and measurements of weight and height for body mass index (BMI) calculations. Genotyping for PPARG Pro12Ala, LPL (Pvu M/P), IL-6 (-174G>C), ACE (I/D) and AT1R (1166A>C) was performed by PCR restriction fragment length polymorphism (PCR-RFLP) method.

**Results:** In the group of participants with PPARG ProAla or AlaAla genotype, carriers of LPL M/P or P/P genotype have about six times greater odds for developing MetS compared to

PPARG ProPro genotype carriers (OR=5.98, 95% CI:1.46-24.47). Interaction of PPARG and LPL genotypes was also statistically significant for HDL-C, where the combination of Ala/Pvu(P) contributes to low HDL-C (specific Ala/Pvu(P) vs. others  $\chi^2=11.750$ ,  $p=0.0006$ ). In the group of patients with MetS, carriers of combination of IL-6 -174 GG and PPARG ProAla or AlaAla genotypes have 90% smaller odds of having high glucose compared to PPARG ProPro genotype carriers (OR=0.10, 95% CI:0.02-0.57). In the group of patients with MetS carriers of combination of genotypes IL-6 -174 GC or CC with PPARG ProAla or AlaAla have almost 2.5 times larger odds of having high glucose compared to PPARG ProPro genotype carriers (OR=2.39, 95% CI:1.11-5.17).

**Discussion:** PPARG gene variants in the interaction with target genes may contribute to the development of MetS.

**Acknowledgments:** This study was supported by grant of Croatian Ministry of Science, Education and Sports as part of Project No. 108-1080134-0136 „Functional genomics and proteomics of risk factors for atherosclerosis”.

**MeSH/Keywords:** Metabolic Syndrome, Genetic Polymorphisms, PPAR gamma, Angiotensin Converting Enzyme, Angiotensin Type 1 Receptor, Lipoprotein Lipase, Interleukin-6

**Poster code:** A-6-29

## POSTER TITLE: WHOLE GENOME SEQUENCING ANALYSIS OF HUMAN LIVER SINUSOIDAL ENDOTHELIAL CELLS REVEALS EVIDENCE FOR AN ANTI-INFLAMMATORY ROLE DURING HCV INFECTION

**PhD candidate:** Neven Papić, MD

**Part of the thesis:** The role of liver sinusoidal endothelial cells in HCV infection.

**Mentor/s:** Assistant Professor Adriana Vince, MD, PhD, Professor Curt Hagedorn, MD, PhD

**Affiliation:** University Hospital for infectious diseases Zagreb, Croatia. University of Utah, School of Medicine, Salt Lake City, Utah, USA.

**Introduction:** Liver sinusoidal endothelial cells (LSEC) due to their extraordinary scavenger activity are playing a pivotal role in blood-borne virus clearance. LSEC account for the 20% of hepatic cells and are unique organ-resident cell population with diverse functions, including degradation of bacterial by-products, antigen presentation and induction of tolerance. While these processes are particularly relevant to HCV infection, the role of LSEC in chronic hepatitis C is not defined.

**Materials and methods:** Aim of this study was to apply systems biology approaches to evaluate the role of LSEC in HCV infection. Poly(A) RNAs from HCV, MOCK or LPS treated primary LSEC cultures were analyzed by RNA-sequencing (Illumina) to identify differentially expressed genes (DEG) and biological pathways. Cell transcriptomes were compared to similar analysis with mild (no fibrosis) and severe (cirrhosis) hepatitis C livers, hepatoma and Kupffer cells.

**Results:** Following exposure LSEC internalized HCV, but failed to support HCV replication. LSEC overall displayed 754, 245 and 2543 DEG at 8, 24 and 48h after HCV exposure, respectively. While LPS stimulation triggered exceptionally potent activation, HCV in general induced a downregulation of inflammatory signals. This involve changes in network of transcriptional regulators (>100 DEG), such as MAFB (4x) and NURP1 (7x) that antagonize anti-viral inflamma-

tory responses, a decrease in transcription of cytokines and increase in inhibitors of their biological functions (ACP5 9x, A2M 6x, SERPING1 7x), an unaffected IFNs and ISGs expression. Gene pathway analysis highlighted changes associated with angiogenesis (40), adhesion (142), ECM-organization (107), signaling (153), apoptosis (109) and regulation of immune responses (104). Interestingly, most of these pathways showed significant overlap with HCV infected livers, in contrast to HCV infected hepatoma and Kupffer cells that presented with distinct gene expression profiles.

**Discussion:** This is the first comprehensive gene expression analysis of LSEC that provided insight into the broad portrait of genomic changes associated with HCV infection. These genes are critical components of host immune and inflammatory pathways and provide new evidence that LSEC downregulate inflammation during HCV infection.

**Acknowledgments:** This study was financially supported by Croatian Ministry of Science (143-0000000-0117) and Division of Gastroenterology, Hepatology and Nutrition at University of Utah.

**MeSH/Keywords:** HCV, chronic hepatitis C, liver sinusoidal endothelial cells, next-generation RNA sequencing, gene expression

**Poster code:** A-6-37

## POSTER TITLE: EXPRESSION OF BORIS AND MYC IN HYPOPHARYNGEAL SQUAMOUS CELL CARCINOMA - PRELIMINARY RESULTS

**PhD candidate:** Ivan Rašić MD

**Part of the thesis:** Clinical Significance of BORIS and MYC Expression in Hypopharyngeal Squamous Cell Carcinoma

**Mentor/s:** Renata Novak Kujundžić DVM., PhD, Professor Mirko Ivkić MD, PhD

**Affiliation:** Ruder Bošković Institute, Zagreb, University Hospital Center „Sestre milosrdnice“, Zagreb

**Introduction:** Exposure to risk factors for hypopharyngeal squamous cell carcinoma (SCC) results in complex epigenomic changes and derailment in expression of cancer relevant genes. Proteins CTCF and its paralogue BORIS associate with regulatory regions genomewide and organize chromatin into domains with different transcriptional activity. It has been well established that activity of c-MYC, coding for important regulator of cell proliferation and differentiation, is tightly regulated by CTCF. Its related protein BORIS, homologous in its DNA-binding domain with CTCF, has long been regarded as cancer testis antigen, due to lack of awareness of its transcript variants and protein isoforms. Discovery of its ubiquitous expression and role in cell cycle points to the need for evaluating regulatory role of BORIS isoforms on c-MYC activity.

**Materials and methods:** Total RNA was extracted from 68 hypopharyngeal SCC and 30 adjacent tissue samples and reversely transcribed into cDNA. Up to now, we have analyzed the expression of BORIS and MYC transcripts in 30 tumor/surrounding tissue sample pairs by RT-PCR. Products were visualized on agarose gels, photographed and analyzed by Image J software.

**Results:** The amplification of cDNA with primers constructed to detect different BORIS transcripts revealed expression of three BO-

RIS transcript variants in hypopharyngeal SCC and adjacent tissue samples. The full length BORIS transcript was detected in 6 tumor samples (20%) and none of the tumor-adjacent tissue samples. The two splice variants (lacking exons 7 and 6-8, respectively) were detected both in tumor and adjacent tissue. The level of MYC mRNA was not significantly associated with patients' survival. Lower MYC transcript level in tumor compared to adjacent non-tumorous tissue was associated with poor survival (hazard ratio 5.134,  $p=0.0328$ ).

**Discussion:** Full length BORIS transcripts were confined only to tumors, while its other transcript variants were present in tumor and adjacent non-tumorous tissue in accordance to report on its ubiquitous expression and association with cell cycle. Association of lower MYC expression in tumors, relative to adjacent tissue, with poor outcome in patients is in line with recent report on increased invasiveness of tumors with low MYC expression.

**Acknowledgments:** This work is funded by grant No. 098-0982464-2511 from the Ministry of Science, Education and Sport, Republic of Croatia.

**MeSH/Keywords:** hypopharynx, squamous cell carcinoma, BORIS, MYC, transcript variant, protein

**Poster code:** A-6-65

## POSTER TITLE: PHOSPHORYLATED HER2 RECEPTOR AS AN INDICATOR OF BREAST CANCER RESISTANCE TO TRASTUZUMAB

**PhD candidate:** Snježana Ramić, M.Sc. Molecular Biology

**Part of the thesis:** Phosphorylated HER2 receptor as an indicator of breast cancer resistance to trastuzumab

**Mentor/s:** Associate Professor Fabijan Knežević, MD, PhD

**Affiliation:** University Hospital for Tumours, University Hospital Centre „Sisters of Charity“, Ilica 197, Zagreb, Croatia

**Introduction:** Overexpression of the epidermal growth factor receptor 2 (HER2) leads to oncogenic transformation of cells. HER2 is overexpressed in 15-25% of breast cancer (BC) resulting with a poor prognosis. Patients with HER2-positive BC receive trastuzumab (Herceptin® Roche), an anti-HER2 therapy that reduces recurrence and improves survival. Still, some patients develop metastasis during treatment as a result of resistance to trastuzumab. HER2 can be overexpressed, but not activated. Phosphorylation of HER2 (pHER2) is the final step of its activation and results in downstream signalling. Therefore, pHER2 is a true indicator of receptor activity and function. Variations in HER2 phosphorylation indicate changes in receptor or its signalling pathway. Lack of pHER2 expression might determine patients who will be resistant to trastuzumab.

**Materials and methods:** pHER2 was determined in 88 cases of HER2-positive and 50 cases of HER2-negative BC. All patients with HER2-positive BC received trastuzumab-based therapy and 16 of them (18.2%) had disease progression during treatment. A monoclonal antibody against phosphorylated-Tyr1248-HER2 was used for immunohistochemical analysis. Intensity of membrane/cytoplasmic staining was categorized as negative (0, without staining and 1, weak staining) and positive (2, moderate and 3, strong staining). The difference in the pHER2 expression between trastuzumab-sensitive and

-resistant tumours was analysed using Fisher's exact test ( $P < 0.05$ ).

**Results:** Our results showed that overexpressed HER2 is generally in its phosphorylated form. pHER-2 was positive in 62.5% (55/88) of HER2-positive BC with HER2 score 3 in 51 cases and score 2 with gene amplification in four. Although pHER2 was predominantly expressed in HER2-positive BC it cannot be used as a surrogate for HER2 positivity. Six cases of HER2-negative BC (12%) displayed positive pHER2. Trastuzumab-resistant tumours had a low level of phosphorylation. They had negative pHER2 in 62.5% of cases. Trastuzumab-sensitive tumours had only 22% of pHER2-negative cases. pHER2 expression between trastuzumab-resistant and sensitive tumours differed significantly ( $P = 0.017$ ).

**Discussion:** Although trastuzumab is the most widely used anti-HER2 therapy, some patients does not benefit from it. The pHER2 expression could have clinical impact on the application of trastuzumab therapy. Combined with HER2 positivity, pHER2-positive cases could be categorized as good candidates for trastuzumab therapy.

**Acknowledgments:**

**MeSH/Keywords:** Breast cancer, HER2, phosphorylation, trastuzumab, drug resistance

**Poster code:** A-6-111

## POSTER TITLE: SELECTION OF FORENSICALLY SIGNIFICANT SNPS INSIDE BIH POPULATION

**PhD candidate:** Rijad Konjhodžić

**Part of the thesis:** Identification of the mitochondrial DNA control region polymorphisms in population of Bosnia and Hercegovina and the development of the protocol for their forensic application

**Mentor/s:** Prof. dr. Milovan Kubat

**Affiliation:** Clinical Center Sarajevo

**Introduction:** Analysis of the hypervariable region of the human mitochondrial DNA is one of the widely accepted tools in forensic genetics. It is especially useful in cases where degradation of nucleic genetic material has rendered it useless, since the mitochondrial DNA has shown itself more resilient to degradation. The control region is 610 base pairs long, and is consisted of hypervariable regions 1 and 2 (HV1 and HV2). Both hypervariable regions can be sequenced from one run each, with both forward and reverse primers, which are well documented. Sequencing of the HV regions is essentially a comparative study, where we compare sequences from the DNA extracted from the samples collected at the crime scene with the ones collected from the persons of interest. However, rate of mutations at certain SNPs (Single Nucleotide Polymorphisms) varies from population to population, and its determination is very important for the precise statistical analysis essential in every forensic report. Analysis is based on the identification of the SNP's characteristic for the population in which the testing is performed, primarily their rate of occurrence.

**Materials and methods:** DNA was extracted from 300 buccal swabs taken from unrelated individuals from the entire territory of Bosnia and Hercegovina. DNA was amplified using PCR, and subsequently sequenced using primers spe-

cific for the hypervariable regions 1 and 2. Electrophoresis was done on the ABI 3130 Genetic Analyzer. Obtained sequences were analyzed and compared using DNA VIEW software.

**Results:** Comparison of sequences obtained with the Anderson sequence has shown presence of 15 potentially significant SNPs. Nine of those SNPs are explained in literature, but the other 6 are unique for the territory tested. Primers necessary for the single base extension protocols were designed, and their results are to be compared with the Sanger sequencing results.

**Discussion:** Rate of mutations at certain SNPs varies between populations, and its determination is very important for the precise statistical calculation. Analysis is based on the identification of the SNP's characteristic for the population in which the testing is performed, primarily their rate of occurrence. This enables generation of forensic reports, but also opens the possibility of the creation of the alternative protocol based on single nucleotide extension that will simplify the procedure, and give it mixed sample testing potential.

**Acknowledgments:**

**MeSH/Keywords:** mtDNA, SNP, single-base extension, Sanger sequencing, PCR

**Poster code:** A-6-144

## POSTER TITLE: AICAR INDUCES DIFFERENTIATION OF ACUTE MYELOID LEUKEMIA CELLS

**PhD candidate:** Hrvoje Lalić, MD

**Part of the thesis:** The role of AMPK/mTOR signaling pathway in differentiation of leukemia cells

**Mentor/s:** Associate Professor Dora Višnjić, MD, PhD

**Affiliation:** Department of Physiology and Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Salata 3, 10 000 Zagreb, Croatia

**Introduction:** The most successful therapy of acute myeloid leukemia (AML) is differentiation therapy with all-trans-retinoic acid (ATRA), but so far, it has been restricted only to acute promyelocytic leukemia (APL). Pharmacological modulators of AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) pathway have been reported to exert antiproliferative effects in leukemia, but their role in differentiation is less explored. The aim of this study was to test for the effects of AMPK/ mTOR modulators in combination with differentiating agents in AML, especially in non-APL cell lines.

**Materials and methods:** Myeloblastic HL-60, promyelocytic NB4 and monocytic U937 were differentiated in the presence of ATRA or dimethyl-sulfoxide (DMSO) and incubated with AMPK/mTOR-modulators: rapamycin, 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR), metformin and compound C. The number of viable cells was determined by hemocytometer. The expression of differentiating markers, cell cycle analysis and apoptosis were determined and analyzed by FACSCalibur, Cell Quest and ModFit software (Becton Dickinson). Total cell lysates were analyzed for the level of total and phosphorylated p70 S6K, AMPK $\alpha$  and mitogen-activated protein kinase (MAPK) by Western blot. The data are shown as means $\pm$ S.E.M. and analyzed using Student t-test.

**Results:** Rapamycin alone had cytostatic effects but enhanced ATRA-mediated differentiation and DMSO-mediated growth arrest and apoptosis. AMPK activators, AICAR and metformin, significantly reduce the number of viable cells.

Morphologic and FACS analysis shows the significant increase in apoptosis in cells treated with AICAR. Western blot analysis confirms that both agents activate AMPK and inhibit mTOR activity. AICAR enhances ATRA-mediated differentiation of NB4, a typical APL cell line. In U937 cells, AICAR alone induces the expression of cell surface markers associated with mature monocytes and macrophages. In both cell lines, AICAR increases the activity of MAPK, and the increase in the expression of CD64 and CD14 is inhibited in the presence of MAPK and AMPK inhibitors.

**Discussion:** AICAR inhibits proliferation, increases apoptosis and induces expression of differentiation markers in monocytic U937 cells. This is, to our knowledge, the first report showing that AICAR has some differentiating properties in leukemia cells. These results suggest that a strategy using combination of differentiation agents with drugs targeting AMPK/mTOR may improve differentiation therapy for non-APL AML.

**Acknowledgments:** We thank Ms Dunja Tankovic for valuable technical help and assistance. This study was supported in part by the Ministry of Science, Education and Sport of the Republic of Croatia, grant No. 108-1081347-1448 (to Dora Višnjić). A part of presented results regarding rapamycin and DMSO has already been published (Lalic et al., *Leuk Lymphoma* 2012; 53: 2253-2261).

**MeSH/Keywords:** AICAR, Leukemia, Differentiation Markers, AMP-Activated Kinase

**Poster code:** A-7-68



## POSTER TITLE: ANDRIJA ŠTAMPAR'S REJECTION OF EUGENICS

**PhD candidate:** Martin Kuhar, MD

**Part of the thesis:** Eugenics in Croatian Medicine and its Public Influence 1859-1945

**Mentor/s:** Professor Stella Fatović-Ferenčić

**Affiliation:** Department for the History of Medicine, Croatian Academy of Sciences and Arts

**Introduction:** Andrija Štampar (1888-1958), the main figure of public health in the 1920s Yugoslavia, a leading Rockefeller Foundation and League of Nations health expert and one of the founders of the World Health Organization, certainly represents one of the most important people in the history of public health in the 20th century. However, it is a less known fact that he was also an advocate of negative eugenics prior to his international work. Here I present Štampar's initial acceptance, and the reasons of his eventual abandonment of eugenics.

**Materials and methods:** The historical documents used in this research consist of Štampar's own articles and books, his correspondence, the works of his contemporaries, health statistics and health decrees and, finally, secondary literature on the history of left-wing eugenics and Darwinism.

**Results:** Štampar initially accepted eugenics as one of the means of fighting the presumed biological degeneration made visible by the effects of World War I. In time, he became more careful in his assessment of the validity of eugenic measures, and all but discarded eugenics by the start of World War II.

**Discussion:** I propose four reasons for Štampar's eventual marginalization of eugenics. First, when Štampar started his work in

the Ministry, Yugoslavia had atrocious health statistics and its rural population had very limited availability of health care, making the establishment of basic public health institutions a priority. Therefore, eugenic measures were difficult to prepare and execute, and also there were criticisms addressed to proposals of eugenic measures, mainly by Croatian physicians. Second, Štampar was relieved of his duties in the Ministry in 1931 due to the national tensions during the King Alexander dictatorship. His enemies were radical right-wing eugenicists and nationalists, the episode which could have made Štampar reluctant to pursue with eugenics. Third, Štampar spent the majority of the 1930s abroad, especially in China where he helped in the building of public health system as an expert of the League of Nations and the Rockefeller Foundation. Fourth, Štampar's personal diaries reveal deep scorn towards Nazism and Fascism, totalitarian systems which increasingly became associated with negative eugenics.

**Acknowledgments:** I'd like to thank Stella Fatović-Ferenčić and Tatjana Buklijaš for their valuable comments.

**MeSH/Keywords:** eugenics, Andrija Štampar, public health, social medicine, World Health Organization

**Poster code:** A-8-170

## **POSTER TITLE: REGIONAL DIFFERENCES IN DENDRITIC MORPHOLOGY AND SPINE DENSITY OF STRIATAL MEDIUM SPINY NEURONS IN FOXP2 MICE**

**PhD candidate:** Ivana Bičanić, MD

**Part of the thesis:** Changes in morphology of medium spiny striatal neurons in mice with humanized versions of *Foxp2* gene

**Mentor/s:** Zdravko Petanjek, MD, PhD, Professor

**Affiliation:** University of Zagreb, School of Medicine, Department of Anatomy and Clinical Anatomy, Croatian Institute for Brain Research

**Introduction:** The extent of language capability sets humans apart from their closest living relatives, the chimpanzees. The transcription factor FOXP2, which is required for speech and language development, carries two amino acid substitutions (T303N, N325S) on the hominine lineage which were likely positively selected during human evolution. When the human variant of the FOXP2 protein is expressed in mice these animals show an increased dendritic complexity of neurons that are a part of the basal ganglia circuitry and highly express FOXP2, e.g. striatal medium spiny neurons (MSN).

**Materials and methods:** The current investigation involves analysing dendritic morphology and spine density in Golgi-Cox impregnated MSN in adult mice homozygous for the FOXP2 human variant (*Foxp2*<sub>hum/hum</sub>-T302N, N324S) and in two additional mouse strains where one carries substitution at position 302 (T302N) while the other carries it at position 324 (N324S) in their endogenous *Foxp2* gene. Analysis will include regional comparison of dendritic morphology and spine density of MSN striatum (dorso-medial, dorso-lateral, rostral and caudal region) in all mice lines, as well as a comparison with the wild-type (*Foxp2* wt/wt) line.

**Results:** The previous study has shown that in *Foxp2*<sub>hum/hum</sub> mice MSN tend to have around 20% longer dendritic trees, but present results

of dendritic morphology of MSN in dorso-medial striatum in *Foxp2*<sub>hum/hum</sub> mice did not show any significant differences. Interestingly, in T302N line there was a tendency for terminal segments to be longer and thinner when compared to *Foxp2*<sub>wt/wt</sub>, both in dorso-medial and dorso-lateral striatum.

**Discussion:** Present results did not confirm previous observation of increased dendritic morphology of MSN in *Foxp2*<sub>hum/hum</sub> mice line. In addition, the results do not fit with electrophysiological data, as well as with decrease in dopamine levels in some striatal regions. It is possible that the effect is related only to a part of MSN population or it has a clear regional effect (MSN in rostral and caudal striatum will be reconstructed). It is also possible that changes are related with spine density (analysis in process) and not with the dendritic size. Present results support the hypothesis that human specific changes at position T302N are responsible for neuronal changes related with „language“ circuitry and a view that expansion of cerebral cortex is needed to allow significant functional changes related with appearance of language.

**Acknowledgments:** Supported by MSES project

**MeSH/Keywords:** *Foxp2*, speech development, cortico-striatal circuitry, dopamine

**Poster code:** A-9-109

## POSTER TITLE: DOSE-DEPENDENT DEPRESSION OF PREBÖTZINGER COMPLEX (PBC) REGION NEURONS BY LOCAL APPLICATION OF THE

**PhD candidate:** Tomislav Radočaj

**Part of the thesis:** The Role Of 5HT1A and 5HT2A Receptors within the PreBötzingner Complex (pBC) And Ventral Respiratory Column (VRC) In Eliciting Respiratory Responses To Systemic Administration Of Selective Serotonin Ag

**Mentor/s:** Associate Professor Mladen Perić, MD, PhD

**Affiliation:** Medical College of Wisconsin, Department of Anesthesiology, Milwaukee, WI, USA, University Hospital Centre „Sestre milosrdnice“, Zagreb, Croatia

**Introduction:** Intravenous administration of the 5HT1a agonist 8OH-DPAT increases breathing rate and reverses opioid-induced respiratory depression. The mechanism by which 8OH-DPAT produces its effect is unclear. The purpose of this study was to determine the dose-dependent effects of 8OH-DPAT on single pBC respiratory neurons and gain insight in the role of 5HT1a receptors on pBC neurons in producing tachypnea.

**Materials and methods:** Acute non-survival experiments were performed in decerebrate, vagotomized, paralyzed and mechanically ventilated dogs during isocapnic hyperoxia. Four-barrel micropipettes were used to record neuronal activity of single pBC neurons and picroject 8OH-DPAT (1, 10 and 100  $\mu$ M), D,L-homocysteic acid (DLH, 20mM) and the artificial CSF (aCSF) vehicle. Ejected volumes were measured via the meniscus of the pipette with a microscope (resolution 2nl). Inspiratory duration (TI) and expiratory duration (TE) were measured from the phrenic neurogram (PNG). The pBC within the ventral respiratory column (VRC) was functionally located via stereotaxic coordinates, the presence of a mixture of respiratory neuron subtypes and by its typical tachypneic response to microinjection of DLH. Cycle-Triggered Histograms (CTH) of single pBC neurons triggered by the phrenic neurogram (PNG) were used to quantify the peak and time-averaged discharged frequencies (Fn).

**Results:** Picoejection of aCSF and 5HT2a agonist DOI had no effect on single pBC neurons.

$\mu$ M of the 5HT1a agonist 8OH-DPAT depressed peak and average discharge of I neurons by ~36% but had no effect on E neurons. 8OH-DPAT at 10 and 100  $\mu$ M depressed both I and E neurons similarly with a maximum depression of ~42% at 100  $\mu$ M. In contrast, unilateral 8OH-DPAT (200 $\mu$ M, 100nl) injections made in 1mm increments from the obex to 7mm rostral within the VRC (including the pBC) had no effect on the TI, TE, and peak PNG.

**Discussion:** 5HT1A receptors are able to inhibit pBC region neurons by ~40%. I-neurons are more sensitive than E-neurons to 5HT1a agonist-induced inhibition (~1  $\mu$ M). 5HT2a receptors are not present on pBC respiratory neurons or non-functional. 5HT1a receptor-mediated inhibition within the VRC has no effect on phase timing, even at agonist concentrations (200  $\mu$ M) sufficient to produce ~40% inhibition. Systemic administration of an 5HT1a agonist produced tachypnea at expected effect-site concentrations in the nanomolar range (< 100 nM). This is most likely due to effects outside the VRC.

**Acknowledgments:** Supported by VA Medical Research Funds and NIH grant GM 059234 funds

**MeSH/Keywords:** pBC, preBötzingner, 8OH-DPAT, DOI, 5HT1a, 5HT2a, VRC, respiration

**Poster code:** A-9-47



**1.2.**  
**RESEARCH ABSTRACTS**  
**- CLINICAL MEDICAL SCIENCES**



## POSTER TITLE: STUDY ON THE IMPACT OF PSORIASIS ON QUALITY OF LIFE: PHYSICAL, PSYCHOLOGICAL, SOCIAL AND FINANCIAL IMPLICATIONS

**PhD candidate:** Vedrana Bulat, MD

**Part of the thesis:** Study on the impact of psoriasis on quality of life: physical, psychological, social and financial implications

**Mentor/s:** Mirna Šitum, PhD

**Affiliation:** Department of Dermatology and Venereology University Hospital Center „Sestre milosrdnice“

**Introduction:** Psoriasis as a chronic condition with stigmatising features poses significant and hard to meet challenges in patient management. The impact of psoriasis on quality of life is significant given its chronicity and visibility. Psychological stress has been associated with initial presentation of the disease as well as exacerbations of pre-existing psoriasis.

**Materials and methods:** Fifty-one consenting patients fulfilled the inclusion criteria, being hospital-based outpatients of either sex, aged 18 to 65 years, with conclusive diagnosis of mild to moderate plaque psoriasis, and managed by topical or phototherapy. After dermatological examination and determination of Psoriasis Area and Severity Index (PASI) score, patients were referred to a psychological consult. Assessment was done through standardized psychological questionnaires concerning quality of life, depression, anxiety, illness perception, financial domain and personal data.

**Results:** Results of our study indicate that psoriasis has a strong impact on patients' life. There is a strong correlation between time spent on skin care and feelings of anger and resentment ( $p < 0.01$ ,  $r = 0,58$ ). Higher PASI score is associated with lower health satisfaction ( $r = -0,32$ ). Higher PASI score correlates with stronger influence of illness on eating and drinking habits ( $r = 0,57$ ). Higher PASI score negatively influences social be-

haviour ( $r = 0,46$ ) and has a significant impact on psychological aspect of quality of life in patients with psoriasis ( $r = 0,41$ ). Significant positive correlations are shown between PASI score and perception of illness-related consequences ( $r = 0,30$ ), perception of symptoms ( $r = 0,42$ ), illness-related concern ( $r = 0,31$ ) and emotional representation ( $r = 0,35$ ). Also higher PASI score correlates with increased anxiety (momentary and in general) and depression ( $r = 0,33$ ,  $r = 0,35$ ,  $r = 0,35$ ). Psoriasis influences working habits, creates a significant financial burden, but most of all, significantly impairs quality of life and psychological status of affected individuals.

**Discussion:** Psoriasis poses a substantial threat in several dimensions concerning quality of life. Patients feel that the current treatment, although often effective, does not provide a satisfactory long-term solution. Emotional and social consequences are greatest for economically deprived individuals, who already bear the burden of difference and discrimination. Thus, long-term psychologic and social support for patients with psoriasis is desirable.

**Acknowledgments:**

**MeSH/Keywords:** psoriasis, quality of life, illness perception, anxiety, depression, psycho-dermatology

**Poster code:** B-2-164

## POSTER TITLE: TROPHOBLAST DIFFERENTIATION IN NORMAL AND PATHOLOGICAL PREGNANCY

**PhD candidate:** Jasenka Zmijanac Partl MD

**Part of the thesis:** Differentiation of Human Trophoblast Cells in Normal and Pathological Pregnancy

**Mentor/s:** Associate Professor Ljiljana Šerman MD PhD

**Affiliation:** University of Zagreb, School of Medicine, University Hospital Merkur

**Introduction:** During placentation, trophoblast cells undergo epithelial - mesenchymal transition (EMT) which results in acquisition of mesenchymal characteristics. This is achieved by the interaction of factors that activate or inhibit Wnt signaling pathway. SFRP1 and SFRP3 act as Wnt antagonists and play an important role in development by maintaining epithelial cell characteristics. On the other hand, TCF1 activates genes linked with growth and invasion and therefore serves as marker of mesenchymal transition. The aim of the present study is to analyze the distribution of the SFRP1 and SFRP3 proteins as well as transcription factor TCF1 in normal and IUGR human placentas.

**Materials and methods:** Placentas were delivered in the third trimester from uncomplicated pregnancies (control group, n = 7) and those complicated by IUGR (n = 7). Intrauterine growth restriction (IUGR) was defined as birth weight less than 10th percentile for gestational age, parity and sex of the newborn. IUGR population was considered idiopathic. SFRP1, SFRP3 and TCF1 antigen distribution was analyzed by immunohistochemistry. Antigen expressions were scored using quantitative stereological analysis of volume density. Statistical significance was set at  $p < 0.05$ .

**Results:** A statistically significant difference was found between SFRP1, as well as SFRP 3 protein expression in placental tissues of IUGR

group in comparison to control group ( $p < 0.05$ ). There was no statistical difference between TCF1 expression in normal and IUGR placentas ( $p = 0.7117$ ). SFRP1 positive staining was found in cytoplasm of syncytiotrophoblast, decidua, extravillous intermediate trophoblasts, and rare cytotrophoblasts of terminal villi. SFRP3 protein was expressed in nuclei (of Hofbauer cells, stromal cells of terminal villi) and cytoplasm (in cytotrophoblasts, decidua, extravillous intermediate trophoblasts and rarely in syncytiotrophoblast. TCF1 expression was positive in nuclei of extravillous intermediate trophoblasts and decidual cells.

**Discussion:** Statistically higher expression of SFRP1 and SFRP3 in human IUGR placentas may indicate a role of inadequate EMT in pathogenesis of IUGR. Those placentas show higher expression of epithelial phenotype markers. TCF1 is a part of Wnt transcriptional circuit. We succeeded to show that active transcription occurs in cells that acquire mesenchymal characteristics, such as extravillous intermediate trophoblast cells. Preliminary results gain insight into the etiology of intrauterine growth restriction.

**Acknowledgments:**

**MeSH/Keywords:** trophoblast, Wnt signaling pathway

**Poster code:** B-5-60



## **POSTER TITLE: AN ADEQUACY OF LOW MOLECULAR WEIGHT HEPARIN TREATMENT IN PATIENTS WITH HEREDITARY TROMBOPHILIA AS A CAUSE OF RECURRENT PREGNANCY LOSS.**

**PhD candidate:** Vesna Sokol, MD

**Part of the thesis:** Treatment with low molecular weight heparin improves perinatal outcome in women with hereditary trombophilia as a cause of recurrent pregnancy loss

**Mentor/s:** Professor Marina Ivanišević, MD, PhD

**Affiliation:** Clinical Hospital Centre Zagreb, Department of obstetrics and gynaecology

**Introduction:** Approximately 5% of women trying to conceive experience miscarriages, and in 50% of these women the cause of it remains unknown. Inherited trombophilia could be associated with recurrent miscarriage. The goals of this research are to investigate the successful perinatal outcome in hereditary thrombophilic patients with recurrent early pregnancy loss treated with low molecular weight heparin and to evaluate the prevalence of hereditary trombophilia in healthy patients with negative obstetric history and according to that investigate the perinatal outcome in hereditary trombophilic patients without treatment.

**Materials and methods:** Ninety-eight patients with the history of recurrent pregnancy loss and hereditary trombophilia were included in this study. The cause of their preceding miscarriages was unknown. They were treated with prophylactic dose of LMWH in period from visualisation of gestational sac till after delivery. Their perinatal outcome was observed. The second group included 98 healthy pregnant women that were examined for trombophilic mutations.

**Results:** These are preliminary results of prospective study (from January 2012). During this period 24 patients with recurrent miscarriages and hereditary trombophilia were admitted to our Clinic. The most common type of the gene mutation was heterozygosity for factor V Leiden mutation and PAI-1 polymorphism. 75% of

women that underwent treatment with LMWH had successful perinatal outcome. In the group of 24 healthy pregnant women with no obstetric history 40% was carrier of trombophilic mutation. The most common types were heterozygosity for PAI-1 polymorphism and MTHFR polymorphism. They were not treated with LMWH. 3% of these women had intrauterine growth retardation

**Discussion:** There is a large and contradictory literature on the association between maternal inherited trombophilia and recurrent pregnancy loss. According to that, the statistical and clinical heterogeneity across the studies led the authors to conclude that there was insufficient evidence to support the routine use of LMWH to improve pregnancy outcomes in women with trombophilia and a history of pregnancy loss. Our study showed association between these two entities and emphasised that heparin improved live birth rate of women with recurrent miscarriages. The study also highlighted the high percentage of inherited trombophilia in asymptomatic, healthy population of women. Further research into the link between the observed association, causality and heterogeneity is required.

**Acknowledgments:**

**MeSH/Keywords:** hereditary trombophilia, recurrent pregnancy loss, low molecular weight heparin, perinatal outcome

**Poster code:** B-5-166

## **POSTER TITLE: QUALITY OF LIFE IN FEMALE PATIENTS WITH GENITAL CHRONIC GRAFT VERSUS HOST DISEASE**

**PhD candidate:** Tajana Klepac Pulanić

**Part of the thesis:** Characteristics of female patients with genital chronic Graft Versus Host Disease

**Mentor/s:** Prof Slavko Oreskovic, Prof Zivko Pavletic

**Affiliation:** 1. University of Zagreb, School of Medicine, University Hospital Center Zagreb, 2.National Institute of Health, Bethesda

**Introduction:** Chronic graft versus host disease (cGVHD) is a multisystemic disorder and a major complication after allogenic hematopoietic stem cell transplantation (HSCT). One of the manifestations of cGVHD is genital cGVHD which is not well studied and possibly underdiagnosed disease. Quality of life (QOL) in female patients with cGVHD who have genital cGVHD changes has not been described. Features found in genital cGVHD patients such as clitoral agglutination can impair QOL.

**Materials and methods:** By using single-visit, we evaluated 99 consecutive female patients with cGVHD at the National Institutes of Health enrolled onto cross-sectional prospective cGVHD natural history study. QOL was determined using Short Form (36) Health Survey - (SF -36), a generic questionnaire used to assess general life satisfaction. Descriptive statistics and Chi-square test for dichotomous variables were used in the statistical analysis. Comparison of global QOL between cGVHD patient with and without genital cGVHD was made by Mann-Whitney U test. A P value <0,05 was considered to indicate statistical significance.

**Results:** At the time of evaluation, 60(60,6%) female patients with cGVHD were diagnosed to have genital cGVHD. 39(65%) had severe, 6(10%) had moderate and 15(25%) had mild genital cGVHD.36(36,4%) were sexually active. Majority of patients with genital cGVHD (70,1%) had severe global NIH cGVHD. There was no difference in QOL measured by SF-36 questionnaire between group of cGVHD female patients with and without genital cGVHD (32,50 vs 35,28,  $p=0,367$ ).

**Discussion:** Our finding suggest that having genital GVHD does not impair overall QOL in patients with cGVHD measured by SF-36 generic questionnaire which is used to asses general life satisfaction. Further investigations regarding specific sexual functioning and more specific questionnaires are needed

**Acknowledgments:** dr. Pamela Stratton, National Institute of Health, Bethesda

**MeSH/Keywords:** alloHSCT, GVHD, Gynecology, Quality of life

**Poster code:** B-5-176

## POSTER TITLE: SEPSIS SEVERITY ESTIMATION AND INFLUENCE ON OUTCOME OF PATIENTS WITH INFECTIVE ENDOCARDITIS

**PhD candidate:** Vladimir Krajinović, MD

**Part of the thesis:** Severity of sepsis, along with other well-known complications significantly influences the outcome of patients with infective endocarditis

**Mentor/s:** Bruno Baršić

**Affiliation:** University hospital for infectious diseases Zagreb

**Introduction:** Infective endocarditis (IE) is infection of endocardial surface of heart. Despite improvements in diagnostics and treatment of IE mortality is still high (11-26%). Infective endocarditis is septic disease and severe sepsis and septic shock are common complications of IE. However, clinical characteristics of these complications in patients with IE, use of surgical treatment, and their associations with patient outcome are scarcely presented. We investigated the influence of different stages of sepsis on outcome of patients with IE and impact of cardiac surgery on outcome in these patients.

**Materials and methods:** A prospective, single-center observational study in patients with definite native or prosthetic valve IE admitted between January 1, 2000 and December 31, 2011. We compared clinical characteristics and outcome (in-hospital mortality) in different stages of sepsis during IE. We also compared characteristics of surgically and only medically treated patients stratified on the severity of sepsis.

**Results:** The cohort included 294 patients with definite IE known septic status enrolled. Patients were stratified into two groups. There were 199 (67.7%) with sepsis and 95 (32.3%) patients with severe sepsis and/septic shock (SSS). In-hospital mortality was significantly higher in SSS group 43/95 (45.3%) compared

with S group 11/199 (5.53%),  $p < 0.001$ . Valve replacement was performed in 37 (38.9%) patients in SSS group, and 71 (35.7%) in S group,  $p = 0.587$ . The impact of valve replacement was the most conspicuous in the SSS group. The mortality in this group was significantly higher in medically treated patients 39/58 (67.2%) vs. 5/37 (13.4%),  $p < 0.001$ . However, solely medically treated patients in SSS group had more severe disease: the APACHE II score was higher (median 19.5 vs. 13.0,  $p = 0.001$ ) as well as SOFA score (median 7.5 vs. 3.0,  $p = 0.005$ ). After the adjustment for APACHE II score, SOFA score, age, and congestive heart failure, the beneficial impact of cardiac surgery remained significant. Cardiac surgery decreased the risk of in-hospital death about five times in SSS group (OR=0.096, 95%CI 0.027 to 0.335).

**Discussion:** Our study showed that different stages of sepsis during IE have important impact on in-hospital mortality. Also, in the most severe, septic patients with IE, cardiac surgery improves patients outcome.

**Acknowledgments:**

**MeSH/Keywords:** endocarditis, bacterial, sepsis, shock, septic, cardiac surgery procedure, hospital mortality

**Poster code:** B-7-50

## **POSTER TITLE: EFFICACY OF THERAPEUTIC HYPOTHERMIA IN PATIENTS WITH INFLAMMATORY DISEASES OF THE CENTRAL NERVOUS SYSTEM**

**PhD candidate:** Marko Kutleša, MD

**Part of the thesis:** Efficacy of therapeutic hypothermia in patients with inflammatory diseases of the central nervous system

**Mentor/s:** Prof.dr.Bruno Baršić, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine

**Introduction:** Despite the advances in critical care and powerful antimicrobial treatment central nervous system infections still impose significant mortality and disability rates. To decrease mortality and disability improvement in the treatment of the brain edema and intracranial hypertension are mandatory in these patients. Furthermore, if cerebral chemoregulation in these patients is impaired standard treatment of the brain edema with hyperosmolar solutions, hyperventilation and barbiturate induced coma are futile and may be even harmful. In these circumstances new treatment strategies ought to be explored. Primary goal of our study is to assess the efficacy of therapeutic hypothermia in the mentioned clinical scenario.

**Materials and methods:** Adult patients with severe inflammatory disease of the central nervous system(CNS)will be included in this prospective study from January 2009 until January of 2013. Indications for therapeutic hypothermia and variables of importance are included in the previously designed treatment protocol. After enrolment is finished the impact of therapeutic hypothermia on the outcome will be analyzed in comparison to the historic control group.

**Results:** 131 patients with community acquired bacterial meningitis were included in the study. 41 were treated with therapeutic hypothermia and 90 were historic control patients. The patients with non-bacterial CNS inflammatory

disease were excluded from the analysis due to the sample insufficiency. The results revealed that therapeutic hypothermia is a independent predictor variable of the favorable outcome. Logistic regression detected significant mortality reduction in the therapeutic hypothermia treatment group(OR 0.059,  $p < 0.001$ ). Unfavorable outcome (GOS 1-3) was also significantly reduced in the therapeutic hypothermia treatment group(OR 0.209,  $p = 0.0011$ ). Cox-regression revealed hazard ratio of 0.367 in the therapeutic hypothermia treatment group which was also statistically significant ( $p = 0.0107$ ).

**Discussion:** Our results confirm that implementation of therapeutic hypothermia is a significant predictor of a favorable outcome in patients with severe form of community acquired bacterial meningitis. Reduction in mortality, as well as decrease in unfavorable neurological outcome were confirmed. These results justify the recommendation to implement this method in patients with community acquired bacterial meningitis on a wider scale.

**Acknowledgments:** Staff of the department of neuroinfectology and intensive care medicine at the University hospital for infectious diseases in Zagreb.

**MeSH/Keywords:** Therapeutic hypothermia, bacterial meningitis

**Poster code:** B-7-33

## POSTER TITLE: FIBROBLAST GROWTH FACTOR 23 AND ACUTE KIDNEY INJURY

**PhD candidate:** Sanja Sakan

**Part of the thesis:** Fibroblast growth factor 23 augmentation and postoperative acute kidney injury progression

**Mentor/s:** Prof. Nikolina Bašić-Jukić

**Affiliation:** University Hospital Center Zagreb, University of Zagreb School of Medicine

**Introduction:** Fibroblast growth factor 23 (FGF23) is a novel peptide hormone with the regulatory role of phosphate metabolism. Present studies have shown that in patients with chronic kidney disease FGF23 is significantly elevated and responsible for the development of Chronic Kidney Disease - Mineral and Bone Disorders. FGF23 is a strong predictor of progressive development of chronic kidney disease and lethal outcome. Studies about the prognostic role of FGF23 in acute kidney injury are insufficient and contradictory. Early identification of the new onset of reversible acute kidney injury imports early initiation of the treatment, which includes dialysis as well.

**Materials and methods:** Plasma FGF-23 levels were measured in 6 patients with acute kidney injury and 2 control healthy subjects with baseline eGFR > 60 ml/min/1,73m<sup>2</sup>. Plasma samples obtained from cases were immediately spun at 3000 rpm for 10 minutes and were aliquoted and stored at -80 C until biomarker measurements were made. FGF-23 measurements were made using a C-terminal FGF-23 ELISA (Immutoxics, San Clemente, CA).

**Results:** We studied 6 cases who developed at least Stage I acute kidney injury according to RIFLE/AKIN criteria. FGF-23 levels were significantly higher in cases with acute kidney injury compared with healthy subjects, with a median

FGF-23 level of 511 RU/ml ( IQR, 133-1059) on the first postoperative day, 677.9 RU/ml ( IQR 106-133,9 ) on the third postoperative day, 957.8 RU/ml ( IQR 62,5-1159) on the fifth postoperative day. However, FGF-23 levels in control subjects were in the reference range with a median FGF-23 levels 52 RU/ml ( IQR 38-54 ).Owing to serum creatinine values measured on the seventh postoperative day five cases with acute kidney injury had normal renal function, except one who developed renal insufficiency ( serum creatinine 173 μmol/l).

**Discussion:** We provide novel data that demonstrate that FGF-23 levels are elevated in cases with acute kidney injury compared to healthy control cases. Also, data suggest that FGF-23 dysregulation occurs in acute kidney injury as well as chronic kidney disease. However, a larger sample size and better statistical analyses are required to determine the role of FGF-23 as early prognostic indicator in the acute kidney injury outcome. Moreover, FGF 23 connection to serum and urinary phosphatase, calcium and creatinine values should be investigated likewise. As well, for the first time FGF23 values in healthy control subjects for our population were determined.

**Acknowledgments:**

**MeSH/Keywords:** Acute kidney injury

**Poster code:** B-8-118

## POSTER TITLE: NECK CIRCUMFERENCE ASSOCIATION WITH METABOLIC RISK FACTORS IN PATIENTS UNDERGOING NECK SURGERY

**PhD candidate:** Danijela Grizelj, MD

**Part of the thesis:** Relationship of adiponectin and omentin in neck adipose tissue and serum

**Mentor/s:** Vlatka Pandžić Jakšić, MD, PhD

**Affiliation:** Dubrava University Hospital, Zagreb

**Introduction:** Increasing amounts of adipose tissue which we recognize clinically as obesity are associated with the development of insulin resistance, diabetes, dyslipoproteinemia and cardiovascular disease. Ectopic compartments of adipose tissue, which originate from its redistribution in obesity, are the source of predominantly proinflammatory adipocytokines and they contribute to the development of metabolic disorders. Recent data have shown that the increased neck circumference is associated with metabolic risk.

**Materials and methods:** The study will include 40 participants. Samples of adipose tissue will be taken during routine neck surgery. Gene expression of omentin and adiponectin in the tissue will be analyzed by RQ-PCR method. Serum samples will be taken preoperatively for the analysis of adipocytokine levels by ELISA and for the analysis of standard laboratory parameters. Standard anthropometric measurements, body composition analysis by bioelectrical impedance and ultrasound measurement of intima-media thickness of common carotid artery will be also made.

**Results:** So far we made analysis of standard laboratory parameters, anthropometric measurements, body composition analysis and ultrasound measurement of intima-media thickness of common carotid artery in 36 participants.

Statistically significant positive correlations were found between neck circumference, other anthropometric measures of obesity and body fat mass ( $p < 0.05$ ). Neck circumference also positively correlated with levels of insulin, glucose and triglycerides, but negatively with HDL-cholesterol ( $p < 0.05$ ). Neck circumference was associated with carotid intima-media thickness ( $p < 0.05$ ). Patients with carotid plaques had significantly larger neck circumference ( $p < 0.05$ ).

**Discussion:** The preliminary results of our study support the hypothesis that neck circumference is associated with metabolic risk factors. Considering probable paracrine effect of adipose tissue in the development of atherosclerosis we might expect that at least part of neck adipose tissue has a metabolically adverse role similar to ectopic fat. In that context we plan to proceed with molecular analysis of adipose tissue samples taken from subcutaneous and perivascular locations. We expect that adipocytokine expression patterns will help us in understanding the metabolic role of individual sections of neck adipose tissue.

**Acknowledgments:**

**MeSH/Keywords:** adiponectin, omentin, neck, adipose tissue

**Poster code:** B-9-89

## POSTER TITLE: CHARACTERIZATION OF LIVER TUMORS USING QUANTITATIVE SONOELASTOGRAPHY - PRELIMINARY RESULTS

**PhD candidate:** Tomislav Bokun

**Part of the thesis:** Characterization of liver tumors using quantitative sonoelastography

**Mentor/s:** Ivica Grgurevic

**Affiliation:** University Hospital Dubrava, Zagreb University School of Medicine, Zagreb, Croatia

**Introduction:** Shear Wave Elastography (SWE™) is a new quantitative elastography technique for measuring tissue stiffness. Studies with other elastography-based imaging methods have demonstrated some differences in stiffness with respect to tumor etiology. The aim of this study was to investigate the possibility of using SWE™ to differentiate between the most common hepatic tumors - haemangiomas and metastases. The results for this study were pulled from an ongoing study which is a part of my PhD research. The third group of hepatic tumors (HCC) in the ongoing study was not included in this preliminary report due to small numbers.

**Materials and methods:** Two groups of liver tumors were investigated: haemangiomas and metastases. The nature of the tumors was defined through a standard diagnostic workup according to current guidelines, including contrast enhanced multi-slice CT, MRI and/or cytology/histology, as applicable. Tumors verified in cirrhotic liver were excluded. After obtaining good quality B-mode ultrasound images the stiffness was measured by intercostal approach, and exhalation, five times for each tumor, and the mean value was taken for the analysis.

**Results:** In the first group, 53 haemangiomas were included, and the mean haemangioma

stiffness was 15.05 kPa ± 7.34 kPa (95% CI 13.02-17.07 kPa). In the second group, 44 metastases were included, and the mean tumor stiffness was 36.2 kPa ± 10.32 kPa (95% CI 33.06-39.34 kPa). Haemangiomas were softer compared to metastases, and the difference was statistically significant ( $p < 0.0001$ ). Cutoff value for the differentiation of haemangiomas from metastases was set to 24.65 kPa, with a 92.45% sensitivity (95% CI 81.8-97.9%) and 93.18% specificity (95% CI 81.3-98.6%).

**Discussion:** Haemangiomas were significantly softer comparing to metastases when measured with SWE™. It was possible to differentiate between haemangiomas and metastases with relatively high sensitivity and specificity. Assessment of tumor stiffness by SWE™ could potentially reduce the number of diagnostic procedures, costs of diagnostic workup and monitoring of patients with liver tumors. Introduction of SWE™ to the diagnostic algorithms and monitoring should be considered.

**Acknowledgments:**

**MeSH/Keywords:** sonoelastography, hepatic tumors, shear wave elastography

**Poster code:** B-9-108

## POSTER TITLE: ANESTHETIC TECHNIQUES FOR OPEN INGUINAL HERNIA REPAIR IN ADULTS

**PhD candidate:** Bore Bakota

**Part of the thesis:** Meta-analysis of efficacy and safety of general, regional and local anesthesia in open surgical repair of inguinal hernia in adults

**Mentor/s:** Prof. Leonardo Patrlj, MD, PhD, Prof. Diana Šimić, PhD

**Affiliation:** School of Medicine, University of Zagreb, Croatia

**Introduction:** Inguinal hernia operative repair is one of the most common worldwide surgical procedures. It can be undertaken under general, regional or local infiltration anesthesia, and can be performed as a day case procedure. Outcome measures, such as postoperative pain, postoperative recovery, return to work, complications and length of stay, considerably vary among the mentioned anesthetic techniques. Despite the procedure's long tradition, there is no consensus regarding the best choice of anesthesia. Therefore, further benefits and drawbacks clarification associated with each of the anesthetic techniques are important as it would have both patient and health resource implications.

**Materials and methods:** This study is focused on randomized controlled clinical trials comparing different open inguinal hernia repair anesthetic techniques. We searched MEDLINE, CINAHL, EMBASE, SCI-EXPANDED, Cochrane Central Register of Controlled Trials (CENTRAL), SCOPUS and other sources without language restrictions.

**Results:** Search strategies identified 5385 abstracts. Twenty six trials contributed to this review. 2854 patients were analyzed with 1075 (37,66%) in local anesthesia group, 950 (33,29%) in regional anesthesia group and 829 (29,05%) in general anesthesia group. Complications rate with general and regional anesthesia techniques were higher than when local

anesthesia technique was applied. Local and regional anesthesia have presented as more convenient regarding nausea, patient satisfaction, postoperative recovery, time to full mobility and return to work. Post-operative hematoma remains the main problem in local anesthesia. When general anesthesia applied, there is less incisional pain, hospital stay is shorter and conversion possibility is equal to zero.

**Discussion:** Direct comparison of local, regional and general anesthesia has shown significant differences. Despite more adverse effects, such as postoperative pain, nausea and longer time to full mobility, general anesthesia in some of the outcomes (no conversions, less incidence of postoperative hematoma, incisional pain) has the advantage over the other two types. Regional anesthesia application is associated with postoperative hematoma lower rate and less postoperative pain together with nausea lower incidence in comparison with general anesthesia. Compared with regional and general anesthesia, local anesthesia is the best technique in terms of complications, postoperative recovery, postoperative analgesia, patient satisfaction, and return to work.

**Acknowledgments:**

**MeSH/Keywords:** Hernia, Anesthesia, Local, Regional, General

**Poster code:** B-10-67



## POSTER TITLE: ATTITUDES OF CROATIAN INTERNAL MEDICINE RESIDENTS REGARDING AVAILABLE ONLINE RESOURCES FOR CLINICAL DECISION MAKING SUPPORT

**PhD candidate:** Ivana Čegec, MD

**Part of the thesis:** The impact of UpToDate concerning point-of-care clinical decision making at the University Hospital Centre - Zagreb

**Mentor/s:** Assistant Professor Robert Likić, MD, PhD

**Affiliation:** University Hospital Centre - Zagreb

**Introduction:** The aim of this survey was to evaluate attitudes and experience of internal medicine residents concerning varieties of information sources available to guide point-of-care (POC) clinical decision making.

**Materials and methods:** A pilot online electronic questionnaire was distributed among 60 internal medicine residents at the University Hospital Centre - Zagreb during April 2013 with a response rate of 66%.

**Results:** When internal medicine residents were asked to select (Likert scale 1 to 5, 1=always, 5=never) from a list of different types of information sources available to guide clinical decision making, the majority opted for finding out the answers using electronic search engine (Google, yahoo, etc) ( $1.97 \pm 0.63$ , mean $\pm$ SD), direct colleagues ( $2.03 \pm 0.58$ ) and clinical practice guidelines consultation ( $2.03 \pm 0.71$ ). Concerning different resources relevant to EBM (Evidence Based Medicine) the largest number of responders (79%) use UpToDate in clinical decision making, since they consider it to (Likert scale 1 to 5, 1=strongly agree, 5=strongly disagree) improve patient care ( $1.59 \pm 0.59$ ) and outcomes ( $1.82 \pm 0.72$ ), help in clinical decision making ( $1.46 \pm 0.55$ ), as well as introduce quick knowledge updates ( $1.41 \pm 0.59$ ). In contrast, most

of the residents find the lack of EBM resources in their native language (74%) and the insufficiency of basic EBM skills (43%) to be some of the possible barriers for EBM application. However, when asked to describe their confidence of understanding of basic EBM skills (Likert scale 1 to 5, 1=very good, 5=very poor), they consider themselves to be either very good or good (1.77-2.10) in all of the mentioned skills (clinical question formulation, literature search, critical appraisal, patient extrapolation, evaluation).

**Discussion:** Electronic resources are a vital addition in delivering quality patient care and can help physicians at point-of-care decision making. Majority of our residents rely on and use UpToDate, because it is an online tool which provides prompt and practical clinical information for doctors with a compendium of regularly revised, evidence-based monographs on a variety of topics in adult internal medicine and its subspecialties.

**Acknowledgments:** I would like to thank to my mentor assistant professor Robert Likić, MD, PhD

**MeSH/Keywords:** information sources, point-of-care decision making, UpToDate

**Poster code:** B-13-69

# POSTER TITLE: ETHICS AND PROFESSIONALISM: MEDICAL ETHICS AS PHYSICIANS PROFESSIONAL COMPETENCY ILLUSTRATED THROUGH PATIENTS' AUTONOMY ISSUES

**PhD candidate:** Lucija Murgić

**Part of the thesis:** Professional Ethics Competences Questionnaire (PECQ): an Assessment Tool for Evaluation of Medical Students' Professional Ethics Characteristics and Competences

**Mentor/s:** Professor Gordana Pavleković, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, „Andrija Štampar“ School of Public Health, Zagreb

**Introduction:** Ethical behavior is a core attribute of every physician and, together with other cognitive and practical skills, is regarded as a constituent element of medical professionalism. However, the latter term carries many connotations and implied meanings. This qualitative study investigates what physicians, hospital clinicians, medical ethics teachers, medical students and patients perceive as ethical problems regarding patient's autonomy and explores how best to incorporate related competencies into medical training.

**Materials and methods:** A qualitative study involving 6 focus groups, held separately with 9 family physicians, 8 hospital clinicians, 6 medical teachers engaged in medical ethics, 9 patients, 8 first year and 8 final (6th) year students from Zagreb University, School of Medicine, was conducted. Participants were included through purposeful sampling. Interviews were audio-recorded, transcribed verbatim, and data was analyzed by means of thematic analysis.

**Results:** A number of frequent ethical dilemmas regarding patient autonomy were mentioned. In general, informed consent was not regarded as ethically problematic since more accent was given to legal and practical aspects missed while delivering it to patients. Regarding medical secret which protects patient's pri-

vacancy, major problems were detected in terms of medical informatization, health insurance conception and medical education organization. However, as the most troublesome professional ethic problem broke forth the patient right to truth and information which in practice means when? How? Who? What? to whom? And why? To inform/announce the diagnosis, prognosis and needed further procedures, due to general lack of communication as well as moral competences.

**Discussion:** Results evidence that both, medical students and medical doctors are aware of ethical issues in their everyday contact with patients. They tend to respect patients' autonomy and strive to behave professionally, yet their professional moral conceptions and attitudes are frequently questionable or even wrong. All groups acknowledged that additional education in professional medical ethics should be organized for all medical specialists as part of their continuous medical education.

**Acknowledgments:** I would like to thank all focus group participants for sharing their time, experience and opinions in group discussions.

**MeSH/Keywords:** Medical ethics, professionalism, medical education

**Poster code:** B-15-52

## POSTER TITLE: PUBLIC PERCEPTION OF PHYSICIANS' INTERPERSONAL RELATIONSHIPS - ARE CROATIAN PHYSICIANS PROFESSIONAL IN THE EYES OF THE PUBLIC?

**PhD candidate:** Marko Ćurković, MD

**Part of the thesis:** Development of an instrument for evaluation of physicians' professional interpersonal relationships in hospitals

**Mentor/s:** Assistant Professor Ana Borovečki, MD, PhD. Milan Milošević, MD, PhD.

**Affiliation:** University Psychiatric Hospital Vrapče, Zagreb. University of Zagreb School of Medicine, Andrija Štampar School of Public Health

**Introduction:** Professionalism is a key competence of every practicing physician and is also a crucial segment of social contract between medicine and society. Although physicians usually adhere to universal norms of professionalism, they often fall short in everyday practice. This study investigates beliefs, attitudes and experiences of the social contract's particular segments related to physicians and their professional interpersonal relationships in the view of the broader public.

**Materials and methods:** A survey was conducted using an independently created questionnaire on a nationally representative sample of 1008 adults. Sampling methods used in the research included stratified random sampling and was conducted using the field survey method.

**Results:** While almost the half of responders evaluated the collaboration among physicians as mediocre, poor or nonexistent, the vast majority of responders (94 %) consider collaboration and communication to be important and very important for adequate provision of health care. One in five of responders (18 %) experienced physicians' comments on their fellow colleagues' work, and 6% witnessed a conflict between physicians. Vilification, humiliation, discrimination or intimidation of physicians by their colleagues was witnessed by three percent of responders. One in six believe physicians always or almost always put their own interest in front of the pa-

tients', while one third consider that sometimes they do and sometimes they don't. However, 58% of the respondents believe that physicians do their work conscientiously and responsibly in most cases or always. Half of the respondents consider physicians to be inadequately paid for their work, while the majority of them (87 %) think that they are underpaid. Bribe and corruption in the health care system were witnessed by 14% of respondents, and every fourth had to utilize personal connections in order to be treated adequately.

**Discussion:** While the public recognizes the importance of collaboration among physicians, their experiences tell a different story. The current public perception of physicians' priorities and interests can raise some concerns, as well as the public view of their inadequate adherence to professional standards. The findings about evident corruption in the Republic of Croatia's health care system are alarming. These results only scratched the surface of potential problems in our country's health care system. Further research is needed to explain the findings and increase the awareness of existing problems.

**Acknowledgments:**

**MeSH/Keywords:** public, professionalism, physicians

**Poster code:** B-15-119

## POSTER TITLE: COMPARISON OF AZITHROMYCIN AND DOXYCYCLINE IN VITRO ACTIVITY AGAINST *CHLAMYDIA TRACHOMATIS* STRAINS ISOLATED FROM CERVICAL SWABS

**PhD candidate:** Tomislav Meštrović, MD

**Part of the thesis:** In vitro efficacy of azithromycin, doxycycline and levofloxacin against urogenital *Chlamydia trachomatis* strains

**Mentor/s:** Associate Professor Sunčanica Ljubin-Sternak, MD, PhD

**Affiliation:** Croatian National Institute of Public Health, Polyclinic „Dr. Zora Profozić”

**Introduction:** Although the resistance of *Chlamydia trachomatis*, the most frequently reported bacterial sexually transmitted infection today, is currently not of great concern, clinical treatment failures have been described and some of them linked to laboratory proved resistance. Therefore in vitro susceptibility testing to commonly used antimicrobials is needed, particularly in countries with high antibiotic consumption rates like Croatia.

**Materials and methods:** Susceptibility testing of *C. trachomatis* was performed in 96-well microtiter plates containing McCoy cell monolayers. Azithromycin and doxycycline were obtained from PLIVA Pharmaceuticals, Inc. (Zagreb, Croatia). 20 strains isolated from cervical swabs were tested. Each well was inoculated with 100  $\mu$ l of the isolated test strain known to yield 5 000 to 10 000 inclusions. After centrifugation and incubation, 100  $\mu$ l of each drug dilution has been added to appropriate wells, providing a concentration range of 0.008 to 8  $\mu$ g/ml. Following 72-hour incubation at 35 °C in 5% CO<sub>2</sub>, cultures were fixed and stained with fluorescein-conjugated antibody (Pathfinder®, Bio-Rad Laboratories, France). The minimal inhibitory concentration (MIC) was defined as the lowest concentration of antibiotic without visible inclusions. The minimal chlamydicidal concentration (MCC) was determined after one passage in the absence of antibiotics.

**Results:** MIC values of strains isolated from cervical swabs ranged from 0.064 to 0.125  $\mu$ g/ml for azithromycin, and from 0.016 to 0.125 for doxycycline. MCC values ranged from 0.064 to 1.0  $\mu$ g/ml

for azithromycin, and from 0.032 to 0.25  $\mu$ g/ml for doxycycline. MCC values for both drugs were equal to MIC values, or were up to four dilutions higher. Median MIC value (MIC<sub>50</sub>) was 0.064 for azithromycin and 0.032 for doxycycline. Median MCC value (MCC<sub>50</sub>) was one dilution higher for both drugs. Nonparametric Kruskal-Wallis test showed the significant difference between in vitro activity of the drugs ( $p < 0.001$ ), and Spearman's correlation test did not reveal any significant correlation pattern between the concentrations for different antibiotics.

**Discussion:** Our preliminary results did not show antimicrobial resistance in clinical isolates from cervical swabs. As we still lack information on whether *C. trachomatis* is evolving in vivo in response to antibiotic selection pressure, this kind of surveillance for resistance (even though methodologically cumbersome) remains essential in detecting shifts in antimicrobial susceptibilities in vitro.

**Acknowledgments:** This work is part of the project „Research on the etiology, epidemiology, diagnosis and treatment of patients with prostatitis syndrome” (P.I. Professor V. Škerk) funded by The Croatian Foundation for Science, Higher Education and Technological Development No 04/30.

**MeSH/Keywords:** microbial sensitivity test, *Chlamydia trachomatis*, azithromycin, doxycycline, minimum inhibitory concentration, minimum chlamydicidal concentration

**Poster code:** B-16-84

# POSTER TITLE: ANALYSIS OF CHANGES OF BACTERIAL ISOLATES FROM SEVERE INFECTIONS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS WITH EMPIRIC ANTIMICROBIAL THERAPY IN UNIVERSITY HOSPITAL FOR INFECTIOUS DISEASES

**PhD candidate:** Irina Pristaš, MD

**Part of the thesis:** yes

**Mentor/s:** Prof Arjana Tambić Andrašević

**Affiliation:** University Hospital for Infectious Diseases

**Introduction:** Sepsis is a clinical syndrome that complicates severe infection and patients with bacteremia are of major concern in clinical microbiology. The most common source of bacteremia that can lead to sepsis is urinary and respiratory tract infections. Other sources are intraabdominal infections, wound infections, central nervous system (CNS) and cardiovascular infections (CVS) and skin and soft tissue infections. In a significant number of septic episodes, source of bacteremia is not defined.

**Materials and methods:** In PhD thesis, data about source of bacteremia, the most frequent agents of severe bacterial infections and their antibiotic susceptibility patterns together with empiric antimicrobial therapy will be determined in patients admitted to University Hospital for Infectious Diseases over the years 2002 - 2013. Results shown here refer to year 2010.

**Results:** Overall 537 isolates were identified from 489 patients in year 2010. The most common diagnosis were: urinary tract infections (UTI) 37.6%, sepsis with unknown origin 29.2%, lower respiratory tract infections (RESP) 10.4%, skin and soft tissue and bone and joint infections (SST and BJ) 5.8%, intraabdominal infections (IA) 5.02%. Nosocomial infections accounted for 17.9% of cases. The most prevalent isolates

were *Escherichia coli*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter baumannii* (34.5%, 10.2%, 7.1%, 5.8%, 5.4% and 4.8% respectively). Out of 185 *E. coli* isolates, 17 (9.2%) were resistant to third generation of cephalosporins, and only three were resistant to carbapenems. Out of 55 *Streptococcus pneumoniae* isolates, 14 (25.5%) had reduced susceptibility to penicillin, and 24 out of 38 (63.2%) *Staphylococcus aureus* isolates were resistant to penicillin. Only three cases of MRSA bacteremia were present in 2010. Carbapenem resistance in *Pseudomonas* was present in 10 (32.2%) out of 31 isolates and in 19 (73.1%) out of 26 *Acinetobacter* isolates.

**Discussion:** The results that will be shown in this study will provide insight on changes in susceptibility patterns of the most common isolates of positive blood cultures over the defined period of time, rate of nosocomial infections and changes in rationale of empirical antimicrobial prescribing.

**Acknowledgments:** Marija Čulo

**MeSH/Keywords:** Sepsis, Microbial Sensitivity Test, Antimicrobial therapy

**Poster code:** B-16-150

# POSTER TITLE: COMPARISON OF FEMTOSECOND LASERS AND MECHANICAL MICROKERATOMES FOR LASER IN SITU KERATOMILEUSIS - PRELIMINARY RESULTS

**PhD candidate:** Maja Boháč, MD

**Part of the thesis:** Comparison of femtosecond lasers and mechanical microkeratomes for laser in situ keratomileusis

**Mentor/s:** professor Nikica Gabrić, MD PhD

**Affiliation:** Eye Specialty Hospital

**Introduction:** Laser in situ keratomileusis (LASIK) is mostly used refractive procedure today. Procedure implies photoablation of corneal stroma with excimer laser under the superficial corneal flap. Today LASIK flap can be created with mechanical microkeratome or femtosecond laser. Guiding idea of femtosecond lasers is precision. Lasers are less surgeon and gear dependent and more software controlled than microkeratomes. The idea implies that flaps of more reliable thickness and shape provide more accurate refractive and optical results. Idea is still waiting for its complete scientific evidence since technology is relatively new and not widely used.

**Materials and methods:** First 40 out of 200 patients planned in prospective comparative study were evaluated. Follow up is 3 months. Flap was created either with Moria SBK one use-plus mechanical microkeratome or Ziemer FEMTO LDV laser. Mean preoperative spherical equivalent was  $-3,13D$ , central corneal thickness  $562\pm 27\mu m$  and keratometry values  $44\pm 4D$ . Measurements included flap thickness and profile at 5 points in two axis ( $90^\circ, 180^\circ$ ) with Visante OCT, complication rate, time of procedure, flap and stromal bed quality, visual outcome, patients discomfort, and postoperative dry eye.

**Results:** Mean flap thickness for right eye was  $98 \pm 12\mu m$ (SBK),  $107 \pm 10\mu m$ (LDV) and for the

left eye  $97\pm 15\mu m$ (SBK),  $102\pm 10\mu m$ (LDV). All flaps aligned perfectly to corneal bed. Intraoperative and postoperative complications were unremarkable in both groups. Flap and corneal bed quality were slightly better in SBK group. Patients discomfort was greater in LDV group. There was no difference in postoperative visual acuity between groups. SBK group had better Schirmer values during the follow up.

**Discussion:** Current researches are mainly focused on the central portion of the flap and residual bed. Decreased postoperative visual quality (halo, glare, decreased contrast sensitivity) may be related to peripheral corneal distortions. In our study flap measurements showed that flaps were thinner in the center and thicker at the periphery. Central and variation in peripheral flap thickness were not significant between groups (Student t-test  $p>0.05$ ). The difference in dry eye between the groups can be explained with the hinge position. Nasal hinge created with SBK preserves more corneal nerves than superior hinge in LDV. Both machines showed similar results, however more patients need to be analyzed to support this theory.

**Acknowledgments:**

**MeSH/Keywords:** LASIK, mechanical microkeratome, femtosecond laser, corneal flap

**Poster code:** B-18-41

## **POSTER TITLE: CLASSIFICATION AND QUANTIFICATION OF THE RISK FACTORS AND TREATMENT STRATEGIES FOR OCULAR HYPERTENSION AND PRIMARY OPEN- ANGLE GLAUCOMA**

**PhD candidate:** Qendrese Daka, MD

**Part of the thesis:** Part of the thesis: Classification and quantification of the risk factors and treatment strategies for ocular hypertension and primary open-angle glaucoma

**Mentor/s:** Associate Professor Vladimir Trkulja, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb University of Prishtina Faculty of Medicine, University Clinical Centre of Kosova

**Introduction:** Late detection with a consequent delayed treatment of POAG is a major risk factor for blindness. Individual or combined contributions of the risk factors to the risk of POAG and possible relationship with OHT have not been systematically evaluated thus far. A comprehensive quantification of the effects and classification of IOP-lowering treatment options based on their efficacy/safety has not been performed thus far. It is unclear if preventive treatments are cost effective in terms of long term avoidance of blindness.

**Materials and methods:** A comprehensive search of electronic databases PUBMED, SCOPUS and HTA was performed till July 2012 for potentially relevant articles of risk factors for POAG. The authors reviewed 1413 abstracts. They selected 41 abstracts to review in full text. Reference lists of these articles were reviewed to identify any other trials eligible for inclusion in the meta-analysis. Authors independently reviewed all studies, 15 articles where yield for methodological review. Electronic databases PUBMED, SCOPUS, HTA, Cochrane Library and ACP Journal Club were searched till April 2013 for potentially articles of RTCs vs. placebo, no treatment or an active treatment, for any pharmacological or non-pharmacological intervention for the treatment of POAG. The authors reviewed 676 abstracts. They selected 160 articles to review in full text to determine their relevance to the effectiveness of the treatments and 37 articles

for the cost-effectiveness profile of the IOP-lowering treatments.

**Results:** Prior to meta-analysis, studies will be evaluated for quality assessment. Data extraction will be performed. Pooled estimates of effects (risks, efficacy/safety) will be performed for each outcome. In the case of high heterogeneity, the priority will be given to random effects estimates. Reporting of the prognostic studies will be in line with the MOOSE criteria, for intervention studies based on the current Cochrane Handbook for Systematic Reviews.

**Discussion:** Identification and categorization of risk factors for POAG will provide the basis for improved identification of subpopulations at the highest risk. Comprehensive evaluation of available preventive treatments will help establish evidence-based criteria for their selection. This will be particularly useful for developing countries with restricted public health resources.

**Acknowledgments:** I would like to thank Professor Vladimir Trkulja, for agreeing to be my mentor on long distance and providing me with much needed advice regarding this research, Mrs Davorka Granic and Adea Kelmendi for helping me with the searching of studies.

**MeSH/Keywords:** primary open angle glaucoma, ocular hypertension, risk factors, treatments

**Poster code:** B-18-152

# POSTER TITLE: THE DIAGNOSTIC VALUE OBTAINED BY OPTIC NERVE HEAD ANALYSIS OF OPTICAL COHERENCE TOMOGRAPHY IN RELATION TO THE STAGE OF GLAUCOMA

**PhD candidate:** Sonja Jandroković MD

**Part of the thesis:** Characteristics Of Optic Disc Morphology And Comparison Of Rates Of Change In Retinal Nerve Fiber Layer Thickness In Different Stages Of Glaucoma Disease

**Mentor/s:** Associate Professor Smiljka Popović Suić MD, PhD

**Affiliation:** Department of Ophthalmology, University Hospital Center Zagreb, Croatia, Kišpatićeva 12

**Introduction:** Glaucoma can be characterized as a slowly progressing optic neuropathy that damages the retinal ganglion cells RGCs and their axons. This damage causes thinning of the retinal nerve fiber layer RNFL, leads to cupping of the optic nerve head ONH, and usually results in observable visual field loss. Because glaucomatous damage is irreversible, early detection is crucial for effective treatment of the disease. Studies have shown that up to half of the RGCs could be damaged before defects are reported on the visual field. OCT has been shown to correlate well with histological retinal measurements and to allow direct visualization and quantification of the structures of the retina and ONH.

**Materials and methods:** We recruited one hundred seventeen (117) glaucoma patients. All patients underwent OCT optical coherence tomography SOCT Copernicus (Optopol Technology SA) and SAP (Haag Streit Octopus 900, G program). The discrimination power of each OCT parameter was statistically evaluated in all groups and all data were compared. Subjects were divided into three groups according to the GSS II system (Glaucoma Staging System, Brusini and Filcordia). The control group (O B) 48 subjects, the early glaucoma group (S1 S2) 39 subjects and the advanced glaucoma group (S3 S4 S5) 30 subjects.

**Results:** Rim area showed the strongest correlation with glaucoma progression. As is well

known that the disk size has an impact on the results of OCT examinations, it is important to emphasize that all groups had equal average size of the disk. Comparison of parameters for the cup area and cup volume has shown that there is a difference that was statistically significant between the control group and advanced glaucoma group. There was no statistically significant difference in any ONH parameter between control and early glaucoma group. We must take into account that the progression clearly see the differences in certain parameters.

**Discussion:** Imaging technologies provide objective and quantitative measurements that are highly reproducible and show very good agreement with clinical estimates of optic nerve head structure and visual function. As with other technologies, imaging may produce false identification of glaucoma and its preoression thus, clinicians should not make management decisions based solely on the results of one single test or technology. There is a need for an individualistic approach to the management of patients in glaucoma as standard approach cannot be applied to every patient.

**Acknowledgments:** I would like to thank my mentor Professor Smiljka Popović Suić MD, PhD

**MeSH/Keywords:** glaucoma, optic nerve head, optical coherence tomography, retinal nerve fiber layer

**Poster code:** B-18-159



## POSTER TITLE: ANALYSIS OF SALIVA PEPSIN IN PATIENTS WITH VOICE PROSTHESIS

**PhD candidate:** Ana Đanić Hadžibegović, MD

**Part of the thesis:** Influence of extraesophageal reflux on the occurrence of voice prosthesis complications and voice quality after total laryngectomy and voice prosthesis implantation

**Mentor/s:** prof. Drago Prgomet, MD, PhD

**Affiliation:** University of Zagreb School of Medicine

**Introduction:** Extraesophageal reflux (EER) is one of the risk factors for voice prosthesis (VP) complications. After gastric acid, pepsin is the most studied gastric component and has been proven to be the most sensitive and specific marker of EER. The aim of this study was to investigate the relationship between EER and the occurrence of VP complications in laryngectomized patients.

**Materials and methods:** We assessed and compared concentrations of pepsin in saliva in 60 laryngectomized patients with VP and 30 control subjects and correlated it with the incidence of VP complications and voice quality. Voice quality was assessed by Harrison-Robilard - Schultz (HRS) scale. Pepsin levels were measured by enzyme-linked immunoadsorbent assay (ELISA).

**Results:** Thirty four (57%) patients had VP complication. The most common complications were transprosthetic (24%) and periprosthetic (21%) leakage. Patients without miotomy had more often transprosthetic leakage. Patients with VP complication had longer median time since last

prosthesis change. There was no significant difference in median value of pepsin concentration in all patients and control subjects, 0.633 pg/ml vs. 0,698 pg/ml respectively. We found no significant difference in pepsin concentrations between patients with and without VP complications and patients with and without adjuvant radiotherapy. In addition, we found statistically insignificant negative correlation between pepsin levels and voice quality measured by HRS scale.

**Discussion:** Our results do not confirm previous studies of influence of EER on VP complications. We did not find any statistically significant correlation between pepsin levels and occurrence of VP complications and voice quality.

**Acknowledgments:** I thank prof. Davorin Đanić MD, PhD for critical revision, Ana Kozmar, PhD for help in pepsin ELISA test, Irzal Hadžibegović, MD, PhD for statistical guidance.

**MeSH/Keywords:** total laryngectomy, voice prosthesis, extraesophageal reflux, pepsin

**Poster code:** B-21-58

## **POSTER TITLE: RELATIONSHIP BETWEEN SPECIFIC AND NONSPECIFIC NASAL HYPERREACTIVITY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS**

**PhD candidate:** Dejan Tomljenović

**Part of the thesis:** Relationship between specific and nonspecific nasal hyperreactivity in patients with seasonal allergic rhinitis

**Mentor/s:** Professor Livije Kalogjera, MD, PhD

**Affiliation:** University Hospital Centre „Sestre milosrdnice”

**Introduction:** Allergic rhinitis is defined as an IgE-mediated inflammation of the nasal mucosa, induced by allergen exposure. Activation of mast cells in the early stage and eosinophils in late stage of allergic reactions, after contact allergen with respiratory mucosa, is the fundamental pathophysiological mechanism which leads to inflammation. Allergic inflammation leads to the characteristic symptoms of allergic rhinitis, such as runny nose (rhinorrhea), post-nasal dripping, nasal congestion, nasal itching and sneezing. Nasal symptoms are often combined with ocular symptoms (watery and itchy eyes).

**Materials and methods:** This study is designed to include 30 patients of both genders, aged 18 to 65, with monoallergy to grass or ambrosia pollen. An out-of-allergy-season provocation test with allergen, histamine and hypertonic solutions is planned to be administered to the nasal mucosa. Stimulation of two types of nasal mucosa receptors who respond to nonspecific provocation stimulus (H1 and TRPV) is expected. A before and after evaluation of nasal patency, symptom intensity, tryptase concentration, eosinophilic cationic protein and substance P in nasal secretion and tears will be conducted.

The markers of inflammation and symptoms in selected models of nasal provocation will be correlated statistically. The control group encompasses ten patients with symptoms of non-allergic rhinitis, with negative skin prick test and negative specific IgE tests.

**Results:** The study is currently in the phase of data collection and preliminary result processing, with almost 75% of planned applicants interviewed and their samples analyzed. Out of the planned 30 patients, 24 have completed study protocol testing and their samples are being analyzed.

**Discussion:** The aim of the study is to compare the reactivity of inflammatory cells in the early and late phase of allergic reactions, measure non-allergic inflammation intensity and neurokinin release after specific and nonspecific provocation.

**Acknowledgments:** Professor Livije Kalogjera - as my mentor and teacher.

**MeSH/Keywords:** allergy, ambrosia, grass pollen, provocation test, substance P, tryptase, nasal patency.

**Poster code:** B-21-112

## POSTER TITLE: DETERMINATION OF EGFR, BCL-2 AND KI67 IN PATIENTS WITH ORAL LICHEN PLANUS

**PhD candidate:** Ivana Pavić, MD

**Part of the thesis:** The significance of immunohistochemical expression of FHIT, EGFR and Bcl-2 in patients with oral lichen planus

**Mentor/s:** Associate Professor Drinko Baličević, MD, PhD

**Affiliation:** Ljudevit Jurak Department of Pathology, Sestre milosrdnice University Hospital Centre, Vinogradska cesta 29, 10000 Zagreb, Hrvatska

**Introduction:** Oral lichen planus (OLP) affects 1 to 2% of the population. Typically it affects middle-aged and elderly women although it can affect men, and rarely children. The cause of OLP is not known, but it is known that the OLP is mediated through T-lymphocytes to a still unknown antigen. There is about a 1% risk to cancerous change over a 10-year period. The main problem is in identifying lesions that will actually transform into cancer.

**Materials and methods:** Normally, tumor markers are used to identify cancer, but in some instances they can suggest potentially malignant lesions. Therefore, we evaluated OLP 64 lesions using immunohistochemistry markers (epidermal growth factor receptor (EGFR), bcl-2, Ki67) in comparison to the density of subepithelial band inflammatory infiltrate (low, medium and high). OLP patients were divided into smokers and non-smokers.

**Results:** There were 15 OLP patients in smoker group (range 28-70 years) while non-smoker group included 49 OLP patients (range 21-72 years). The mean age at which OLP was diagnosed was lower in smoker ( $48.7 \pm 10.6$ ) than non-smoker group ( $55.8 \pm 11.5$ ). Conventional hemalaun and eosine staining showed no difference in diagnosis OLP in smoking and non-

smoking group, nor EGFR expression by itself (Spearman's correlation test  $p=0.4$ ). Significant difference was found comparing EGFR, Ki67 and bcl-2 expression in squamous epithelium in relation to the density of subepithelial band inflammatory infiltrate between smokers and non-smokers with OLP ( $p<0.01$ ) (Table 1,2).

**Discussion:** We might conclude that at the time of OLP diagnosis, smokers were younger when compared to the OLP non-smokers which can implicate the possibility of cancer development in younger age than it is statistically reported for oral carcinoma. Additional immunohistochemical analysis showed that smokers with OLP, compared to non-smoker group, showed statistical significant expression of EGFR, Ki67 and bcl-2 markers in squamous epithelium in relation to the density of subepithelial band inflammatory infiltrate. These findings could contribute to the carcinogenesis and pathogenesis of OLP. Additional studies on a larger sample are needed to confirm this assumption.

**Acknowledgments:**

**MeSH/Keywords:** oral lichen planus, oral carcinogenesis, oral carcinoma

**Poster code:** B-23-31

## POSTER TITLE: BIOMARKERS OF UNCONTROLLED CHILDHOOD ASTHMA

**PhD candidate:** Marta Navratil, MD

**Part of the thesis:** Biomarkers of Systemic and Lung Inflammation in Controlled and Uncontrolled Childhood Asthma

**Mentor/s:** Mirjana Turkalj, MD, PhD, Assistant Professor Davor Plavec, MD, PhD

**Affiliation:** Srebrnjak Children's Hospital, Zagreb

**Introduction:** Asthma is a chronic inflammatory airway disease with a multifactorial pathophysiology. Although several clinical markers of asthma have been evaluated in many previous studies, an ideal measure of asthma activity and control has not been determined. The aim of study was (1) to compare different biomarkers (BMs) in children with controlled and uncontrolled asthma and (2) to investigate their relationship with other clinical indices of asthma control (Asthma Control Test [ACT], quality of life, lung function, serum IgE, prn beta-agonist use, time from last exacerbation [TLE] and (3) with each other.

**Materials and methods:** This cross-sectional study comprised 103 consecutive patients (age 6-18 years) with uncontrolled ([UA], n=53) and controlled asthma ([CA], n=50). Measured lung function and BMs included: spirometry, eosinophilic cationic protein (ECP), high-sensitivity C-reactive protein (hs-CRP), exhaled NO (FENO), pH and urates from exhaled breath condensate (EBC), exhaled breath temperature (EBT).

**Results:** The values of EBC pH, EBC urates and EBT showed statistically significant differences between studied groups (UA vs CA: EBC pH, mean [SD]. 7,2 [0,17], vs 7,33 [0,16], P=0,002. EBC urates, median [IQR],  $\mu\text{mol/L}$ . 10 [6] vs 45 [29], P<0,001. EBT mean [SD],  $^{\circ}\text{C}$ . 34,26 [0,83], vs 33,9 [0,6], P=0,014). Serum hs-CRP significantly positively correlated with prn salbutamol use, and EBT ( $r=0,240$ , P=0,014.  $r=0,445$ , P<0,0001. respectively) and inversely with FEV1 ( $r=-0,366$ , P=0,007). EBC

urates showed significant association with TLE and FENO ( $r=0,518$ , P<0,001.  $r=0,369$ , P=0,007, respectively) in UA, and EBC pH ( $r=0,351$ , P=0,0003), FEV1 (as % predicted) ( $r=0,222$ , P=0,024), ACT ( $r=0,654$ , P $\leq$ 0,0001), PAQLQ ( $r=0,686$ , P<0,0001), and prn salbutamol use ( $r=-0,527$ , P<0,0001) in all asthmatics. Discriminant analysis depicted EBC urates as the best single significant predictor of asthma control (F=62,969, P<0,0001) with an 80,6% diagnostic accuracy.

**Discussion:** In CA EBC urates and EBC pH were increased compared to UA. Significant association of serum hs-CRP with EBT, and of EBC urates with EBC pH reflect an association of inflammation, oxidative stress and acid stress in asthmatics. Our results provide the evidence supporting the potential utility of a panel of non-invasive BMs of inflammation, acid stress and oxidative stress as additional tools for monitoring childhood asthma.

**Acknowledgments:** The results presented were obtained in the scope of a scientific project 277-0000000-3436, entitled Comparing effects of two ways of driving asthma therapy in children 12-18 years, carried out with support from the Ministry of Science, Education and Sports of the Republic of Croatia. We would also like to thank to Srebrnjak Children's Hospital for financial support and contribution to this study.

**MeSH/Keywords:** asthma, biomarkers, child, exhaled breath condensate, inflammation

**Poster code:** B-24-51

## POSTER TITLE: 17Q12-21 AND ASTHMA - INTERACTIONS WITH EARLY LIFE ENVIRONMENTAL EXPOSURES

**PhD candidate:** Mario Blekić, MD

**Part of the thesis:** Association between chromosome 17q12-21 gene variants and asthma in childhood

**Mentor/s:** Prof. Neda Aberle, MD PhD

**Affiliation:** General Hospital „Dr. Josip Bencevic“ Slavonski Brod

**Introduction:** 17q12-21 polymorphisms are associated with asthma presence and severity across different populations. We sought to extensively investigate the genes in this region amongst Croatian schoolchildren in a case-control study, taking account of early-life environmental exposures.

**Materials and methods:** We included 423 children with asthma and 414 controls aged 5-18 years. 51 haplotype tagging SNPs were genotyped (GSDMA, GSDMB, ORMDL3, IKZF3, ZPBP2, TOP2). Data on exposure to smoking and furry pet ownership were collected using a validated questionnaire. Information on severe asthma exacerbations with hospital admission were retrieved from hospital notes. All cases underwent spirometry.

**Results:** We found two SNPs (one novel rs9635726 in IKZF3) to be associated with asthma. Among children with asthma, 4 SNPs (in ZPBP2, GSDMB and GSDMA) were associated with hospital admissions and 8 SNPs with lung function. One SNP (rs9635726) remained significantly associated with FEV1% predicted after FDR correction. Nine markers across five genes showed interaction with early-life ETS ex-

posure in relation to asthma and two with furry pet ownership. Amongst children with asthma, we observed significant interactions between early-life ETS exposure and 3 SNPs for lung function, also between early-life ETS exposure, 3 SNPs (in ORMDL3 and GSDMA) and hospital admission with asthma exacerbation. Three SNPs (in ORMDL3) interacted with current furry pet ownership, in relation to hospital admissions for asthma exacerbation.

**Discussion:** Our results indicate that several genes in the 17q12-21 region may be associated with asthma. This study confirms that environmental exposures may need to be included into the genetic association studies.

**Acknowledgments:** I thank my mentors Prof Adnan Custovic, Prof Angela Simpson and Prof Neda Aberle. We acknowledge all patients, physicians, clinical trial nurses, data managers and other collaborators who contributed to the study.

**MeSH/Keywords:** children, asthma, pet, smoking, polymorphism

**Poster code:** B-24-95

## POSTER TITLE: ANALYSIS OF TREATMENT OUTCOME IN CHILDREN WITH HYPOPLASTIC LEFT HEART SYNDROME

**PhD candidate:** Andrea Dasović Buljević, MD

**Part of the thesis:** Survival and quality of life in children with hypoplastic left heart syndrome

**Mentor/s:** Full professor Ivan Malčić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** In patients with congenital heart disease, according to a Croatian national population study, there are 2.3% patients with hypoplastic left heart syndrome - (HLHS). During the 12 year study all the children with HLHS were sent into two international cardio-surgery centres. They underwent three staged palliative surgery which can transform only existing right ventricle into the system ventricle: 1) Norwood procedure (creation of neo-aorta and subclavio-pulmonary anastomosis), 2) Glenn procedure (partial cavo-pulmonary connection PCPC) and 3) Fontan procedure (total cavo-pulmonary connection TCPC). Aim: to demonstrate treatment success in patients with HLHS, especially survival rate and quality of life, during the time span of 12 years.

**Materials and methods:** Patients: 58 neonates with HLHS were born in Croatia from 3 Nov 1999 till 1 Sep 2011. Initial management and diagnostic evaluation were performed in University Hospital Centre Zagreb. After that they were sent either to Deutsches Herzzentrum (München) or Frauen- und Kinderklinik (Linz). Between different stages of surgery they were treated in UHC Zagreb.

**Results:** Patients were categorized according to the gestational age (8% born before and 92% after achieved 37th week of gestation)sex (68 % male and 32% female)anthropometric characteristics at birth (BW: 3%<2499 g, 97%>2500g,

BL: 35%<49 cm, 65%>50cm)and Apgar score in fifth minute(4%<6, 96%>7. According to anatomical characteristics the patients were categorized in four groups, with predominance of near 80% of the most serious anatomy-aortal and mitral atresia. Prenatal diagnosis was made in 21% (66,6% before 34th gestational week, 33,3% after that), and postnatal in 79% of patients 69 % of them in the first two days and 31 % in more than 2 days after birth.

**Discussion:** Mortality: Between the 1st and the 2nd surgery 53,3 % patients died: between the 2nd and the 3rd 33,3% patients died. After the Fontan circulation was established, no one died. There are no data for 13,3% of patients. Total survival rate of children with HLHS over 12 years period is 74.4%. Even better results one can expect with a diagnostic shift into foetal period. That would allow an early treatment, immediately after delivery. Quality of life: According to Warmes- Sommerwill criteria 6% patients have seriously impaired quality14% have moderately impaired and 80% live normal life. The latter is possibly a consequence of non-observation of late complications during only 12 years of follow up.

**Acknowledgments:**

**MeSH/Keywords:** hypoplastic left heart syndrome, survival, quality of life

**Poster code:** B-24-171

## **POSTER TITLE: COMPARISON OF DIFFERENT DIAGNOSTIC PROTOCOLS IN THE DIAGNOSIS OF ASSOCIATED FRACTURES OF THE FACE AND SKULL BASE COMPUTED TOMOGRAPHY**

**PhD candidate:** Jasminka Igrec, MD

**Part of the thesis:** Role of defined computed tomography protocol in evaluation of the associated facial and skull base fractures

**Mentor/s:** Gordana Ivanac, MD, PhD

**Affiliation:** Clinical Institute for Diagnostic and Interventional Radiology, Clinical Hospital Dubrava

**Introduction:** Craniofacial fractures are complex injuries of the head associated with the incidence of skull base fractures ranging from 4% to 71%. Because they are not initially diagnosed, part of the skull base fractures remains unnoticed with development of late complications.

**Materials and methods:** A retrospective study was performed from 12th January 2007 till 31th December 2011 in Clinical Hospital Dubrava. Source of data are archived CT examinations of the head in patients with blunt head trauma. The research is going to be carried out on two groups of patients. In the first group, we intend to determine the incidence of associated facial and skull base fractures based on original single slice CT axial slices. In the second group, we intend to determine the incidence of associated facial and skull base fractures based on multiplanar MSCT reconstruction analysis. Proceeding on the assumption that the extended MSCT protocol is optimized for our analysis we will determine the time interval from the initial CT examination and radiological diagnosis of associated fractures mounted on MSCT device, classify certain types of fractures in the fracture patterns, and according to the radiographic appearance establish the relationship between the skull base and facial bones fractures, contusion markers, radiological detectable, post-traumatic

neuro-viscerocranial changes and outcome of diagnostic tests.

**Results:** For comparison and statistical analysis stored data is encrypted according to the anatomical localization units. In CT analysis we determine the number of fracture lines in one localization unit, length of the longest fracture line, dyastasis of the fragments, correlating our findings with associated neuro-viscerocranial injuries and outcome of the diagnostic tests. When classifying fracture patterns we analyze age, sex, mechanism of trauma and contusion marker. Our preliminary results indicate that some fracture patterns can be recognized and extended MSCT protocol is preferable for the analysis of complex fractures of the head.

**Discussion:** We believe that we will be able to confirm that our MSCT protocol is optimal for radiologic analysis of the fractures in complex head trauma which will enable the recognition of fracture patterns and could result in development of new classification system and help in selection of the treatment procedure.

**Acknowledgments:** /

**MeSH/Keywords:** blunt head injury, facial bone fracture, skull base fracture, computed tomography, multiplanar reconstructions

**Poster code:** B-25-30

## **POSTER TITLE: THE RELATIONSHIP OF PEER PRESSURE, BODY SHAME AND BODY DISSATISFACTION WITH ADOLESCENT EATING BEHAVIOURS**

**PhD candidate:** Jelena Mustapić, psychologist

**Part of the thesis:** The Relationship of Peer Pressure, Body Shame and Body Dissatisfaction with Adolescent Eating Behaviours

**Mentor/s:** Assistant Professor Darko Marčinko, MD, PhD, psychiatrist and psychotherapist

**Affiliation:** Technical School Rudjer Bošković, School of Applied Arts and Design and Fifth Gymnasium Zagreb, Ministry of Justice of the RoC, Prison System Directorate, Center for Diagnostics

**Introduction:** Eating disorders are associated with serious biological, psychological, and sociological morbidity and significant mortality. Rapid physical growth and development in adolescence constitute the unique background for development of disordered eating behaviours and/or eating disorders at this stage of life. There is an increased value placed on peer acceptance and approval, and a heightened attention to external influences and social messages about cultural norms. The experience of body shame and body dissatisfaction can lead to poor health habits and low self-esteem. These negative feelings may affect health behaviors associated with poor eating habits, dieting, low self-esteem and eating disorders.

**Materials and methods:** A sample of 400 adolescents 14-19 years of age completed self-reported measures of body dissatisfaction, body shame, peer pressure and eating attitudes and behaviours. The assessment tools included: a social-demographic questionnaire, Body Shape Satisfaction Scale (BSSS), Drive for Muscularity Scale (DMS), Body Shame Scale (BS-OBCS), Eating Attitudes Test (EAT-26), Peer Pressure Questionnaire and Body Mass Index (BMI) which is calculated using person's weight in kilograms divided by the square of the height in metres (kg/m<sup>2</sup>). Up to date, 328 adolescent participated in research.

**Results:** Preliminary data indicated that disordered eating attitudes and behaviours were positively correlated with peer pressure, drive for muscularity, body shame and body dissatisfaction, but not with body mass index. Body shame and body dissatisfaction were positive predictors of eating disturbance in female sample, while peer pressure and drive for muscularity were positive predictors of eating disturbance in male sample.

**Discussion:** The aetiology of eating disturbances and/or disorders may be different for male and female samples. Among adolescents, disturbed eating attitudes and behaviors were associated with various psychological and sociocultural factors some gender-related differences are also evident. The limitations and importance of these results will be discussed, and directions for future research and treatment of eating disorders will be indicated.

**Acknowledgments:** I would like to express my gratitude to all those who gave me the possibility to complete this thesis, especially to my supervisor, Darko Marčinko, MD, PhD.

**MeSH/Keywords:** Body Shame, Body Dissatisfaction, Peer Pressure, Eating Behaviours, Adolescents

**Poster code:** B-29-56



## POSTER TITLE: INCIDENCE, ACUTE MANAGEMENT AND LONG-TERM FOLLOW-UP OF PATIENTS WITH VESTIBULAR NEURITIS

**PhD candidate:** Ivan Adamec, MD

**Part of the thesis:** Acute Management of Patients with Vestibular Neuritis

**Mentor/s:** Mario Habek, MD, PhD

**Affiliation:** Department of Neurology, University Hospital Centre Zagreb

**Introduction:** Vestibular neuritis (VN) is one of the three most common causes of vertigo. Aims of this study were: [1] to determine incidence of vestibular neuritis in Zagreb and Velika Gorica, Croatia, [2] to assess efficacy of intravenous administration of dexamethasone on recovery of clinical symptoms of VN patients treated in the emergency department, and [3] to evaluate the recovery of vestibular nerve function after VN by ocular (oVEMP) and cervical (cVEMP) vestibular evoked myogenic potentials.

**Materials and methods:** Patients older than 18 fulfilling clinical criteria for VN were included. They were randomized into two groups: group 1 received intravenous dexamethasone 12 mg and group 2 received placebo. Clinical examination, number of vomiting episodes in the past 24 hours, nausea according to the visual-analogue scale, The European Evaluation of Vertigo scale and need for hospitalization were noted or performed at the time of presentation and two hours later. All patients underwent brain MRI during the first three months from initial presentation. In order to evaluate the recovery of vestibular nerve function after VN, all patients underwent VEMP recordings at six days and at six months after their initial presentation of symptoms.

**Results:** The incidence of VN in 2011 was 11.7 per 100000 people, and in 2012 it was 15.5 per 100000. The preliminary results of efficacy of

dexamethasone therapy showed improvement in patients in group 1 in the grade of nystagmus and The European Evaluation of Vertigo Scale ( $p=0.03$  and  $p=0.03$ , respectively). In the VEMP long-term follow-up part of the study we included 26 patients. 14 of them showed improvement on oVEMP at month 6 and 12 showed no change or worsening on oVEMP at month 6. Inability to perform Fukuda test and chronic white matter supratentorial lesions present on brain MRI were more frequent in patients with worse outcome on oVEMP ( $p=0.044$  and  $0.045$ , respectively). oVEMP latencies were associated with improvement or worsening of oVEMP amplitudes, showing that prolonged latencies correlate with 6 month improvement in oVEMP amplitudes ( $p=0.041$  and  $p=0.009$ , respectively).

**Discussion:** Preliminary results have shown a positive role of corticosteroids in the treatment of VN. The incidence we noted was higher than previously reported. This study identified clinical, MRI and neurophysiological predictors of recovery in patients with VN and offers additional insight in better understanding the role of VEMP in diagnosis and prognosis of VN patients.

**Acknowledgments:**

**MeSH/Keywords:** vestibular neuritis, dexamethasone, vestibular evoked myogenic potentials.

**Poster code:** B-30-80

# POSTER TITLE: EFFECT OF BOTULINUM TOXIN - TYPE A ON NONMOTOR SYMPTOMS AND COGNITION IN PATIENTS WITH PRIMARY FOCAL DYSTONIA

**PhD candidate:** Vladimir Miletić

**Part of the thesis:** Effect of Botulinum Toxin - Type A on Nonmotor Symptoms in Patients with Primary Focal Dystonia

**Mentor/s:** Professor Maja Relja, Md, PhD

**Affiliation:** University of Zagreb School of medicine, University Hospital Centre Zagreb, Department of Neurology

**Introduction:** Dystonia is the third most common movement disorder characterized by sustained muscle contraction causing abnormal posture. Cervical dystonia (CD) is the most frequent type of focal dystonias. Dystonia is considered as pure motor disorder, while nonmotor symptoms and cognition are often disregarded. Our previous results showed higher level of depression, anxiety and fatigue in CD patients. Mild executive dysfunction, although statistically insignificant was also observed in CD patients. Local application of botulinum toxin-type A (BTX-A) represents first line treatment for CD. It was thought that BTX-A only has local, peripheral effect. However, recent experimental data provided evidence for central effect of BTX-A. Considering central effect of BTX, investigation of BTX-A treatment on nonmotor symptoms including cognition was conducted.

**Materials and methods:** Up to now, our prospective study included 19 CD patients (10 females and 9 males, aged  $48 \pm 9$  and  $47 \pm 8,5$ ). Dystonia symptoms were assessed with Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). Non-motor symptoms were assessed with validated scales: Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Starkstein Apathy Scale (AS), Fatigue Severity Scale (FSS) and Pittsburgh Sleep Quality Index (PSQI). Cognitive functions were examined with computerized 'COGTEST' battery set of 5 tests examining several cognitive domains: 'Auditory Number

Sequencing', 'Spatial Working Memory', 'Strategic Target Detection', 'Continuous Performance Test - Flanker version' and 'Tower of London'. The Medical Outcome Study 36-item short-form health survey (SF-36) was used to assess health related quality of life in its various dimensions. All CD patients were examined prior to BTX-A treatment and 6-12 months after treatment.

**Results:** Our preliminary results showed that there was no statistically significant difference ( $p > 0,05$ ) in level of depression, anxiety, sleep quality, apathy, fatigue and in cognitive domains when comparing testing results prior and 6-12 months after BTX-A treatment. There was statistically significant improvement in dystonia symptoms when comparing results of TWSTRS ( $p < 0,05$ ) before and after treatment. Improvement was also found in domain of SF-36 referring to bodily pain ( $p < 0,05$ ).

**Discussion:** Results of our study conducted so far, indicate that BTX-A may be considered as effective and safe form of treatment, although longer follow-up period with larger number of patients is required for appropriate conclusions.

**Acknowledgments:** I would like to thank my mentor for advices and support during this investigation

**MeSH/Keywords:** Primary Focal Dystonia, Botulinum Toxin, Nonmotor Symptoms, Cognition

**Poster code:** B-30-140

## **POSTER TITLE: THE ROLE OF ULTRASONOGRAPHIC ANALYSIS OF MESENCEPHALIC NUCLEI IN PATIENTS WITH PARKINSON'S DISEASE WITH AND WITHOUT DEPRESSIVE SIMPTOMS**

**PhD candidate:** Katarina Blažina

**Part of the thesis:** Ultrasonographic Analysis of Mesencephalic Nuclei Can Play a Significant Role in Recognition of Early Nonmotor Sign of Idiopathic Parkinson's Disease.

**Mentor/s:** Professor Maja Relja, MD, PhD

**Affiliation:** University Hospital Centre Zagreb, University of Zagreb School of Medicine, Department of Neurology

**Introduction:** Transcranial ultrasonography (TCS) is low-cost, non-invasive, short duration neuroimaging method that allows high resolution imaging of deep brain structures in patients with movement disorders. On TCS, about 90% of patients with idiopathic Parkinson's disease (iPD) exhibit abnormal hyperechogenicity of the substantia nigra (SN). In addition, the TCS finding of reduced echogenicity of midbrain raphe is frequent in depressive disorders. Since depression is an early premotor sign of iPD and also a risk factor for iPD, aim of our study was to investigate TCS differences of mesencephalic nuclei in iPD with and without depression. Based on those findings we can estimate the role of ultrasonographic analysis of mesencephalic nuclei in diagnosis nonmotor sign of idiopathic Parkinson's disease.

**Materials and methods:** Up to now, a total of 124 patients with diagnose of iPD (82 males and 42 females, mean age 64.7 /-13.3) was included in the study. Depression in iPD was assessed with „Beck Depression Inventory“ (BDI) (score 0-63, pathological values over 18). Down cut-off value of SN hyperechogenicity is 0.21 cm<sup>2</sup>.

**Results:** In 8.1% (n=10) of iPD patients TCS could not be performed due to unsuitable temporal bone window. BDI score of more than 18, indicating depression was found in 31 (27.2%) of iPD patients. Among them 28 (90.3%) patients have changes in SN and 27 (87.1%) in nuclei raphe findings. Eighty three patients (72.8%) have BDI under 18, among them 70 (84.3%) with SN changes and 42 (50.6%) with nuclei raphe changes on TCS. Enlargement of SN is always contralateral to the clinically more affected side. We found no correlation between SN enlargement and clinical stage of disease ( $p>0,05$ ).

**Discussion:** Our preliminary results indicate that TCS is useful method of imaging of deep brain structures in patients with movement disorders, although its significance in detecting midbrain structures changes in early, premotor iPD still remains to be elucidated.

**Acknowledgments:**

**MeSH/Keywords:** Parkinson disease, ultrasonography of mesencephalic nuclei, depression.

**Poster code:** B-30-149



**1.3.**  
**RESEARCH ABSTRACTS**  
**- PUBLIC HEALTH AND HEALTH CARE**



## POSTER TITLE: ARE PHYSICIAN-PATIENT COMMUNICATION PRACTICES SLOWLY CHANGING IN CROATIA? - A CROSS-SECTIONAL QUESTIONNAIRE STUDY

**PhD candidate:** Luka Vučemilo, MD

**Part of the thesis:** Respecting Patients' Right to Information Regarding the Medical Procedure during Hospital Treatment in Croatia

**Mentor/s:** Assistant Professor Ana Borovečki, MD, PhD

**Affiliation:** University of Zagreb School of Medicine Andrija Štampar School of Public Health. University Hospital Merkur, Zagreb

**Introduction:** Good communication between health care professionals and patients ensures good patient-physician understanding, which in turn influences patient satisfaction, compliance, medical outcomes cost-containment, and overall good quality of healthcare. Effective communication is a prerequisite for the informed consent-obtaining process. This process emphasizes collaboration between physician and patient and the patients are allowed to co-decide by being provided all the information related to their illness, specific diagnostic and therapeutic procedures, as well as alternative treatment procedures. The analysis of the informed consent process can be a useful tool for understanding the physician-patient communication practices. This is why, the aim of this research was to explore the practices of physician-patient communication during the process of obtaining informed consent in a hospital setting in Croatia.

**Materials and methods:** Two hundred and fifty patients (response rate 78%) from five tertiary level hospitals in Zagreb, Croatia, anonymously filled in the questionnaire on informed consent and communicational practices by Nemcekova et al in the period from April to December 2011.

**Results:** Eighty five percent of patients received complete, understandable information, presented in a considerate manner. Higher

level of information was provided to patients in surgical than in internal medicine departments. Patients were informed about health risks of the proposed treatments (in 74% of cases) and procedures (76%), health consequences of refusing medical intervention (69%), and other methods of treatment (46%). However, patients pointed out a number of problems in physician-patient communication.

**Discussion:** Communication practices during informed consent-obtaining process in hospitals in Zagreb are based on a model of shared decision-making, but paternalistic physician-patient relationship is still present. Our results indicate that Croatia is undergoing a transition in the physician-patient relationship and communication.

**Acknowledgments:** I would like to thank Marko Čurković, MD, Milan Milošević, MD, PhD, and Professor Jadranka Mustajbegović, MD, PhD for contribution as co-authors in paper: Vučemilo L, Curkovic M, Milosevic M, Mustajbegovi J, Borovecki A. Are physician-patient communication practices slowly changing in Croatia? - a cross-sectional questionnaire study. Croat Med J. 2013

**MeSH/Keywords:** 54:185-91

**Poster code:** C-2-53

## POSTER TITLE: QUALITY ASSESSMENT IN GENERAL PRACTICE

**PhD candidate:** Slavica Sović

**Part of the thesis:** Development of Quality Indicators in General Practice

**Mentor/s:** Professor Hrvoje Tiljak, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, Andrija Štampar School of Public Health

**Introduction:** Quality improvement methods used to be focused on the reduction of differences between practices. However, efforts to improve quality of care by reducing undesirable variability in the delivery of services must avoid reducing desirable variability that reflects personalizing, integrating, and prioritizing care.

**Materials and methods:** Participants were 124 medical doctors, students of Postgraduate study in Family medicine at the School of Medicine, University of Zagreb, enrolled into the study in academic years 2004/05 through 2009/10. As a part of the course „Quality improvement”, students completed structured questionnaire on quality of their own work in general practices, composed of 23 quality indicators, each of them explained with five criteria. Based on the number of fulfilled criteria, adding 1 point for each fulfilled criterion, indicator score was calculated for each quality indicator. It ranged from 0 (no criterion fulfilled) to 5 (5 criteria fulfilled). Data were analyzed using factor analysis. Additionally, each student provided written description of their own work. It was in form of free text, analyzed based on grounded theory which was carried out manually.

**Results:** Two factors were derived through a factor analysis. Factor 1 „Scope of professional competencies and practice” encompassed quality indicators related to diagnostic equipment in doctor’s office, preventive measures

provided, cooperation and communication in medical team, clinical competences of a doctor, continuing medical education of a doctor, rate of immunization of the patients in care and doctor’s activities in society. Factor 2 „Organization of work” encompassed quality indicators related to getting practice on the phone, waiting time to get an appointment, well organized working time and absence of delayed diagnosis. Qualitative analysis explained that a part of variability of factor 2 is related to differences in accessibility to health care, socioeconomic and health status of the population in care, organization of health care and characteristics of medical staff.

**Discussion:** Factor analysis derived two factors, two dimensions of quality in general practice. A part of variability of factor 2 „Organization of work” reflects adoptability to characteristics of the practice, and in that way it is a desirable variability. This should be considered in quality assessment and quality improvement processes.

**Acknowledgments:** I would like to thank my mentor Professor Hrvoje Tiljak for patient guidance and advices he has provided me throughout preparing my doctoral thesis.

**MeSH/Keywords:** primary health care, general practice, quality indicator, quality assessment, quality improvement

**Poster code:** C-2-117



## POSTER TITLE: DOES NURSES' ABSENTEEISM AFFECT PATIENT SAFETY?

**PhD candidate:** Hana Brborović

**Part of the thesis:** Presenteeism and Absenteeism of Health Care Workers and Patient Safety Culture

**Mentor/s:** Professor Jadranka Mustajbegović, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, Andrija Štampar School of Public Health

**Introduction:** Health care is considered to be one of the high-risk occupations in Croatia because health care workers (HCW) are exposed to numerous occupational hazards and harm. Repeated exposure of HCW to negative or demanding conditions results in psycho-physiological imbalance that results in long-term chronic health problems and the emergence of presenteeism and absenteeism in the workplace. Absenteeism is considered to be any absence from work. Research showed that absenteeism of HCW could potentially threaten a large number of patients, which further increases costs in the healthcare system and compromises the quality of their work and the quality of health care. It was our aim to investigate the prevalence of nurses' absenteeism in Croatia and to investigate whether nurses' absenteeism affects patients' safety.

**Materials and methods:** This is a cross-sectional study which included medical nurses. Data were collected during April and May 2012. The study was conducted in a general hospital in Croatia. A total of 194 questionnaires were distributed and 147 returned, yielding response rate of 75,77%. Nurses from non-surgical, surgical, pediatric, obstetrics, psychiatry departments and anesthesiology/ICU participated in this research. Two questionnaires were used, The World Health Organization Health and Work Performance Questionnaire short form (WHO HPQ) and Hospital Survey on Patient Safety Culture.

**Results:** The data were not normally distributed ( $p > 0,005$ ). Median for relative absenteeism (4-week estimate) was 0,9 (minimum was 0,83, maximum 1). Out of 147 nurses participating, 68,03% (100/147) had experienced absenteeism in the last 4 weeks. Nurses who experienced absenteeism had statistically significantly ( $p < 0,005$ , Independent Samples Mann-Whitney U Test) higher median 0,92 than nurses who have not experienced absenteeism in the last 4 weeks (median 0,88). Overall patient safety was graded as „excellent“ by 34% of participants, as „very good“ by 43% participants, as „acceptable“ by 21% and as „poor“ by 3% of participants. Binary logistic regression was conducted to assess whether the 12 dimensions of the HSOPSC are associated to the absenteeism 4-week estimate. The model was not statistically significant ( $X^2(12)=13,59$ ,  $p=0,328$ ).

**Discussion:** Our results show high rate of absenteeism among respondents. However, patient safety was graded as „excellent“ and „very good“ by majority of participants. No association between absenteeism and patient safety was found.

**Acknowledgments:** This study was supported by Ministry of Science, Education and Sports, project title: „Health at the workplace and healthy working environment“, 108-1080316-0300

**MeSH/Keywords:** nurse, absenteeism, patient safety culture

**Poster code:** C-3-32

## POSTER TITLE: HOW GOOD ARE WE IN ACHIEVING GUIDELINES-RECOMMENDED GOALS FOR T2DM PATIENTS IN GP OFFICES IN CROATIA?

**PhD candidate:** Valerija Bralić Lang, MD, Family Physician

**Part of the thesis:** Family physician's clinical inertia in glycemetic control among patients with type 2 diabetes

**Mentor/s:** Prof. Biserka Bergman Marković, MD, GP, PhD

**Affiliation:** Private GP office affiliated to Department of Family Medicine, University of Zagreb, Zagreb, Croatia

**Introduction:** The typical patient with T2DM has multiple cardiovascular risk factors, each of which should be treated in accordance with existing guidelines in order to reduce the risk of microvascular and macrovascular complications. The aim of the study was to determine the achieved treatment targets in patients with type 2 diabetes set by European guidelines on cardiovascular disease prevention in clinical practice in GP offices.

**Materials and methods:** Between 2008 and 2010, 453 GP from all Croatian regions recruited first 20-25 participants of both sex with T2DM diagnosed at least 3 year prior to study entry, aged  $\geq 40$  years, who visited a practice for any reason (10274 participants). Blood samples were analyzed in accredited laboratories (HbA1c, fasting glycaemia, total cholesterol), measurements were made (blood pressure, body mass index, waist circumference) and physical activity and smoking habits were analyzed. Patients were stratified for gender and age groups.

**Results:** Mean age among participants was 65,7 yrs (range 40-96), female 5335 (51,9%). Mean HbA1c was 7,57% (range 3,8-15,4, 95% CI for the mean 7,54-7,60, SD 1,58) and 41,3% of analyzed diabetic patients had HbA1c less than 7%. Mean fasting glycaemia was 8,6 mmol/l (range 2,9-32,3 95% CI for the mean 8,55-8,66 SD 2,86) and 14,3% had fasting glycaemia level less than 6 mmol/l. Mean total cholesterol was 5,34 (range 2,0-14,9 95% CI for the mean 5,32-5,36

SD 1,12) and 18,6% had total cholesterol level less than 4,5 mmol/l. 66,81% of analyzed diabetic patients had hypertension. Mean systolic pressure was 139 mmHg (range 90-220 95% CI for the mean 138,7-139,3 SD 16,36) and mean diastolic pressure was 83 mmHg (range 45-130 95% CI for the mean 82,7-83,0 SD 8,56). Goal systolic pressure  $< 140$  mmHg reached 46,3% patients and 17% diastolic pressure  $< 80$  mmHg. 41,3% of analyzed diabetic patients were overweight and 44,7% were obese. 87,3% had waist circumference  $> 94$  (M), 80(F). 65,8% were physically active less than five times a week, and 19,4% were smokers.

**Discussion:** The degree of achieved treatment targets is not satisfactory. Most of analyzed T2DM patients are overweight or obese with the lack of physical activity and represent the typical patient with T2DM that have multiple cardiovascular risk factors, each of which should be treated in accordance with existing guidelines. Greater efforts are required for improving T2DM patient healthcare and outcome.

**Acknowledgments:** I would like to thank my mentor Professor Bergman Marković for her help and guidance that made this study possible and all GP colleagues who participated in this study.

**MeSH/Keywords:** T2DM, guidelines, cardiovascular prevention, general physician

**Poster code:** C-4-61

## **2. RESEARCH PROPOSALS**

### **2.1. RESEARCH PROPOSALS - BASIC MEDICAL SCIENCES**



## POSTER TITLE: EXPRESSION OF PLAKOPHILIN 3 IN DIFFUSE MALIGNANT PLEURAL MESOTHELIOMA

**PhD candidate:** Silvija Mašić, MD

**Part of the thesis:** Expression of plakophilin 3 in diffuse malignant pleural mesothelioma

**Mentor/s:** Professor Sven Seiwert, MD, PhD

**Affiliation:** Institute of Pathology, University of Zagreb School of Medicine, Šalata 10, Zagreb Department of Emergency Medicine, City of Zagreb, Heinzlova 88, Zagreb

**Introduction:** Diffuse malignant pleural mesothelioma is the most common primary malignant neoplasm of pleura. It represents diagnostic and also clinical challenge due to its histological heterogeneity and clinical outcome. There are 3 main histological types: epitheloid, sarcomatoid and biphasic. Epitheloid type is the most common and has the most favourable prognosis, while sarcomatoid is related to the worst prognosis. Plakophilins are structural proteins important for stability, adhesion of cells, intercellular interactions and cellular signaling, but there are little data about their role in tumorigenesis and tumor progression. Research on different types of tumor demonstrated that the change of plakophilin 3 expression is related to biological characteristics of tumor and patient survival.

**Hypothesis:** Expression of plakophilin 3 is increased in samples of diffuse malignant pleural mesothelioma compared to normal mesothelia and is related to more aggressive tumor growth and shorter patient survival.

**Aims:** The aim of this study is to classify samples of diffuse malignant mesothelioma into main types and subtypes of epitheloid mesothelioma, to analyze expression of plakophilin 3 in diffuse malignant pleural mesothelioma and study its prognostic value in this tumor.

**Materials and methods:** Archival samples of tissue of patients with established diagnosis

of diffuse malignant pleural mesothelioma and samples of normal pleural tissue will be used. Samples will be classified into 3 main histological types of diffuse malignant pleural mesothelioma and subtypes of epitheloid mesothelioma based on the prevalent histological component of the tumor. After immunohistochemical staining, levels of plakophilin 3 expression in cytoplasm and membranes of immunopositive tumor cells will be evaluated. Expression of plakophilin 3 with consideration to histologically estimated aggression in tumor growth and its prognostic value in diffuse malignant pleural mesothelioma will also be studied.

**Expected scientific contribution:** Many research performed on different types of tumors demonstrated that the expression of plakophilin 3 is connected with patient survival and aggression in tumor behaviour, but no research based on expression of this protein in diffuse malignant pleural mesothelioma was performed. Therefore, the expression and prognostic value of plakophilin 3 in diffuse malignant pleural mesothelioma will be analyzed.

**Acknowledgments:**

**MeSH/Keywords:** plakophilin 3, diffuse malignant pleural mesothelioma, prognostic value, immunohistochemistry

**Poster code:** A-3-36

## **POSTER TITLE: MICRONUCLEUS INDEX IN EPITHELIAL EXFOLIATED CELLS OF UROTHELIUM AND BUCCAL MUCOSA, AND PERIPHERAL BLOOD LYMPHOCYTES OF PATIENTS WITH PAPILLARY UROTHELIAL CARCINOMA**

**PhD candidate:** Arjeta Podrimaj Bytyqi, MD

**Part of the thesis:** Micronucleus index in epithelial exfoliated cells of urothelium and buccal mucosa, and peripheral blood lymphocytes of patients with papillary urothelial carcinoma

**Mentor/s:** Professor Isa Elezaj, MD, PhD, Dr. Ana Borovečki, MD, PhD, Research associate

**Affiliation:** University of Zagreb, School of Medicine, University of Prishtina, University Clinical Centre of Kosova and Faculty of Natural Sciences, Department of Biology

**Introduction:** Urothelial carcinoma comprises approximately 90% of all primary tumors of the bladder. The association between micronuclei (MN) induction and cancer development is supported by a number of scientific researches. The presence of MN in cells is a reflection of chromosomal aberration and also an important initiating event in cancer. Exfoliated epithelial cells are used traditionally for cancer screening by cytopathologists and for biomonitoring of the genotoxic effects in humans. The frequency of MN in peripheral blood lymphocytes (PBLs) is extensively used as a biomarker of chromosomal damage and genome stability.

**Hypothesis:** The micronucleus index (MNI) in epithelial exfoliated cells of urothelium in patients with bladder papillary carcinoma increases with the gradus of the cell atypia. The increase of MNI in urothelial cells of patients with bladder papillary carcinoma correlates with MNI in epithelial cells of buccal mucosa and PBLs of the same patients.

**Aims:** GENERAL AIM: The aim of this study is to establish the relationship of the MNI between the urothelial and buccal exfoliated cells, and PBLs in patients with bladder papillary carcinoma. SPECIFIC AIMS: 1. To analyze whether the MN-index in exfoliated urothelial and buccal cells, and in PBLs increase with the extent of cell

atypia in bladder cancer. 2. To propose MN test as potential to diagnose the asymptomatic disease in general population. 3. To establish the coexistence of genetic instability in different cell types which are distant from the primary lesion.

**Materials and methods:** 60 male participants will be classified into three groups (20 individuals per each group): healthy individuals, patients with low and high grade papillary urothelial carcinoma. The MN test will be performed in urothelial, buccal mucosa smears and PBLs according to adequate methods (Realı et al, Tolbert et al and Fenech and Morley). Statistical analysis will be performed using Sigma Stats Program, One Way ANOVA and Bonferroni post test.

**Expected scientific contribution:** In case of positive correlation between critical stages of epithelial bladder cell transformations and MN-index in buccal and PBLs, this method can be proposed as an additional criterion for prediction of bladder cancer risk.

**Acknowledgments:**

**MeSH/Keywords:** Micronucleus test, micronuclei, urothelial exfoliated cells, papillary urothelial carcinoma, cancer risk, screening.

**Poster code:** A-3-160

## **POSTER TITLE: THE INCIDENCE OF MICRONUCLEI IN PERIPHERAL BLOOD LYMPHOCYTES AND BUCCAL EXFOLIATED CELLS IN WOMEN WITH AND WITHOUT CERVICAL CANCER**

**PhD candidate:** Goneta Gashi, MD

**Part of the thesis:** The incidence of micronuclei in peripheral blood lymphocytes and buccal exfoliated cells in women with and without cervical cancer

**Mentor/s:** Professor Isa Elezaj, PhD, Prim. Dr. Sci. Vesna Mahovlic, MD, PhD, Research associate

**Affiliation:** University of Zagreb School of Medicine, University of Prishtina Faculty of Medicine, University Clinical Centre of Kosova, Univeristy of Prishtina, Faculty of Science, Department of Biology

**Introduction:** Cancer is a multistage process that results from an accumulation of multiple genetic changes. Therefore, it is imperative to use some biomarkers of DNA damage due to genetic instability to predict cancer risk as well as to identify high-risk individuals. Micronucleus (MN) is a biomarker of genotoxic events and chromosomal instability. Micronuclei (MN) are cytoplasmatic chromatin masses with the appearance of small nuclei that arise from chromosome fragments or intact whole chromosomes lagging behind at the anaphase stage of cell division.

**Hypothesis:** The effect of pre-cancer and cancer lesions of cervix on induction of the genetic instability can be determined using the (MN) assays in exfoliated buccal cells and peripheral blood lymphocytes.

**Aims:** The aim of this research is to evaluate the effect of different stages of cervical precancerous lesions and cervical cancer in the induction of genetic instability using frequency of micronuclei in the peripheral blood lymphocytes and buccal exfoliated epithelial cell.

**Materials and methods:** The study will be carried out at Gynecology and Obstetrics Hospital, University Clinical Centre of Prishtina, including 100 women who will be diagnosed and classified on the bases of the Papanicolaou (PAP) test and colposcopy/biopsy into group of low grade squamous intraepithelial lesions (LGSIL) and high-

grade squamous intraepithelial lesions (HGSIL) as well as invasive squamous carcinoma and control group, under supervision of gynecologists and pathologists. Two kinds of samples will be taken: blood and buccal mucosa smears. In each type of cells will be performed the MN test according to the original authors (MNI in buccal cells after Tolbert et al and MNI in lymphocytes after Fenech and Morely). Statistical analysis will be performed using Sigma stats program, One Way ANOVA, and Bonferroni post test.

**Expected scientific contribution:** The eventual positive correlation between critical stage of epithelial cervical cell transformations and MN frequency in buccal and peripheral blood lymphocytes will support the predictive value of micronucleus test as a biomarker of genetic instability for evaluation of risk level of cancer diseases. Aim of the research: The aim of this research is to evaluate the effect of different stages of cervical precancerous lesions and cervical cancer in the induction of genetic instability using frequency of micronuclei in the peripheral blood lymphocytes and buccal exfoliated epithelial cell.

**Acknowledgments:**

**MeSH/Keywords:** Micronucleus, Cervical cancer, Exfoliated cells, LSIL, HSIL, Buccal epithelial cells, Lymphocytes, Predictive value, Cancer risk.

**Poster code:** A-3-162

## POSTER TITLE: GENETIC POLYMORPHISM OF CYP2C19, CYP2C9 AND VKORC1 IN KOSOVO'S POPULATION

**PhD candidate:** Valon Krasniqi, MD

**Part of the thesis:** Genetic Polymorphism of CYP2C19, CYP2C9 and VKORC1 in Kosovo's Population

**Mentor/s:** Associate Prof. Nada Božina (Zagreb), Full Prof. Aleksandar Dimovski (Skopje)

**Affiliation:** University „Ss Cyril and Methodius“, Faculty of Pharmacy, Center for Biomolecular Pharmaceutical Analyses, Skopje (Macedonia). University of Prishtina, Faculty of Medicine, University Clinical Centre

**Introduction:** Determination of polymorphisms' frequencies in drug detoxification genes among different ethnic groups, as well as the influence of these allelic variants on clinical drug response, have become a major focus of many recent studies.

**Hypothesis:** There are certain specificities in the pharmacogenetic profile in Kosovo's population that deserve closer examination.

**Aims:** GENERAL AIM: Conduct a pharmacogenetic screening in Kosovo's healthy population. Information obtained from this research will be used to compare the allele frequency in Kosovo's population with that of other ethnic groups. SPECIFIC AIM: Investigate the frequency of CYP2C9, CYP2C19 and VKORC1 polymorphisms in Kosovo's healthy population.

**Materials and methods:** Distribution of allelic variants of CYP2C9 (\*1\*2\*3), CYP2C19 (\*1\*2\*3), and VKORC1 (position -1639) in Kosovo's population will be analyzed using a population sample of 150 individuals, aged between 18 and 65 years. The research will involve healthy persons without blood relationship between them, representing a mixed population from all parts of Kosovo. The gender ratio of participants in the

research will be nearly equal between women and men. In the process of DNA extraction (isolation), 5 ml of fresh blood together with the anticoagulant ethylene diamine tetraacetic acid (EDTA) will be used from each research participant. Genotyping of CYP2C9, CYP2C19, and VKORC1 will be carried out using ABI TaqMan® assays on Stratagene Real-time PCR machine.

**Expected scientific contribution:** This research will be the first study that examines CYP2C9, CYP2C19 and VKCOR1 gene polymorphisms in Kosovo's population. Therefore, this investigation will contribute to the completion of the European „map“ of different ethnic groups pharmacogenetic profile.

**Acknowledgments:** I would like to express my utmost gratitude to Professor Nada Bozina and Professor Aleksandar Dimovski for accepting to be my external mentors as well as for their continuous support, advice and encouragement with regard to my research.

**MeSH/Keywords:** CYP2C9, CYP2C19, VKORC1, Kosovo healthy population, pharmacogenetics, allelic variant, Real-Time PCR assay.

**Poster code:** A-4-88



## POSTER TITLE: EFFECT OF PENTADECAPEPTIDE BPC 157 ON MONOCROTALINE INDUCED COR PULMONALE IN RATS

**PhD candidate:** Mario Udovičić, MD

**Part of the thesis:** Effect of Pentadecapeptide BPC 157 on Monocrotaline Induced Cor Pulmonale in Rats

**Mentor/s:** Prof. Sven Seiwerth, MD, PhD and Prof. Predrag Sikirić, MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, Department of Pathology and Department of Pharmacology

**Introduction:** Pentadecapeptide BPC 157 antagonizes the incidence of a series of gastrointestinal lesions, it has a positive impact on healing processes of various wounds, proven angiogenic effect, protective effect on endothelium and it modulates synthesis of NO. BPC 157 furthermore reduces the duration of arrhythmias induced by ischemic-reperfusional injury in isolated pig heart, and also has antihypertensive effect in the model of L-NAME induced hypertension.

**Hypothesis:** Pentadecapeptide BPC 157 will prevent the development of pulmonary hypertension and cor pulmonale in rats induced by monocrotaline as well as alleviate already existing pulmonary hypertension and cor pulmonale induced by monocrotaline.

**Aims:** General aim is to prevent lesions of pulmonary vasculature and hypertrophy of right ventricle or to remove already existing lesions of pulmonary vasculature and hypertrophy of right ventricle by intraperitoneal or peroral application of BPC 157. Furthermore, the efficacies of BPC 157 applied in two different dosages, given either perorally or intraperitoneally and in two different regimens (cotreatment and post-treatment after the onset of pulmonary hypertension) will be compared between each other.

**Materials and methods:** This study will include 13 groups by 6 rats (male, body weight 150-200 grams). After initial application of monocrota-

line (80 mg per 1 kg body weight subcutaneously), the animals will be randomized. There will be 5 control groups and 8 experimental groups: cotreatment or posttreatment, with BPC given daily, either orally or intraperitoneally, in two different dosages (10 µg/kg i 10 ng/kg). During the experiment several parameters will be monitored (survival, activity, respiratory rate, body weight, peripheral edema, cyanosis, regular ECGs). On day 30 (or day 15 for one control group) animals will be killed and the lungs will be fixed for histology. After staining by van Gieson, the remodeling of pulmonary arteries will be assessed by measuring muscularization of arterioles with diameters 25-200 µm using computerized morphometric system ISSA. Hearts will be dissected, and the ratio of the right ventricle to left ventricle plus septum weight will be calculated as index of right ventricular hypertrophy.

**Expected scientific contribution:** This study could offer a new therapeutic option for pulmonary hypertension, which is an important cause of morbidity and mortality. It will also improve our understanding of pentadecapeptide BPC 157.

**Acknowledgments:**

**MeSH/Keywords:** BPC 157, monocrotaline, cor pulmonale, pulmonary hypertension, rats

**Poster code:** A-4-134

## POSTER TITLE: PENTADECAPEPTIDE BPC 157 AND WOUND HEALING AFTER HIND LIMB ISCHEMIA

**PhD candidate:** Andrej Šitum dr.med.

**Part of the thesis:** The effect of pentadecapeptide BPC 157 on the wound healing after hind limb ischemia

**Mentor/s:** Prof.dr.sc.Leonardo Patrlj, Prof.dr.sc.Predrag Sikirić

**Affiliation:** Medical Faculty University of Zagreb Department of Farmacology and Pathology

**Introduction:** Numerous recent studies have shown the positive effect of pentadecapeptide BPC 157 on lesions of various organic systems and its effect on the NO system. Considering that no study on the effect of the pentadecapeptide BPC 157 on hind limb wound healing in ischemic conditions has been made, in this paper we have analysed its effect produced by permanent ligation of common iliac artery.

**Hypothesis:** The implementation of the pentadecapeptide BPC 157 accelerates the wound healing process on the hind limb in induced ischemic conditions during the permanent ligation of the common iliac artery. The effect of BPC 157 is mediated by the action of the NO system.

**Aims:** The aim of this study is to show that wound healing on the hind limb is possible through the implementation of the BPC 157 in ischemic conditions during the permanent ligation of the common iliac artery and that its effect is mediated by the action of the NO system.

**Materials and methods:** The experiment is performed on 255 male Wistar Albino rats. The animals undergo surgery aimed at the ligation of common iliac artery and hind limb wound (3x3 cm) under deep anaesthesia. In line with the treatment regime and experimental period the animals are randomly divided into 11 groups (9 groups of 25 rats per group and 2 groups of 15) and are treated with saline (per os and 5ml/kg,i.p.), BPC 157 (10 µg/kg and 10 ng/kg,i.p.and per os), L arginine (200 mg/kg,i.p) and L NAME

(5 mg/kg,i.p) and cream (neutral cream and BPC 157 50µg(50ng)/2ml saline/50g neutral cream, topically). The first treatment is conducted immediately after the ligation of common iliac artery and the hind limb wounding, whereas the ultimate treatment is carried out 24 hours prior the sacrifice. The animals are sacrificed and assessed at the end of each single experimental period (24 hours, 3 days, 7 days, 14 days and 21 days). The assessed parameters are: macroscopic wound analysis (wound contracture and size), functional analysis (hind limb's EPT- extensor postural thrust/ MFI-motor function index) and microscopic analysis of the hind limb skin wound and ligated common iliac artery.

**Expected scientific contribution:** The expected scientific contribution is the fulfilment of the hypothesis, namely the demonstration that the BPC 157 causes an acceleration of the wound healing process on the hind limb in induced ischemic conditions during the permanent ligation of the common iliac artery and that the BPC 157 action mechanism is strictly correlated to the NO system.

**Acknowledgments:** I would like to express my gratitude to my mentors Prof.dr.sc. Leonardo Patrlj and Prof.dr.sc. Predrag Sikirić on their assistance during my research.

**MeSH/Keywords:** bpc 157, wound healing, ischemia, hind limb, NO system, L-arginine, L-NAME

**Poster code:** A-4-120

## **POSTER TITLE: BPC 157 REDUCED POSTOPERATIVE ADHESIONS FORMATION IN RATS**

**PhD candidate:** Lidija Berkopić Cesar, dr.med.

**Part of the thesis:** BPC 157 reduce postoperative adhesion formation after peritoneal injury.

**Mentor/s:** prof.dr.sc. Hrvoje Vrčić, prof. dr. sc. Predrag Sikirić

**Affiliation:** gynaecology, farmacology

**Introduction:** Peritoneal adhesions even after minor peritoneum injury are common problem after endoscopy or major surgical procedure. We propose for counteraction an orally active, stable gastric pentadecapeptide BPC 157 (GEPP-PGKPADDAGLV, MW 1419) as anti-ulcer peptide efficient in trials for inflammatory bowel disease (PL-10, PLD-116, PL 14736, Pliva, Croatia) and various wound treatment, no toxicity reported) that alleviated adhesions after various intestinal anastomosis in rat.

**Hypothesis:** BPC 157 reduce postoperative adhesion formation after peritoneal injury.

**Aims:** To show that BPC 157 reduces postoperative adhesion after experimental induced peritoneal defect Showing that this effect depend on NO-system.

**Materials and methods:** Excision of parietal peritoneum (1x2cm, 2 cm right from median 3

cm-laparotomy) with underlying superficial layer of muscle tissue was performed in rats (). BPC 157 (10µg, 10ng/kg i.p., 1ml/rat)(or an equivolume of 0.9% NaCl) was applied either (i) immediately after surgery, or (ii) once daily throughout 8 days, last application 24 h before assessment at 9th post-operative day (adhesions scored macro/microscopically (Mazuji's classification)).

**Expected scientific contribution:** To establish that BPC 157 reduces postoperative adhesion after experimental induced peritoneal defect, what is depend on NO-system. BPC 157 as a potential agens in prevention postoperative adhesion formation.

**Acknowledgments:** to my mentors

**MeSH/Keywords:** BPC 157, peritoneal injury, adhesion formation

**Poster code:** A-4-139

## **POSTER TITLE: ASSOCIATION BETWEEN ACTIVITY INTENSITY AND BIOMARKERS OF OXIDATIVE STRESS IN FOOTBALL PLAYERS**

**PhD candidate:** Antonela Nedić

**Part of the thesis:** Association between activity intensity and biomarkers of oxidative stress in football players

**Mentor/s:** Prof.dr.sc. Branka Matković

**Affiliation:** Exercise physiology

**Introduction:** Due to the extreme popularity of soccer in the world, the interest of the world of science in this sport game, which involves both long term and repetitive processes of exceptional physical exertion, is completely understandable. The concept of oxidative stress implies any balance disorder between prooxidant and antioxidant substances which causes the increase of reactive compounds and/or the increase of oxidative biomarker levels (with potential occurrence of molecular damage).

**Hypothesis:** There is a statistically significant difference in the values of the biomarkers of oxidative stress measured immediately after the soccer match in relation to the level of the intensity (during the game).

**Aims:** The goal of this research is to analyze the values of biomarkers of oxidative stress in young soccer players and blood metabolites changes after the soccer game, as well as the analysis of the association of biomarkers of oxidative stress and intensity of the activities during the game.

**Materials and methods:** Forty young soccer players (range: 15 to 18 years) will complete 90 minutes of friendly soccer match. Blood will be sampled before and immediately after the match to measure biomarkers of oxidative stress

(Malondialdehyde, Superoxide Dismutase, Glutathione, Total Antioxidant Status) and blood metabolites (complete blood count, differential blood count, cortisol, myoglobin, creatine kinase, electrolytes). The games will be filmed with 2 digital cameras and the players work profile will be analyzed with the Focus X2 performance analysis software (Elite Sports Analysis). Heart rate will be monitored with the heart rate monitors (Polar) throughout the game. Data will be analyzed using Statistica for Windows, ver.9.0. ANOVA and t-test will be used to determine differences between variables before and after the soccer games while a series of multiple linear regressions will be used to assess the association of biomarkers of oxidative stress and intensity of the activities during the game.

**Expected scientific contribution:** The knowledge of these parameters is of crucial importance in monitoring the growth and development of young football players, prevention of injuries and in the process of talent identification and selection in younger ages.

**Acknowledgments:**

**MeSH/Keywords:** football, oxidative stress, young football players

**Poster code:** A-5-59

## **POSTER TITLE: PROTEOMIC TISSUE PROFILING - A NEW GATEWAY TO UNDERSTANDING EARLY STAGE MELANOMA BIOLOGY**

**PhD candidate:** Andro Košec, MD

**Part of the thesis:** Prognostic significance of tissue proteomic profiling in cutaneous malignant melanoma of the head and neck stage I and II

**Mentor/s:** Professor Vladimir Bedeković, MD, PhD and Assistant Professor Lovorka Grgurević, MD, PhD

**Affiliation:** Department of ENT and Head and Neck Surgery, University Hospital Centre

**Introduction:** Morphohistopathological parameters are currently the basis for malignant melanoma classification and prognosis. An increasing number of molecular biomarkers offer new potential for refining diagnostic and prognostic disease categories. Early stage disease prognosis is only partially encompassed by morphological and histopathological parameters such as primary tumor localization, patient age and gender, mitotic rate, lesion thickness and ulceration. New studies based on direct tissue proteome analyses offer an enormous potential in improving disease prognosis.

**Hypothesis:** The proteomic profile of cutaneous head and neck melanoma tissue in disease stages I and II correlates with known prognostic factors and disease survival.

**Aims:** The aim of this study is to investigate the tissue proteomic profile of cutaneous head and neck melanoma stage I and II. Specifically, the proteomic profile of melanoma tissue specimens will be correlated with those of benign pigmented composite skin naevi and the relative difference in individual protein expression levels (fold change values) in melanoma tissue will be correlated with well-known prognostic factors such as tumor thickness, Clark level of invasion, presence of ulceration, lymphocapillary invasion, tumor-infiltrating lymphocytes, mitotic rate index, AJCC disease stage, disease free survival and disease specific survival rates.

**Materials and methods:** This study is based on tissue proteomic profiling of 40 early stage head and neck malignant melanoma tissue samples and 40 benign pigmented composite skin naevi as a control group for potential identification of biomarkers that will be correlated to known prognostic factors. The results are expected to expand our knowledge on the role of existing and newly discovered melanoma proteins in relation to their prognostic value in an early disease stage through a minimal 3-years follow-up interval.

**Expected scientific contribution:** The principal questions that will be addressed: 1) what is the level of expression of known biomarkers in paraffin-embedded tissue of cutaneous head and neck melanoma in stages I and II, 2) whether paraffin-embedded tissue samples of cutaneous head and neck melanoma expresses new and potentially valuable proteomic biomarkers, 3) does the level of proteomic expression in paraffin-embedded melanoma tissue have a diagnostic or prognostic significance in cutaneous head and neck melanoma stages I and II.

**Acknowledgments:**

**MeSH/Keywords:** malignant melanoma, biomarker, prognosis, head and neck

**Poster code:** A-6-155

## POSTER TITLE: WNT AND SONIC HEDGEHOG SIGNALING PATHWAYS IN PRIMARY AND SECONDARY MYELOFIBROSIS

**PhD candidate:** Marko Lucijanić

**Part of the thesis:** Analysis of genes and proteins of Wnt and Sonic Hedgehog signaling pathways in primary and secondary myelofibrosis

**Mentor/s:** Rajko Kušec

**Affiliation:** University of Zagreb School of Medicine

**Introduction:** Wnt and SonicHedgehog signaling pathways play important role during fetal histogenesis, in homeostasis and morphogenesis of adult tissues, self-renewal, proliferation and differentiation of stem cells/tissue progenitor cells. They are part of larger molecular network. Target genes activated by Wnt and SonicHedgehog signaling are involved in oncogenesis, fibrosis and neoangiogenesis. Primary genetic lesion responsible for primary myelofibrosis is unknown at the time. Current findings suggest possible role of Wnt and Sonic Hedgehog signaling pathways in pathogenesis of this disease.

**Hypothesis:** There is imbalance in gene and protein expression of Wnt and Sonic Hedgehog signaling pathways in tumor tissue of primary myelofibrosis when compared to healthy bone marrow.

**Aims:** General aim is to investigate changes in Wnt and Sonic Hedghog signaling pathways in primary myelofibrosis and their role in pathogenesis of this disease. Specific aims are to analyze expression of Wnt3a,  $\beta$ -catenin, SHH and GLI-1 genes, expression of Wnt3a,  $\beta$ -catenin, SHH, GLI-1 and Sost proteins and to compare obtained results with clinical parameters.

**Materials and methods:** Bone marrow samples of primary myelofibrosis patients obtained by trephine biopsy and fine needle aspiration will

be used for this project. Total of 30 patients with primary myelofibrosis will be analyzed and compared to control groups of 10 patients with secondary myelofibrosis and 10 subjects with healthy bone marrow (patients with aggressive NHL without bone marrow infiltration). Patients included were or will be evaluated in time period from 1st January 2005 to 31st December 2013. RT-PCR methods will be used to analyze gene expression on fine needle aspiration samples. Immunohistochemistry will be used to analyze protein expression on paraffine embedded trephine biopsy samples and level of expression will be expressed semiquantitatively by one pathologist (0 - no positivity, 1 - less than 25% of positive cells, 2 - more than 25% of positive cells). Obtained results will be shown as median and range. Non parametric statistical tests will be used to compare between groups. Percentages will be analyzed using Fisher exact test. Survival curve will be shown for all patients.

**Expected scientific contribution:** Expected scientific contribution is to complement current genetic profile of primary myelofibrosis and clarify the role of Wnt and Sonic Hedgehog signaling pathways in pathogenesis of this disease.

**Acknowledgments:**

**MeSH/Keywords:** Primary myelofibrosis, Wnt, Sonic Hedgehog,  $\beta$ -catenin

**Poster code:** A-6-168

## **POSTER TITLE: CHANGES OF THE NERVE FIBER LAYER THICKNESS EVALUATED BY OPTIC COHERENCE TOMOGRAPHY IN CHILDREN WITH CEREBRAL PALSY AND VISUAL IMPAIRMENT**

**PhD candidate:** Neda Striber MD

**Part of the thesis:** Children with cerebral palsy and visual impairment have structural nerve fiber layer damage

**Mentor/s:** Professor Branko Cerovski, MD PhD

**Affiliation:** Ophthalmology Department University Hospital Sister of Mercy, Zagreb Croatia Department of Pediatric Surgery Children's Hospital Zagreb

**Introduction:** Cerebral palsy (CP) is a clinical entity that refers to the group of no progressive but often variable motor disorders. The cause of CP is brain damage taking place in early perinatal period or early infancy. Children with CP often have associated mild or more severe neurodevelopment impairment visual or hearing disorder epilepsy intellectual deficit speech sensation and perception impairment. Visual impairment is present in a high percentage of children with cerebral palsy including different refractive anomalies strabismus amblyopia nystagmus. The standard ophthalmologic examination of children with CP included anterior eye segment examination, visual acuity, ophthalmoscopy, determination squint angle measurement and VEP. In this study the method of ocular coherence tomography (OCT) for the retinal nerve fiber layer thickness analysis in children with cerebral palsy and visual impairment is applied.

**Hypothesis:** There is a structural disorder of the retinal nerve fiber layer in children with CP which is related to the visual function impairment.

**Aims:** To determine the presence and the degree of optical nerve damage and the relationship between visual impairment and structural eye disorders.

**Materials and methods:** The standard ophthalmologic equipment will be used optotypes for

visual acuity testing slit lamp for anterior eye segment examination, synoptophore for squint angle measurements, ophthalmoscope the fundus of the eye examination, Tropicamide 1% eye drops for skiascopy OCT, VEP. The study will include 50 examinees at the age of 6-17 years with cerebral palsy that satisfy the study criteria. These patients are included in the cerebral palsy registry of Children's Hospital Zagreb. The cerebral palsy classification was conducted according to Surveillance of Cerebral Palsy in Europe (2007) with regard to the basic type subtype etiology imaging methods and associated disorders. Control group children of the same age taking part in the standard ophthalmologic examination at ophthalmology outpatient clinic. The examinees will be chosen by random sampling. The exclusion criteria are cerebral palsy and other associated anomalies.

**Expected scientific contribution:** OCT as a noninvasive and simple method of the laser nerve fiber thickness imaging would provide an insight in the structural retinal damage in children with CP and visual impairment.

**Acknowledgments:**

**MeSH/Keywords:** Cerebral palsy, optical coherence tomography, structural disorder of the retinal nerve fiber layer

**Poster code:** A-9-172





**2.2.**  
**RESEARCH PROPOSALS**  
**- CLINICAL MEDICAL SCIENCES**



## **POSTER TITLE: THE ROLE OF PARATHYROID HORMONE CONCENTRATION MEASUREMENT IN EARLY POSTOPERATIVE DIAGNOSIS OF HYPOCALCAEMIA AFTER THYROID SURGERY.**

**PhD candidate:** Renata Curić Radivojević

**Part of the thesis:** Predictive Value Of PTH Assay In Early Postoperative Diagnosis Of Hypocalcaemia.

**Mentor/s:** Professor Drago Prgomet, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** Hypocalcaemia is the most frequent complication after thyroid surgery with wide range of incidence from 1.2 to 40%. Permanent hypoparathyroidism is less common and occurs in 3 to 10% patients. Postoperative hypoparathyroidism is traditionally detected by serial measurement of serum calcium, requires multiple venepunctures and prolonged hospitalization. In recent years, iPTH assay has been under investigation for thyroid surgery as an early prediction of postoperative hypocalcaemia, guiding the surgeon for parathyroid autotransplantation, and calcium substitution therapy. Still there are many controversies about it, and there are no unique guidelines for PTH use.

**Hypothesis:** iPTH is a better predictor of postoperative hypocalcaemia than serial measurement of ionized calcium (iCa).

**Aims:** This study aims to determine the role of iPTH assay in comparison to ionized calcium as a predictor for hypocalcaemia and its impact on future management of patients with these complications. Further goals are to determine: predictive values of PTH assay in early postoperative diagnosis of hypocalcaemia

**Materials and methods:** A 100 patients going for a thyroid surgery will be followed up pro-

spectively. 63 patients in main group scheduled for thyroidectomy, and 37 patients in control group scheduled for partial resection of thyroid e.g. lobectomy. Exclusion criteria: underage patients, previous thyroid or neck surgery, renal insufficiency, parathyroid disease. Blood samples for iPTH and iCa measurement will be taken 8 times according to the pre-planned time table (during, and after surgery, as well as in outpatient follow up)

**Expected scientific contribution:** Early iPTH measurement may be of value in prediction of postoperative hypocalcaemia, and in guiding surgeon whether to perform parathyroid autotransplantation. iPTH can serve as useful tool for selecting patients requiring substitution therapy and safe discharge home.

**Acknowledgments:** I would like to thank my mentor, nurses and technicians from the Department of ENT and Nuclear Medicine, as well as to OR personnel for their help and patience during this investigation.

**MeSH/Keywords:** Parathyroid hormone, thyroid surgery, hypocalcaemia, complications, hypoparathyroidism

**Poster code:** B-1-57

## POSTER TITLE: INFLUENCE OF DEXAMETHASONE ADMINISTRATION IN SPINAL ANESTHESIA IN FEMUR FRACTURE

**PhD candidate:** Livija Šakić, MD

**Part of the thesis:** Influence of dexamethasone administration in spinal anesthesia in femur fracture

**Mentor/s:** Associate Professor Dinko Tonković, MD, PhD

**Affiliation:** Department of Anesthesiology, Reanimatology and Intensive Medicine, University Hospital „Sveti Duh“, University of Zagreb School of Medicine

**Introduction:** Spinal anesthesia blocks acute pain in older patients with femur fracture. Delirium is a common complication seen after femur fracture, affecting approximately 10-16% of patients. It is associated with increased mortality at 1st year, delayed rehabilitation efforts, prolonged length of hospital stay, poorer functional outcomes, and increased risk of nursing home placement.

**Hypothesis:** Intrathecal dexamethasone administration improves quality of anesthesia in patients with femur fracture compared to conventional spinal anesthesia.

**Aims:** The aim of this research is to establish the influence of intrathecal dexamethasone administration in spinal anesthesia with levobupivacaine on postoperative pain and changes of consciousness, values of cortisol levels and quality of treatment for patients with femur fracture compared to spinal anesthesia with only local anesthetic.

**Materials and methods:** The study is planned as a prospective, interventional, randomized clinical trial. A total of 60 patients ASA2 and ASA3 status, scheduled for surgical procedures will be sorted into two groups and undergo surgery in spinal anesthesia with levobupivacaine with or without dexamethasone. The primary outcome measure will be occurrence of postoperative disturbance of consciousness and plasma cor-

tisol levels. As a secondary outcome measure will be pain intensity, blood glucose levels and recovery. Cortisol and glucose will be analyzed in five measurements. Peripheral venous blood samples will be collected before anesthesia, one hour after surgery, third, fifth and on the tenth day after the surgery. Postoperative delirium will be defined by using Confusion Assessment Method (CAM) criteria. Visual analogue scale (VAS) will be used to record pain severity among patients.

**Expected scientific contribution:** Scientific contribution of this research is to expand knowledge about choosing modalities of anesthesia for femur fracture with better postoperative analgesia and outcome. Specific contribution refers to the collection of evidence on the impact of spinal anesthesia with levobupivacaine and dexamethasone to block pain and how it effects changes on postoperative disturbance of consciousness, by measuring plasma cortisol and glucose levels. The gathered information about cortisol and modality of anesthesia will be useful to define clinical guidelines.

**Acknowledgments:** This work was supported by grants from the Croatian Ministry of Science (projects: 108-0000000-3433)

**MeSH/Keywords:** spinal anesthesia, dexamethasone, delirium, cortisol, pain, femur fracture

**Poster code:** B-1-85

## **POSTER TITLE: A COMPARISON OF THE C-MAC D-BLADE, C-MAC AND DIRECT LARYNGOSCOPY**

**PhD candidate:** Vedran Hostić, MD

**Part of the thesis:** A comparison of the C-MAC D-BLADE, C-MAC and direct laryngoscopy for intubation of anaesthetised patients

**Mentor/s:** Branka Maldini, MD PhD

**Affiliation:** Department of Anaesthesia, Sestre Milosrdnice University Hospital Centre, Zagreb, Croatia

**Introduction:** Difficult and failed tracheal intubation, remains a leading cause of anaesthetic morbidity and mortality. Direct laryngoscopy (DL) has been a mainstay of anaesthetic practice for nearly 100 years, but requires alignment of the oral, pharyngeal, and laryngeal axes in order to facilitate tracheal intubation. In contrast, videolaryngoscopy (VL) only require alignment of the pharyngeal and laryngeal axes. Recent advances in digital technology resulted in the commercial release of numerous competing designs, each purporting to offer the definitive intubation solution.

**Hypothesis:** C-MAC D-BLADE would reduce Intubation difficulty score (IDS) in comparison with the C-MAC and DL.

**Aims:** Primary objective is to compare the C-MAC D-BLADE, C-MAC and DL in respect of intubation difficulty. Secondary objectives are to compare these three devices in respect of efficacy, ease of use and side-effect profile. Finally, standardisation of measured parameters during laryngoscopy and a new scoring system for VL will be proposed.

**Materials and methods:** Ninety patients scheduled for operation in general anaesthesia requiring endotracheal intubation will be enrolled to the study. Patients will be randomised to one of the three devices via computer-generated

randomisation code. Once the patient has been deemed ready for intubation, the researcher will undertake laryngoscopy and intubation using one of the devices as per the study allocation. The researcher will subsequently record VAS scores for ease of device and tracheal tube insertion and the video recording of the intubation will be reviewed for the time to optimal laryngeal view, time for tracheal tube insertion and time to successful intubation. The modified Cormack and Lehane grade and POGO score will also be noted. Finally, the IDS, Fremantle score and the presence of immediate complications will be noted.

**Expected scientific contribution:** Results of this study will contribute to the further development of VL. Standardisation of measured parameters would help in comparing different studies and a new scoring system for VL would make comparing of different videolaryngoscopes possible.

**Acknowledgments:** I would like to thank Professor Branka Maldini and Iljaz Hodzovic for providing me with much needed advice regarding this research.

**MeSH/Keywords:** laryngoscopy, laryngoscopes, intubation

**Poster code:** B-1-91

## POSTER TITLE: HUMAN PAPILLOMAVIRUS - POSSIBLE COFACTOR IN DEVELOPMENT OF NONMELANOMA SKIN CANCER

**PhD candidate:** Vlatka Čavka, M.D.

**Part of the thesis:** The influence of human papillomavirus on nonmelanoma skin cancer etiology

**Mentor/s:** Professor Mirna Šitum, M.D., Ph.D., Professor Nada Brnčić, M.D., Ph.D.

**Affiliation:** Department of Dermatovenereology „Sestre milosrdnice“ University Hospital Centre, „Ljudevit Jurak“ Department of Pathology „Sestre milosrdnice“ University Hospital Centre, Department of Pathology Uni

**Introduction:** Cutaneous HPV types have been established and associated with precancerous lesions, in situ carcinomas and NMSC in numerous studies, but the actual importance of these viruses in the etiology of these lesions still remains unknown. Whereas HPV-DNA has been detected in normal skin and in premalignant lesions „hit and run“ mechanism, which no longer requires the viral agent but the activity of HPV oncoproteins, has been suggested. Recent studies are also trying to establish association between UV radiation and organism's immune response to HPV.

**Hypothesis:** There is an increased prevalence of HPV DNA in precancerous lesions (actinic keratoses- AK) and in situ carcinomas (Mb. Bowen), as well as in basal cell carcinomas localized on permanently sun-exposed skin (face), and basal and squamous cell carcinomas in geographic areas with increased insolation.

**Aims:** To establish the role of HPV in development of NMSC by determining its prevalence in AK, Mb. Bowen, SCC and BCC. To investigate the prevalence and differences between various HPV types according to tumor localization (face/trunk) and patients' geographic distribution (two geographic regions with different insolation- cities of Zagreb and Rijeka).

**Materials and methods:** HPV DNA will be detected from paraffin-embedded biopsy materials of AK, Mb. Bowen, SCC and BCC by reverse hybridization assay. Part of the E1 region of the  $\beta$ -papillomavirus genome will be amplified by PCR. Genotyping of 25 skin HPV types (5, 8, 9, 12, 14, 15, 17, 19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 49, 75, 76, 80, 92, 93 i 96) will be carried out. Identification of high-risk HPV types 16 i 18 will also be performed. To explore differences in sun intensity (dependent of geographical latitude), city-specific data on the erythematous UV index will be obtained and median values will be calculated for cities Zagreb and Rijeka.

**Expected scientific contribution:** To confirm „hit and run“ theory and support a role for HPV infection in skin carcinogenesis as a co-factor in association with UV. To provide a possibility of different therapy approach in treating skin cancers (local immunomodulatory treatment and possible vaccination).

**Acknowledgments:**

**MeSH/Keywords:** HPV, basal cell carcinoma, squamous cell carcinoma, actinic keratosis, carcinoma in situ, ultraviolet rays

**Poster code:** B-2-83

## POSTER TITLE: THE VALUE OF TRICHOSCOPY IN THE DIAGNOSIS OF PRIMARY CICATRICIAL ALOPECIAS

**PhD candidate:** Željana Bolanča, MD

**Part of the thesis:** The value of trichoscopy in the diagnosis of primary cicatricial alopecias

**Mentor/s:** Prof. Mirna Šitum, PHD, MD

**Affiliation:** School of Dental Medicine University of Zagreb

**Introduction:** The scalp biopsy is crucial for the diagnosis of primary cicatricial alopecia. Pathohistological analysis can be quite challenging for the pathologist, especially in the lack of detail disease history, inappropriate specimen, and section cutting. The major mistakes include: too small or too shallow biopsy specimen, artifact while specimen manipulating, cutting through follicles and inappropriate site for the biopsy. The biopsy is usually done at the edge of the active lesion, although sometimes the disease can be focal and disease activity difficult to appreciate with naked eye.

**Hypothesis:** Trichoscopy guided scalp biopsy is a new technique for performing scalp biopsies. It is fast and precise technique that allows choosing individually affected follicles even in early and focal primary cicatricial alopecias.

**Aims:** To investigate the value of trichoscopy in choosing the optimal site for the scalp biopsy.

**Materials and methods:** The Outpatient Clinic patients with primary cicatricial alopecia will be randomized in two different groups. In the first group, the biopsy will be done without trichoscopy, at the edge of the lesion and in the

second group the trichoscopy guided biopsy will be done. The choosing criteria for the appropriate site will be chosen upon the already known trichoscopy criteria for the primary cicatricial alopecia. The two punch biopsy will be performed: one for the vertical section for pathohistological analysis and the other half of the vertical specimen will be used for the DIF. The second 6 mm punch biopsy will be used for the horizontal sections of pathohistological analysis. The biopsy specimen will be stained with hematoxyline and eosin and will be interpreted by the pathologist from the Department for Pathology, University Hospital Center „Sestre milosrdnice“. Biopsy specimen for the DIF will be placed in the fridge.

**Expected scientific contribution:** Trichoscopy guides scalp biopsy allows optimal clinico-pathological correlation and decreases the number of repeated scalp biopsy.

**Acknowledgments:**

**MeSH/Keywords:** primary cicatricial alopecia, alopecia

**Poster code:** B-2-146

## POSTER TITLE: GRIP FORCEFULNESS IN RHEUMATOID ARTHRITIS

**PhD candidate:** Ines Doko, MD

**Part of the thesis:** Correlation between the grip forcefulness, functional ability and disease activity in rheumatoid arthritis

**Mentor/s:** Professor Simeon Grazio, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, 'Sestre Milosrdnice' University Hospital Centre

**Introduction:** Rheumatoid arthritis (RA) is the commonest inflammatory rheumatic disorder which at an early stage already can lead to substantial functional limitations in individuals affected by this disease. The measurement of the hand grip strength is a common method of evaluation and is recommended for assessing the functional ability in RA. New parameters of the functional hand potential measured by a modern dynamic electronic dynamometer represent a unique concept in evaluating the functional status and monitoring the rehabilitation process.

**Hypothesis:** The grip forcefulness as a new parameter of the functional potential of the hand measured by electronic dynamometer is lower in patients with rheumatoid arthritis than in the general population age and sex matched and that change is associated with the degree of functional ability and disease activity.

**Aims:** To determine the correlation between the forcefulness of the grip, measured by newest electronic dynamometer, and functional capacity and disease activity in patients with rheumatoid arthritis.

**Materials and methods:** Eighty adult outpatient participants with diagnosed rheumatoid arthritis according to the ACR criteria will be included. Participants will have age and sex

matched healthy controls. In evaluating the motor function of the hand, a new measuring expert system for the acquisition of dynamic time series of the hand grip force developed at the „Ruder Bošković“ Institute will be used. The outcome measures include: dynamometric parameters of hand grip, ABILHAND-RA questionnaire and Health assessment questionnaire (HAQ) for measuring functional ability, Brief ICF Core Set for Hand conditions, Disease activity score (DAS28), C reactive protein level, Joint Alignment and Motion Scale (JAM) for measuring hand deformity, visual analog scale for pain, Patient and Physician Global Assessment and Steinbrocker score for hand X-rays. Statistical analysis will be performed in the program SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

**Expected scientific contribution:** Evaluation of new parameters of functional hand potential will contribute to the methodology of more detailed clinical assessment of patients with rheumatoid arthritis and possibly also reflect the level of overall functional ability and disease activity.

**Acknowledgments:**

**MeSH/Keywords:** dynamometer, functional ability, disease activity, grip strength, rheumatoid arthritis

**Poster code:** B-3-34



## **POSTER TITLE: ASSOCIATION OF DISEASE ACTIVITY MEASURED BY RAPID3 WITH PHYSICAL FUNCTION OF THE HAND AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS**

**PhD candidate:** Merita Martinaj, Master of Science in Physiotherapy

**Part of the thesis:** Association of disease activity measured by rapid3 with physical function of the hand and quality of life in patients with rheumatoid arthritis

**Mentor/s:** Simeon Grazio, MD, PhD

**Affiliation:** Rheumatology Clinic, University Clinical Center of Kosova

**Introduction:** Rheumatoid arthritis (RA) is progressive, autoimmune disease, characterized by chronic synovitis and joint damage which result in decreased functional ability, especially of the hand.

**Hypothesis:** Disease activities measured by simple disease activity indices are valuable tools that reflect physical function of the hand in patients with rheumatoid arthritis (RA).

**Aims:** The general aim of our study is to evaluate validity and usefulness of RAPID3, simple clinical test for assessment of disease activity in RA and its relationship with functional ability and quality of life (QoL). The specific aims are: to determine the validity of RAPID 3 as index that reflect level of functional disability measured by specific hand related questionnaires (HAQ, SOFI), grip strength, and fingertips-palm distance in patients with RA.

**Materials and methods:** The research will be performed on patients with established diagnosis of RA during their outpatient visit at the Rheumatology Clinic, University Clinical Center

of Kosova. Using a structured questionnaire there will be obtained data regarding demographics, history of the disease, disease activity (RAPID3, DAS28), function of the hand (SOFI, HAQ, grip strength and range of motion for fingers) and quality of life (EQ-5D).

**Expected scientific contribution:** RAPID3 is a simple and for clinic practice very attractive questionnaires measuring disease activity. It takes on average 3-5 minutes to complete. Hand is affected in almost all patients with RA, resulting in significant impairment of its function and consequently in diminished Quality of Life. If our hypothesis will be confirmed it will increase the value of RAPID3 as a measure of disease activity, which reflects physical function of the hand and QoL and widened their usage in clinical practice worldwide.

**Acknowledgments:** Ministry of Education, Science and Technology of Kosova

**MeSH/Keywords:** rheumatoid arthritis, disease activity, function, quality of life

**Poster code:** B-3-107

## POSTER TITLE: MONITORING OF ANTIHYPERTENSIVE THERAPY EFFECTS IN PREGNANCY

**PhD candidate:** Tomislav Kulaš, MD

**Part of the thesis:** Antihypertensive therapy in pregnancy is expected to influence perinatal outcome parameters, depending on the type of antihypertensive therapy used.

**Mentor/s:** Professor Dubravko Habek, MD, PhD

**Affiliation:** Clinical Department of Gynecology and Obstetrics, Merkur University Hospital, Zagreb, Clinical Department of Gynecology and Obstetrics, Sveti Duh University Hospital, Zagreb

**Introduction:** Antihypertensive therapy in pregnancy is expected to influence perinatal outcome parameters, depending on the type of antihypertensive therapy used. Ultrasonography (US) monitoring of biophysical profile variables, Doppler US of uteroplacental and fetal circulation and monitoring of laboratory parameters and other perinatal indicators of treatment with particular antihypertensives will provide an insight into the hemodynamic and biophysical parameters of the fetoplacental unit, in interaction with laboratory findings and overall perinatal outcome.

**Hypothesis:** Antihypertensive therapy in pregnancy is expected to influence the ultrasonography, Doppler ultrasonography, biochemistry and biophysical parameters of fetoplacental circulation and perinatal outcome, depending on the antihypertensive used (methyldopa, nifedipine).

**Aims:** To assess the effects of antihypertensives used on ultrasonography, Doppler ultrasonography and biophysical parameters of fetoplacental circulation. To assess the effects of antihypertensive therapy on blood and urine biochemistry parameters. To assess the effects of antihypertensive therapy on overall maternal and neonatal outcome. To assess which of the two antihypertensives used has better effect on the maternal and neonatal hemodynamic and biophysical parameters.

**Materials and methods:** The study will include more than 100 pregnant women, while the exact number of study women will be determined upon statistical processing of the data obtained. The

study women have been diagnosed with monosymptomatic gestational hypertension, free from proteinuria or target organ lesions. Fetal biometry will be monitored by ultrasonography, whereas uterine artery, umbilical artery, middle cerebral artery, fetal descending aorta, and ductus venosus and/or inferior vena cava circulation will be measured by Doppler ultrasonography. The women included in the study will be randomized into two groups according to the antihypertensive used (methyldopa, nifedipine).

**Expected scientific contribution:** The study will show the effect of treatment for gestational hypertension with the antihypertensives used on ultrasonography, Doppler ultrasonography and biophysical parameters of fetoplacental circulation, maternal blood and urine biochemical parameters, and perinatal outcome. The new knowledge thus acquired will contribute to reducing maternal, fetal and neonatal morbidity and mortality, all this aiming at achieving the best possible perinatal outcome and preventing the sequels of hypertensive disease in pregnancy.

**Acknowledgments:** I would like to thank the mentor Professor Dubravko Habek, MD, PhD, and Maja Predojević, MD who helped me in the preparation of studies and data collection in the study.

**MeSH/Keywords:** hypertension, pregnancy, antihypertensive therapy, ultrasonography, Doppler ultrasonography

**Poster code:** B-5-66

## POSTER TITLE: CHARACTERISTICS OF GASTRIC MYOELECTRICAL ACTIVITY IN PREGNANCY

**PhD candidate:** Damir Zudenigo, MD, MSc, specialist of obstetrics and gynecology, primarius

**Part of the thesis:** Measurement of Gastric Myoelectrical Activity in Pregnant Women

**Mentor/s:** Professor Dubravko Habek, MD, PhD, professor Dragan Jurčić, MD, PhD

**Affiliation:** Department of obstetrics and gynecology, Department of internal medicine, Hospital

**Introduction:** Electrogastrography is a non-invasive technique for recording gastric myoelectrical activity. Koch and coworkers measured gastric myoelectrical activity in 32 women with nausea during the first trimester of pregnancy and found gastric dysrhythmias in 26 women. Riezzo and coworkers studied gastric electrical activity during the first trimester of pregnancy and two months after voluntary interruption of pregnancy (VIP) in nine women with nausea and vomiting. They found that coefficient of variation of gastric frequency during pregnancy was significantly higher than after VIP. Walsh and coworkers measured gastric myoelectrical activity in eight pregnant women with first-trimester nausea and found that gastric dysrhythmias in such pregnancies may be due to a combination of elevated progesterone and estrogen levels. However, in review of available literature, we didn't find publications about the characteristics of gastric myoelectrical activity in normal pregnancy.

**Hypothesis:** Pregnancy is hormonally stimulated state in which placenta produces great amounts of estrogen and progesterone. It is known that progesterone reduces excitability of smooth muscle cells. Therefore we can expect that gastric myoelectrical activity in pregnancy will be changed.

**Aims:** To investigate possible differences in gastric myoelectrical activity between pregnant women with normal intrauterine pregnancy and nonpregnant women and possible changes of gastric myoelectrical activity throughout pregnancy.

**Materials and methods:** Study group: 60 women with normal intrauterine pregnancy, Control group: 60 healthy nonpregnant women. Gastric myoelectrical activity will be measured by cutaneous electrogastrography (POLYGRAM NET, MEDTRONIC). Next electrogastrographic parameters will be analyzed: dominant frequency, percent of dominant frequency in normal range, coefficient of the variation of dominant frequency, dominant power, postprandial power ratio, bradygastria, tachygastria and frequency of the duodeno-respiratory range.

**Expected scientific contribution:** We expect that collected data and results will contribute to better understanding of the physiology and pathophysiology of gastric motility in pregnancy.

**Acknowledgments:** I wish to thank to prof. Habek and prof. Jurčić for past support in preparing of my thesis-

**MeSH/Keywords:** electrogastrography, pregnancy

**Poster code:** B-5-79

## POSTER TITLE: QUALITY OF LIFE AFTER „SLING“ OPERATION

**PhD candidate:** Damir Hodžić, MD, MSc

**Part of the thesis:** Quality of Life in Female Patients After „Sling“ Operation for Stress Urinary Incontinence

**Mentor/s:** Professor Slavko Orešković, MD, PhD

**Affiliation:** Clinical Hospital „Mercur“, Dept.of Obstetrics and Gynecology

**Introduction:** Stress urinary incontinence (SUI) is involuntary discharge of urine caused by the congenital or acquired defect of pelvic organs static with loss of vesicourethral anatomic support. The diagnosis of SUI can be set by the history, because patients referred incontinence in sneezing, coughing, running or similar physical straining, which significantly reduces their quality of life and ability to work.

**Hypothesis:** The „sling“ operation using polypropylene tape or mesh in patients with SUI is a minimally invasive method with a rare post-operative complications and shorter hospitalization compared with conventional surgery. The „sling“ method allows a successful anatomical and functional reconstruction of the anterior vaginal wall and significantly improves the quality of life.

**Aims:** 1. Evaluate the effectiveness of „sling“ method based on Pelvic organ prolapse quantification (POP-Q) system. 2. Compare the quality of life of patients before and after „sling“ operation based on subjective assessments using standard questionnaires. 3. Evaluate the success of „sling“ method through the observed period and possible complications in comparison to patients operated by conventional surgery.

**Materials and methods:** The research will include a minimum of 50 patients treated by „sling“ method, and an equal number of patients operated by conventional anterior vaginal wall repair. All patients will preoperatively make assessment of defect anterior vaginal wall by POP-Q system and fill in two customized questionnaires (PFDI-20 and PFIQ-7) which include questions about the quality of life until the past 3 months before operation. The collection of clinical data and the responses from the questionnaire will continue to be 3, 6 and 12 months after surgery, and will also record any perioperative or late complications.

**Expected scientific contribution:** Surgical treatment of SUI by „sling“ operation is mainly presented as a successful and body integrity preserving method with a low rate of complications. Expected scientific contribution of this study is to evaluate the specific impact of the „sling“ operation on the quality of life in patients with SUI compared with patients operated by conventional surgery.

**Acknowledgments:**

**MeSH/Keywords:** stress urinary incontinence, sling, quality of life

**Poster code:** B-5-97

## POSTER TITLE: THE INFLUENCE OF TOBACCO SMOKE UPON BIOCHEMICAL CHANGES IN CERVICAL MUCUS OF WOMEN IN REPRODUCTIVE AGE

**PhD candidate:** Gordana Planinić Radoš, MD

**Part of the thesis:** Easily reachable material (cervical mucus) can provide useful information about the female genital tract.

**Mentor/s:** Assist. Prof. Tomislav Čanić, MD

**Affiliation:** University Hospital Merkur, Zagreb, Croatia

**Introduction:** Tobacco smoke contains 4000 different compounds, many of which are harmful, teratogenic or carcinogenic. These compounds can have an especially serious effect in women in reproductive age. In this context, the current thesis is an addition to study of the effects of smoking on female genital tract. We will focus on effects of smoking on cervical mucus obtained by common, non-invasive procedure of Papanicolaou smear. In cervical mucus obtained by this method levels of certain molecules, usually assessed from blood, will be established and compared between smoking and nonsmoking women.

**Hypothesis:** We expect to define effects of tobacco smoke on the health of female reproductive tract by studying certain biochemical parameters of cervical mucus.

**Aims:** The aim of the study is to confirm harmful effects of tobacco smoke on women's health by examining levels of different elements in cervical mucus, such as vitamin C. Furthermore, knowing that tobacco smoke contains cyanide, we will establish its levels in cervical mucus and determine if the detoxification of this compound occurs in the genital tract. Smoke contains many harmful oxidative substances such as free radicals, which damage mitochondrial function of cellular structures as well as cervical epithelial cells. We will examine the activity of cytochrome oxidase, a mitochondrial enzyme. Determining the total protein and vitamin C levels, the concentrations

of thiocyanate SCN, cytochrome P450, activity of cytochrome c oxidase and rhodanese, lipid peroxidation and total antioxidant capacity, we will identify differences in the cervical mucus of smoking and nonsmoking women.

**Materials and methods:** 120 women in child-bearing age from 18 to 45 years of life will be included. Subjects will be divided into three groups: non-smokers, light smokers (up to 10 cigarettes a day) and heavy smokers (10 or more cigarettes a day). As a part of the routine gynecologic examination, a cervical mucus sample will be taken and sent to the laboratory. Samples will be stored in a test tube containing 2 ml of phosphate buffer 7.5 to achieve maximum solubility. Homogenized samples will be centrifuged to separate organelles which will be submitted to further processing.

**Expected scientific contribution:** We expect the research to show that easily reachable material (cervical mucus) can provide useful information about the female genital tract. We wish to determine whether the cervical mucus of women smokers may identify some indicators that used to be measured in blood or urine.

**Acknowledgments:**

**MeSH/Keywords:** cervical mucus, smoke, biochemical, cytochrome oxidase, cytochrome P450, cytochrome c oxidase, rhodanese

**Poster code:** B-5-101

# POSTER TITLE: IMPACT OF OBESITY ON THE INFERTILITY OF KOSOVO WOMEN - ASSESSMENT OF OVARIAN RESERVE

**PhD candidate:** Albert Lila, MD

**Part of the thesis:** Impact of obesity on the infertility of kosovo women - Assessment of ovarian reserve

**Mentor/s:** Prof.Dr. Velimir Simunic

**Affiliation:** Prof.Dr. Shefqet Lulaj

**Introduction:** The obesity in women reduces fertility by 20% and the increasing incidence of infertility even up to 33% - two times higher than in women with a normal BMI. Overweight women, as distinct from obese women, are known to be at a higher risk of menstrual dysfunction and anovulation. The mechanisms by which obesity causes or exacerbates sub-fertility are manifold, one suggested theory that hyperandrogenemia results in granulosa cell apoptosis, while peripheral conversion of androgens to estrogen in adipose tissue inhibits gonadotrophin secretion, or possibly due to altered secretion of pulsatile GnRH

**Hypothesis:** 1. Are markers of ovarian reserve disturbed more frequently in overweight and obese group of infertile women? 2. Assessing the diagnostic validity of the specified hormonal markers and ultrasound findings, as well as their combinations, will simplify ovarian reserve assessment standards and procedures.

**Aims:** To assess and compare the two experimental groups/cohorts (first group/cohort with BMI 25-29,9 kg/m<sup>2</sup> and second group/cohort with BMI  $\geq$  30 kg/m<sup>2</sup>) and control group/cohort (with BMI 18-24.9 kg/m<sup>2</sup>), changes in the values of hormones levels of FSH, LH, Estradiol, Progesterone, Testosterone, SHBG, AMH, TSH,

HbA1c, AFC and ovarian volume, on the third day of menstrual cycle in infertile women of Kosovo.

**Materials and methods:** Study Type: Observational, Study Design: Observational, Model: Case Control, Parallel design, Time Perspective: Prospective. The diagnostic performance of tests used as primary outcomes will be evaluated using Receiver Operating Characteristic (ROC) curve analysis. Results will be expressed through Odds Ratio with confidence interval 95% (95% CI). For statistical significance, the value of the factor alpha is  $\leq$  0.05.

**Expected scientific contribution:** This study, which will take place in Kosovo with Kosovo women, will contribute to further professional discussion about the correlation and the level of impact of overweight and obesity on ovarian reserve, simplifying and developing „golden standards“ to assess ovarian reserve, specifically in overweight and obese infertile women.

**Acknowledgments:** Prof. Simunic, Lulaj and Gesitovel, Kosovo Occupational Health Institute and FATI IM private clinic

**MeSH/Keywords:** obesity, ovarian reserve, hormonal status

**Poster code:** B-5-145

## POSTER TITLE: CLINICAL SIGNIFICANCE OF SENTINEL LYMPH NODE DETECTION IN FIGO STAGES IA2 - IIA1 OF CERVICAL CANCER

**PhD candidate:** Pavao Planinić

**Part of the thesis:** Role of sentinel lymph node detection and biopsy in FIGO stages IA2 - IIA1 of cervical cancer

**Mentor/s:** Professor Ante Ćorušić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb, Department of Gynecologic Oncology

**Introduction:** Cervical cancer is the second most common cancer among women worldwide. Treatment of early stage cervical cancer (FIGO IA - IIA1) is primarily surgical. Lymph node metastasis is one of the most important prognostic factors in patients with early cervical cancer. We do not have a good method for evaluation of pelvic lymph nodes, which is why we do a complete pelvic lymphadenectomy in every patient. Sentinel lymph node (SLN) detection and biopsy could help us in assessing the status of the pelvic lymph nodes.

**Hypothesis:** Our hypothesis is that SLN detection and biopsy can predict the possibility and frequency of metastases in the regional lymph nodes in in FIGO stages IA2 - IIA1 of cervical cancer.

**Aims:** To determine the locations of SLN in cervical cancer FIGO stages IA2 - IIA1. To determine the success of detecting SLN in cervical cancer FIGO stages IA2 - IIA1 by application of methylene blue. Determine diagnostic value of SLN biopsy in assessing the status of the regional lymph nodes.

**Materials and methods:** This prospective study will include at least 40 patients diagnosed with cervical cancer FIGO stage IA2 - IIA1, hospitalized in the Department of Gynecologic Oncology, KBC Zagreb, in the next 2 - 3 years. All patients will receive standard preoperative diag-

nostic evaluation. After induction of anesthesia, 8ml of diluted methylene blue (2ml methylene blue 6ml normal saline) is injected in the operating room at 4 quadrants of the cervix and at 4 quadrants of the transition of the cervix to vaginal fornices. After the application of methylene blue, the surgery is performed. Intraoperatively, SLN are identified as being blue. First we determine their location and then we excise them and send them separately for pathophysiological analysis. Afterwards, in all patients, systematic pelvic lymphadenectomy and radical hysterectomy (or trachelectomy) will be performed.

**Expected scientific contribution:** In patients with cervical cancer, lymph node metastasis is the most important prognostic factor for recurrence and death and is a major determinant of treatment. The standard surgical lymph node assessment in early cervical cancer (FIGO stage IA2 - IIA1) is systemic pelvic lymphadenectomy, which is associated with significant short and long-term morbidity. With use of SLN biopsy in patients with cervical cancer we can avoid a complete pelvic lymphadenectomy and its associated complications.

**Acknowledgments:**

**MeSH/Keywords:** sentinel lymph node biopsy, cervical cancer

**Poster code:** B-5-151

## POSTER TITLE: THE IMPACT OF PRE-HOSPITAL EMERGENCY CARE ON OUTCOME IN PATIENTS WITH ACUTE CORONARY SYNDROME

**PhD candidate:** Musli Gashi MD

**Part of the thesis:** The impact of pre-hospital emergency care on outcome in patients with acute coronary syndrome

**Mentor/s:** Associate Professor Vesna Degoricija, MD, PhD, Associate Professor Gani Bajraktari, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Clinical Center of Kosova

**Introduction:** Most deaths from Acute Coronary Syndrome (ACS) occur in the first few hours after the onset of symptoms, mainly from fatal arrhythmias which could be prevented by rapid access to specialized care. Recent studies have demonstrated the effectiveness of Pre-Hospital Emergency in reducing the time between onset of symptoms, diagnosis and beginning of treatment, as well as in reducing mortality in ACS patients.

**Hypothesis:** Implementation of pre-hospital and hospital emergency care will improve outcome of patients admitted to hospital with Acute Coronary Syndrome.

**Aims:** The general aim of this thesis is to evaluate the impact of pre-hospital and hospital emergency care in the management and prognosis of patients admitted to the hospital with acute coronary syndrome. Specific aims are to analyze the outcome of ACS patients admitted to emergency department through pre-hospital emergency care or by self arranged transportation, to illustrate the importance of time in minutes between the onset of symptoms as reported by the patient and admission to the hospital, between the onset of symptoms and the first ECG and between entering the emergency department and the beginning of the therapy.

**Materials and methods:** Observational prospective clinical study included all cases of ACS

patients (defined in accordance with the criteria of the 2000 consensus document „Myocardial Infarction redefined“ of the ESC/ACC Joint Committee) admitted to emergency department of University Clinical Center of Kosova between January 1, 2011 and December 31, 2012. The patients were divided in two different groups: firstly according to the way of admission to the hospital (through pre-hospital emergency care or by self arranged transportation) and secondly by the clinical presentation of ACS, e.g. unstable angina, non-ST-elevation acute myocardial infarction (NSTEMI) and ST-elevation acute myocardial infarction (STEMI).

**Expected scientific contribution:** The performance of the Kosova emergency system for the acute treatment of ACS patients has not been thoroughly studied. Emergency medicine, a field relatively new to even the most developed societies, is in its infancy in Kosova. It is expected to find specific outcome of patients with ACS in studied population, and prognostic factors connected with worse outcome.

**Acknowledgments:** I would like to thank School of Medicine, University of Zagreb and University Clinical Centre of Kosova for support.

**MeSH/Keywords:** Acute Coronary Syndrome, Emergency Department

**Poster code:** B-6-99



## POSTER TITLE: CHEMOKINES IN CENTRAL NERVOUS SYSTEM DISEASES IN CHILDREN

**PhD candidate:** Lorna Stemberger, MD

**Part of the thesis:** Chemokines CXCL10, CXCL11 And CXCL13 In Aseptic Meningitis, Neuroborreliosis And Acute Disseminated Encephalomyelitis

**Mentor/s:** Goran Tešović, MD, PhD, Assistant Professor, Snježana Židovec Lepej, mag.mol.biol., PhD

**Affiliation:** University Hospital for Infectious Diseases „Dr.Fran Mihaljević”

**Introduction:** Chemokines are low molecular weight basic proinflammatory proteins implicated in a variety of diseases within the central nervous system. They play important role in host defense by attracting and activating leukocytes thus modifying process of microbial invasion and have been associated with acute and chronic inflammation as well as with immunologically mediated diseases.

**Hypothesis:** Concentrations of chemokines CXCL10, CXCL11 and CXCL13 in cerebrospinal fluid and sera of patients with aseptic meningitis (AM), neuroborreliosis (NB) and acute disseminated encephalomyelitis (ADEM) differ between themselves and in comparison to group of patients without inflammatory process in CNS. There is a „cut off” value of particular or combination of chemokines which could serve in rapid classification of these diagnoses before definitive diagnosis.

**Aims:** The aim of this study is to help in revealing the importance of chemokines CXCL10, CXCL11 and CXCL13 in pathogenesis of AM, NB and ADEM in children. 1. To determine whether there is a concentration gradient of these chemokines between cerebrospinal fluid and sera. 2. To determine if these concentration gradients differ between themselves and in comparison to the control group. 3. To find a „cut off” value of particular or combination of chemokines which could serve in rapid clas-

sification of these diagnoses before definitive diagnosis.

**Materials and methods:** About 70 patients, 20 with diagnosis of AM, 20 with ADEM, 15 with NB and 15 without inflammatory process in CNS will be included in study. In control group lumbar puncture was made as a routine protocol because of strong clinical suspicion of inflammatory CNS process, which is later excluded. Inclusion criterions were age younger than 18 years and definite clinical/laboratory/radiologic diagnosis of AM, NB and ADEM. To all of these patients lumbar puncture was made in first 24 hours after admission and 1ml of CSF and 2ml of blood was taken to determine chemokine concentration with quantitative enzyme immunoassay and bead-based flow cytometry.

**Expected scientific contribution:** Data on role of these cytokines is very deficient and to the best of our knowledge there is no study which connects and compares them. Our study will enrich existing knowledge about these cytokines in inflammatory CNS diseases. If we find „cut-off value” which could sort these diseases, clinical use will be also possible in future.

**Acknowledgments:**

**MeSH/Keywords:** aseptic meningitis, neuroborreliosis, acute disseminated encephalomyelitis, chemokines CXCL10, CXCL11, CXCL13

**Poster code:** B-7-35

## POSTER TITLE: EPIDEMIOLOGY OF INVASIVE ASPERGILLOSIS IN PATIENTS WITH MALIGNANT HEMATOLOGIC DISEASES

**PhD candidate:** Alen Ostojić, MD

**Part of the thesis:** Epidemiology of Invasive Aspergillosis in Patients with Malignant Hematologic Diseases

**Mentor/s:** Assoc. Professor Radovan Vrhovac, MD, PhD, Assoc. Professor Zdeněk Ráčil, MD, PhD

**Affiliation:** University Hospital Center Zagreb, Department of Internal Medicine, Division of Hematology, Zagreb, Croatia

**Introduction:** Invasive aspergillosis (IA) is an important cause of morbidity and mortality in immunocompromised patients - nowadays a significant, ever growing and heterogenous patient population. Due to the nature of disease and its treatment, patients with malignant hematologic diseases are at highest risk for development of IA. Among them, the ones with acute myeloid leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia/lymphoma treated with intensive chemotherapy, and those undergoing allogeneic hematopoietic stem cell transplantation (HSCT), are the most prone to develop IA (group at high risk). The incidence of IA and IA-related mortality is varying between different studies mostly because of different criteria used to establish diagnosis of IA. In 2008 the European Organization for Research and Treatment of Cancer and the National Institute of Allergy and Infectious Diseases (EORTC/MSG) Consensus Group published revised criteria for diagnosis of IA (De Pauw B et al.). Although those criteria are nowadays being increasingly used in clinical practice, precise data on epidemiology of IA in certain patient subgroups as well as the specific influence of relevant factors to IA related morbidity and mortality are still lacking.

**Hypothesis:** Use of EORTC/MSG 2008 diagnostic criteria for IA changes currently available epidemiologic data on IA among patients with malignant hematologic diseases and those undergoing HSCT.

**Aims:** Aims of this observational study are to determine incidence of IA among patients with malignant hematologic diseases and those undergoing HSCT, and to examine risk factors for IA in group of patients at high risk. Also, occurrence of certain entities of IA will be examined in relation with characteristics of underlying disease, type of immunosuppression, applied prophylaxis and measures of isolation.

**Materials and methods:** Incidence of IA will be evaluated by analyzing Fungal Infection Database (FIND) international registry. Based on EORTC/MSG criteria, incidence of probable and proven IA will be determined. In two-year period or until inclusion of 300 neutropenic episodes, clinical, laboratory, microbiological and radiological data will be collected in consecutive patients and risk factors for IA development will be evaluated.

**Expected scientific contribution:** The study will provide valuable epidemiologic data of IA based on standardized diagnostic criteria. Establishing risk stratification of patients will facilitate development of strategies for diagnosis, prevention and treatment of IA.

**Acknowledgments:**

**MeSH/Keywords:** Invasive Aspergillosis, Epidemiology, Hematologic Neoplasms, Hematopoietic Stem Cell Transplantation

**Poster code:** B-7-72

## POSTER TITLE: THE ROLE OF CYTOKINES IN PROSTATITIS SYNDROME PATIENTS

**PhD candidate:** Adela Kolumbić Lakoš, MD

**Part of the thesis:** The Research of Proinflammatory and Antiinflammatory Cytokines in Prostatitis Syndrome Patients

**Mentor/s:** Višnja Škerk, Professor, MD, PhD

**Affiliation:** University Hospital for Infection Diseases „Dr. Fran Mihaljević“, PLIVA Croatia

**Introduction:** In the available literature we find a limited number of studies which measured levels of cytokines in different samples in patients with prostatitis syndrome (SP). Cytokines are small soluble proteins secreted by immune and inflammatory cells. They have a key role in inflammatory reactions and immune response. Actual NIH classifications distinguish SP into IV categories. According to the NIH classification leukocytes, which are considered traditional markers of inflammation, are not a reliable diagnostic parameter. Taking into consideration that cytokines are secreted and act locally, and can be found in the secretions of the prostate, inflammatory markers such as cytokines have been increasingly studied in order to define their role. The imbalance of pro-and anti-inflammatory cytokines may partly determine the symptoms and outcome of the inflammatory process in SP. This research, which will measure pro-inflammatory cytokines IL-6, IL-8, IL-17 and anti-inflammatory cytokine TGF- $\beta$ , aims to provide new insights on the role of cytokines in patients with SP.

**Hypothesis:** The levels of pro-inflammatory cytokines (IL-6, IL-8, IL-17) and anti-inflammatory cytokine (TGF- $\beta$ ) are higher in patients with chronic bacterial prostatitis and inflammatory form of chronic pelvic pain syndrome compared with patients with non-inflammatory chronic pelvic pain syndrome.

**Aims:** To investigate the levels of proinflammatory and anti-inflammatory cytokines in patients with chronic bacterial prostatitis, inflammatory and non-inflammatory form of chronic pelvic pain syndrome.

**Materials and methods:** Approximately 100 patients will be enrolled in this prospective study. Inclusion criteria: men older than 18 years with chronic prostatitis syndrome confirmed according to NIH criteria. Exclusion criteria: excluded anatomical and functional abnormalities as well as abscess and prostate cancer. The methodology involves detailed history, clinical status, fulfilling the NIH-CPSI questionnaire, digital-rectal examination, US of urogenital tract, the PSA test, „four glasses test“, biochemical and microbiological examination of urine and EPS. Cytokines will be determined in EPS and/or VB3 with ELISA.

**Expected scientific contribution:** New insights on cytokine levels in patients with SP and its potential benefit in differentiating various types of SP in conjunction with other diagnostic methods.

**Acknowledgments:** We thank the National Foundation for Science for funding the project.

**MeSH/Keywords:** prostatitis, cytokines

**Poster code:** B-7-121

## POSTER TITLE: THE ROLE OF SEMEN MICROBIOLOGICAL DIAGNOSTICS IN THE DIAGNOSIS OF CHRONIC PROSTATITIS SYNDROME

**PhD candidate:** Dražen Kovačić, MD

**Part of the thesis:** Rational diagnosis of the chronic prostatitis syndrome

**Mentor/s:** Professor Višnja Škerk, MD, PhD

**Affiliation:** University Hospital for Infectious Diseases (UHID) - Zagreb, Medical Affairs - PLIVA Croatia

**Introduction:** Prostatitis syndrome (PS) is heterogeneous and complex disorder so knowledge about its etiology, diagnosis and therapy is constantly reviewed. Today's standard for research is a classification system approved by a NIH-NIDDK workshop committee in 1999 which divide PS into four categories: Category I Acute Bacterial Prostatitis (ABP), Category II Chronic Bacterial Prostatitis (CBP), Category III Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) and Category IV Asymptomatic Inflammatory Prostatitis (AIP). To differentiate CBP from an abacterial form of PS i.e. CP/CPPS, traditional Meares and Stamey method of four-glass test are used for segmented analysis of urine and expressed prostatic secretions (EPS) specimens. This method is as standard recommended by European association of urology (EAU). Some authors offered method of two-glass test (synonym is pre-massage and post-massage two-glass test) as simplified procedure. As it is often suggested that these segmented tests do not display sufficient sensitivity, some authors have proposed the usefulness of adding semen analysis to a standard four-glass test (five-glass test) for the detection of prostatic pathogens. However, there are few published studies about semen analysis in PS, and these with controversial results.

**Hypothesis:** Microbiological analysis of semen on traditional pathogens improves diagnosis of chronic prostatitis syndrome.

**Aims:** To find if adding microbiological analysis of semen on traditional pathogens to a standard four-glass test improves sensitivity of chronic prostatitis syndrome diagnosis.

**Materials and methods:** We plan to prospectively examine over 100 men 18 years of age and older with signs and symptoms of chronic prostatitis syndrome. All patients will be routinely subjected to the four-glass test, followed by semen culture and analysis on traditional pathogens. Two diagnostic scenarios will be used to compare relative sensitivity of four-glass test with a five-glass test where each patient will be control to himself.

**Expected scientific contribution:** Significant contribution to the knowledge about rational diagnosis of chronic prostatitis syndrome, since research in this area is scarce with controversial results.

**Acknowledgments:** We are indebted to all patients included in this study. We thank Croatian Science Foundation for funding the project

**MeSH/Keywords:** prostatitis syndrome, microbiological diagnosis, traditional pathogens, four-glass test, two-glass test, five-glass test, semen analysis

**Poster code:** B-7-153

## **POSTER TITLE: INCIDENCE AND SIGNIFICANCE OF T. VAGINALIS IN PATIENTS WITH CHRONIC PROSTATITIS SYNDROME**

**PhD candidate:** Martina Vargović

**Part of the thesis:** Incidence and significance of *T. vaginalis* in patients with chronic prostatitis syndrome

**Mentor/s:** Višnja Škerk, MD, PhD, Professor

**Affiliation:** University Hospital for Infectious Diseases „Dr.Fran Mihaljević“

**Introduction:** *Trichomonas vaginalis* (TV) is a protozoa that can cause prostatitis, balanitis, epididymitis and infertility, and has been linked to prostate cancer. In the available literature there is a lack of clinical studies which investigate TV as a cause of chronic prostatitis syndrome (CPS). Data from the National Center for Health Statistics in the USA showed that CPS associated symptoms account for 25 % of urologic outpatient visits. Data on the prevalence of TV as a cause of CPS are scarce, due mostly to the fact that up to 70% of infected men are asymptomatic. In several epidemiologic studies in Croatia TV has been isolated from patients with CPS in 8.66-10.50 % cases.

**Hypothesis:** TV is one of the causative organisms in CPS. With appropriate antimicrobial therapy eradication of the microorganism and clinical improvement can be achieved in patients with CPS.

**Aims:** To determine the prevalence of TV isolates in patients with CPS and the efficacy of the chosen therapeutic regimen in a selected patient group. To determine the most favorable protocol for sample collection with regards to sensitivity and specificity both in diagnostic evaluation and the evaluation of treatment success.

**Materials and methods:** Between 110 - 140 adult patients with at least one symptom of CPS will

be included in the study. Patients with an acute infection, symptoms lasting under three months, a previous surgical intervention and those receiving antimicrobial therapy will be excluded. All patients will fill out the NIH-CPSI questionnaire. Three urine samples (voided bladder 1,2 and 3), an expressed prostatic secretion and an ejaculate sample will be taken and tested per study protocol (Leucocyte count, bacterial cultures, microscopic evaluation and antimicrobial susceptibility). When indicated antimicrobial therapy will be given in accordance with current NIH guidelines. Efficacy of treatment will be assessed clinically by the NIH-CPSI questionnaire 6 weeks and 6 months after treatment, and antimicrobial efficacy (eradication) by repeat sampling at those time intervals.

**Expected scientific contribution:** To supplement existing data on the epidemiology, diagnostic testing and treatment of CPS. Currently available data on these subjects is very limited. Results of this study could be helpful in creating diagnostic and therapeutic guidelines for CPS.

**Acknowledgments:**

**MeSH/Keywords:** chronic prostatitis syndrome, prostatitis, prostatitis epidemiology, prostatitis treatment, *Trichomonas vaginalis*

**Poster code:** B-7-157

## POSTER TITLE: PROGNOSTIC VALUE OF LACTATE CLEARANCE AND CENTRAL VENOUS BLOOD OXYGEN SATURATION

**PhD candidate:** Ivan Tomić, M.D.

**Part of the thesis:** Prognostic value of lactate clearance and central venous blood oxygen saturation for in-hospital outcome in mechanically ventilated patients

**Mentor/s:** prof.dr.sc.Vladimir Gašparović

**Affiliation:** none

**Introduction:** Respiratory insufficiency is a common reason for admitting patients in intensive care units. Often these patients require mechanical ventilation. The outcome of these patients depends on the initial cause of respiratory failure but also depends on medical care procedures. The degree of respiratory insufficiency and care efficiency are measured by parameters such as lactate clearance (LC) and central venous blood oxygen saturation (ScvO<sub>2</sub>). Lactate is indicator of tissue oxygenation, and ScvO<sub>2</sub> is indicator of the ratio of oxygen consumption and delivery. In the literature currently is being intensively discussed about CL and ScvO<sub>2</sub> in severely ill patients as predictors of poor outcome and/or target parameters of resuscitation with a lot of conflicting study results and reviews.

**Hypothesis:** Positive lactate clearance in arterial blood (a decrease of at least 10% between two consecutive measurements) and the central venous blood oxygen saturation above 70% within the first 24 hours of mechanical ventilation are predictors of a positive outcome.

**Aims:** The aim of this study is to determine the prognostic value of the lactate clearance and ScvO<sub>2</sub> for in-hospital outcome in mechanically ventilated patients.

**Materials and methods:** The study will include patients (n 248) with respiratory failure requiring mechanical ventilation. Blood samples

(central venous and arterial blood) will be taken seven times in the first 24 hours of mechanical ventilation (shortly before starting mechanical ventilation, shortly after mechanical ventilation, then after 2, 4 and 6 hours and the other 2 according to the local protocol. Lactate clearance is defined as the difference in lactate concentration between two consecutive measurements. It can be positive or negative. Positive means that the lactate in the blood decreases with time. Statistically significant lactate clearance is if a change in the concentration of lactate is at least 10% compared to the previous measurement, either in a positive or negative direction. The study will determine the predictive value of the overall trend of lactate clearance from the first to the seventh measurement, and predictive value of lactate clearance between any two consecutive measurements within the first 6 hours of mechanical ventilation.

**Expected scientific contribution:** The predictive value of lactate clearance and ScvO<sub>2</sub> for in-hospital outcome in mechanically ventilated patients. Equivalence or complementarity of lactate clearance and ScvO<sub>2</sub> for in-hospital outcome in mechanically ventilated patients.

**Acknowledgments:** none

**MeSH/Keywords:** respiratory insufficiency, lactate clearance, central venous blood oxygen saturation

**Poster code:** B-8-175

## **POSTER TITLE: VALUE OF T-WAVE ALTERNANS IN DIAGNOSTICS OF ISCHEMIC HEART DISEASE**

**PhD candidate:** Mislav Puljević

**Part of the thesis:** T-wave Alternans in Ischemia

**Mentor/s:** Professor Aleksander Ernst, MD, PhD

**Affiliation:** University Hospital Centre Zagreb - Clinical Department for Cardiovascular Diseases, University of Zagreb School of Medicine

**Introduction:** T wave alternans is a periodic beat-to-beat variation in the amplitude or shape of the T wave in an ECG. It is assumed that alternans T-wave is caused by ischemia which makes changes in the configuration and duration of action potential and dispersion of repolarisation. Reason for that could be changes in the intracellular traffic of calcium. Stress test, which is a standard method, has the specificity and sensitivity 0.7 and 0.6.

**Hypothesis:** T-alternans is more specific and more sensitive method for the diagnosing angina pectoris than classic stress test.

**Aims:** We will establish the connection of origin of T-alternans and degree of myocardial ischemia.

**Materials and methods:** Patients with angina pectoris will be included. Exclusion criteria are

atrial fibrillation and low systolic function of left heart ventricle. All patients will undergo classic stress testing and T-alternans test, and then the presence of ischemic heart disease will be verified with coronary angiography.

**Expected scientific contribution:** With this investigation we should be able to verify correlation of origin of T-alternans and ischemia and if the hypothesis appears to be true, we could get more specific and sensitive method for early ischemic heart disease diagnosing.

**Acknowledgments:**

**MeSH/Keywords:** t-alternans, ischemia, angina pectoris

**Poster code:** B-9-177

## **POSTER TITLE: EFFECTS OF POLYPHENOLS FROM GRAPE SEEDS EXTRACT ON BLOOD PRESSURE AND ENDOTHELIAL FUNCTION ON PREHYPERTENSIVE**

**PhD candidate:** Ana Vrdoljak, M.D.

**Part of the thesis:** Pressure and endothelial function on prehypertensive subjects.

**Mentor/s:** prof. dr. sc. Bojan Jelaković

**Affiliation:** University hospital centre Zagreb

**Introduction:** It is generally accepted that hypertension cannot be cured and patients must receive life-long antihypertensive treatment. However the THROPHY study suggested that early treatment of prehypertension may postpone or prevent the development of hypertension. Approximately 37% adults are prehypertensive (BP 130-139/85-89). Clearly current strategies have failed and new strategies are needed. We believe that dietary supplementations are more acceptable to general population and that a wider use of polyphenols isolated from grape seeds extract (GSE) might have a potential salutary effect.

**Hypothesis:** Highly purified polyphenols lower blood pressure in prehypertensive subjects and have a beneficial effect on endothelial function.

**Aims:** To analyse effect of GSE on BP using continuous measurement of arterial pressure. To determine the effect of GSE on BP after 6 months of intake (placebo controlled). Design of study predicts the cross-over study after 6 months which will show whether GSE has a prolonged effect on BP and can it work after 1 month of usage in placebo group. To determine effect of GSE on insulin resistance and other classic risk factors: inflammation and endothelial function.

**Materials and methods:** The examinees: healthy male, non-smoker age 30-40, with BMI 30-40 and BP 130-139/85-89 mmHg. Exclusion criteria: female, age, BP values and BMI outside given parameters, any chronic illness, smoking, taking any prescribed or OTC drug. They will be enrolled by measuring BP 3 times with automatic blood pressure monitor. If average meets prehypertension values other tests will be performed. Day 0: general questionnaire, blood tests (CBC, creatinin, serum lipides, hsCRP, ELISA for VCAM, ICAM, IL-6, albuminuria), CBPM is set. Day 1: participant brings 24h urine sample, returns CBPM and is given GSE or placebo, regarding randomisation number. Day 30: BP control. Day 90: BP control. Day 180: all tests from day 0 will be repeated. Participant will be given capsules from opposite arm of the study. Day 210: all tests from day 0 will be repeated.

**Expected scientific contribution:** To determine the effectiveness of GSE on BP and endothelial function in prehypertensive subjects.

**Acknowledgments:** mentor prof. dr.sc. Bojan Jelaković, prof. dr.sc. Stevo Julius

**MeSH/Keywords:** prehypertension, polyphenols, metabolic syndrome

**Poster code:** B-9-19



## POSTER TITLE: INTRINSIC INSULIN RESISTANCE AMONG NONDIABETICS AND OCCURRENCE OF HYPERGLYCEMIA IN CRITICAL ILLNESS

**PhD candidate:** Edita Lukić

**Part of the thesis:** The association between intrinsic insulin resistance and occurrence of hyperglycemia in critical illness among patients without apparent glucose metabolism disorder

**Mentor/s:** doc.dr.sc. Ivan Gornik

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** Insulin resistance is characterized by the absence of physiologic response of peripheral tissues to insulin action. It plays a major pathophysiological role in type 2 diabetes and it is tightly associated with major public health problems, including obesity, coronary artery disease and metabolic syndrome. Critical illness or injury can lead to hyperglycemia, insulin resistance and glucose metabolism disorder. Patients without apparent glucose metabolism disorder who had hyperglycemia in critical illness have increased risk for the onset of type 2 diabetes mellitus or impaired glucose metabolism (IFG or IGT).

**Hypothesis:** The occurrence of hyperglycemia in critical illness is associated with intrinsically increased insulin resistance among patients without apparent glucose metabolism disorder.

**Aims:** The aim of this study is to explore the association between patients characteristics, intrinsic insulin resistance, critical illness and occurrence of hyperglycaemia in critical illness among patients without apparent glucose metabolism disorder.

**Materials and methods:** This will be a prospective study including 99 patients without apparent glucose metabolism disorder admitted to Intensive Care Unit, Department of Medicine, University Hospital Centre Zagreb due to critical illness (acute coronary syndrome, sepsis, pulmonary edema, pneumonia). Patients will be di-

vided into hyperglycemia group (blood glucose level measured during ICU stay  $>7.7$  mmol/L in at least two occasions) and normoglycaemia group. During their stay in ICU following data will be collected: age, gender, BMI, WHR, family history of glucose metabolism disorders, evaluation of physical activity, history of alcoholic and nicotine consumption. Blood tests including: glucose blood level, HbA1c, cholesterol, FFA, RBC, haematocrit, WBC, platelet number, creatinine, bilirubin will be measured. APACHE II and SOFA will be calculated. Follow up of 6-8 weeks will be conducted and on the ambulatory appointment insulin resistance will be measured by indirect methods (QUICKI, Revised QUICKI, HOMA-IR, 1/HOMA-IR,  $\log(\text{HOMA-IR})$ ) and OGTT test will be performed. Data will be statistically analyzed.

**Expected scientific contribution:** Confirming that increased risk for the onset of type 2 diabetes mellitus among patients who had hyperglycemia in critical illness is caused by intrinsically increased insulin resistance would give a new approach in prevention of type 2 diabetes mellitus among these patients.

**Acknowledgments:**

**MeSH/Keywords:** insulin resistance, hyperglycemia, critical illness, type 2 diabetes mellitus, glucose metabolism disorder

**Poster code:** B-9-87

## **POSTER TITLE: THE CONNECTION BETWEEN HYPOCHLOREMIA AND HYPONATREMIA IN PATIENTS WITH HEART FAILURE**

**PhD candidate:** Bojana Radulović, MD

**Part of the thesis:** The importance of initial hypochloremia in developing hyponatremia and adverse outcome in patients with acute heart failure

**Mentor/s:** Associate Professor Vesna Degoricija MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital „Sestre milosrdnice“ Zagreb, University Hospital Center Zagreb

**Introduction:** Hyponatremia is a significant and independent predictor of outcomes including re-hospitalization and mortality in patients with both acute heart failure and chronic heart failure. Even modest degrees of hyponatremia are associated with a poorer prognosis. Results from some studies of hyponatremia in heart failure suggest the possibility that hypochloremia appears prior to hyponatremia in patients with heart failure.

**Hypothesis:** Hypochloremia is an important factor in the development of hyponatremia and together with low systolic blood pressure, atrial fibrillation and elevated B-type Natriuretic Peptide level has predictive value in patients with heart failure who had normal plasma levels of sodium during presentation in the emergency department prior to admission.

**Aims:** The aim is to investigate the relationship between plasma levels of sodium and plasma levels of chloride in patients with heart failure who will develop hyponatremia during their hospital stay. Also, to investigate laboratory results or/and clinical exam features individually or in combination that are highly predictive for development of hyponatremia in patients who have had normal values of sodium initially. The final

aim is to formulate a novel therapeutic approach in patients with increased risk of development hyponatremia during treatment based on the data collected in this research.

**Materials and methods:** The study is designed as a prospective study that will include 276 patients hospitalised through the emergency department for an acute episode of heart failure. Participants will be divided in two groups depending on initial plasma values of chloride (in one group patients with levels of chloride below 97mmol/L and in the other patients that have higher levels of chloride than 97mmol/L). The two groups will be compared for development of hyponatremia.

**Expected scientific contribution:** Results of this research should offer hypochloremia as a new predictor of outcomes for patients with heart failure and thus improve choice of therapy and quality of life in those patients.

**Acknowledgments:**

**MeSH/Keywords:** Chlorates, hyponatremia, heart failure

**Poster code:** B-9-46

## **POSTER TITLE: THE RELATIONSHIP OF PLASMA CONCENTRATIONS OF GLUCAGONE-LIKE PEPTIDE 1 AND FIBROBLAST GROWTH FACTOR-21 WITH GLUCOREGULATION, LIPIDEMIA AND MICROVASCULAR COMPLICATIONS IN DIABETES MELLITUS TYPE 1 PATIENTS**

**PhD candidate:** Karin Zibar

**Part of the thesis:** The relationship of plasma concentrations of glucagone-like peptide 1 and fibroblast growth factor-21 with glucoregulation, lipidemia and microvascular complications in diabetes mellitus type 1 patients

**Mentor/s:** Prof. dr. sc. Lea Smirčić Duvnjak

**Affiliation:** resident

**Introduction:** The main therapeutic goal in type 1 diabetic mellitus (DM) patients is glucoregulation and prevention of microvascular complications. Glucagon-like peptide 1 (GLP-1) and fibroblast growth factor-21 (FGF-21) are related with glucose and lipid metabolism in DM. The aim of the study is to determine if higher GLP-1 concentration and lower FGF-21 concentration in plasma related with better glucoregulation, better lipid profile and minor risk for microvascular complications development in type 1 DM patients. Considering that the relationship of plasma concentrations of GLP-1 and FGF-21 with glucoregulation, lipidemia and microvascular complications in type 1 DM patients has not been investigated to date, our results could contribute to clarify complex type 1 DM pathophysiology, to upgrade diagnostics of microvascular complications by identification of new markers of their development and progression, which might be followed therapeutic implications towards implementation of incretin drugs as an addendum to current insulin therapy.

**Hypothesis:** Higher GLP-1 concentration and lower FGF-21 concentration in plasma are related with better glucoregulation, better lipid profile and minor risk for microvascular complications development in type 1 DM patients.

**Aims:** The aim of the study is to determine if higher GLP-1 concentration and lower FGF-21 concentration in plasma related with better glucoregulation, better lipid profile and minor risk for microvascular complications development in type 1 DM patients.

**Materials and methods:** Cross-sectional study in 30 type 1 diabetic patients. ELISA method.

**Expected scientific contribution:** Considering that the relationship of plasma concentrations of GLP-1 and FGF-21 with glucoregulation, lipidemia and microvascular complications in type 1 DM patients has not been investigated to date, our results could contribute to clarify complex type 1 DM pathophysiology, to upgrade diagnostics of microvascular complications by identification of new markers of their development and progression, which might be followed therapeutic implications towards implementation of incretin drugs as an addendum to current insulin therapy.

**Acknowledgments:** to laboratory team and colleagues

**MeSH/Keywords:** type 1 diabetic mellitus, GLP-1, FGF-21

**Poster code:** B-9-55

## **POSTER TITLE: THE ROLE OF CAVEOLIN-1 AND TRANSFORMING GROWTH FACTOR BETA IN NONALCOHOLIC FATTY LIVER DISEASE**

**PhD candidate:** Marija Gomerčić Palčić

**Part of the thesis:** Expression and Distribution of Caveolin-1 and Transforming growth factor beta in Hepatocytes of Patients with Nonalcoholic fatty liver disease

**Mentor/s:** Professor Marko Duvnjak, MD, PhD, Professor Božo Krušlin, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Sestre milosrdnice University Hospital

**Introduction:** Nonalcoholic fatty liver disease (NAFLD), a hepatic manifestation of metabolic syndrome is considered to be the most common liver disease in Western countries and also leading cause of cryptogenic cirrhosis. Insulin resistance, of all components of metabolic syndrome, plays the major part in fibrogenesis. Progression of NAFLD is characterized by enhanced accumulation of intrahepatic triglycerides, oxidative stress in hepatocytes and promoted fibrogenesis due to insulin resistance, causing abnormalities in expression and distribution of caveolin-1 and transforming growth factor beta (TGF- $\beta$ ).

**Hypothesis:** Expression of caveolin-1 and TGF- $\beta$  is increased and their distribution is altered in hepatocytes of patients with metabolic syndrome, both correlating with progression of the disease.

**Aims:** This study will be conducted to investigate expression and distribution of caveolin-1 and transforming growth factor beta in hepatocytes according to each NAFLD stage, and their relations with noninvasive biochemical and imaging (abdominal ultrasound) tests. In addition, we will investigate their relations with each component of metabolic syndrome (arterial hypertension, central obesity, atherogenic dyslipidemia and insulin resistance).

**Materials and methods:** This is a prospective study that will involve sixty-five patients of

both genders, aged 18 to 65 years, with NAFLD pathohistological findings and a control group without NAFLD. Blood tests and physical examination will be performed in order to determine whether metabolic syndrome is present in patients with NAFLD, as well as abdominal ultrasound to establish presence of NAFLD. Pathohistological analysis of liver tissues obtained by liver biopsy together with immunohistochemical staining using antibodies on caveolin-1 and TGF- $\beta$  will be performed in both groups. Relations between expression and distribution of caveolin-1 and TGF- $\beta$  with pathohistological findings, components of metabolic syndrome and imaging (abdominal ultrasound) tests will be evaluated.

**Expected scientific contribution:** This would be a first human study investigating role of caveolin-1 in patients with NAFLD. Estimation of expression and distribution of caveolin-1 and TGF- $\beta$  in hepatocytes in patients with different stages of NAFLD will help in understanding pathophysiology of the disease and natural history, as well to improve diagnostic and therapeutic possibilities.

**Acknowledgments:**

**MeSH/Keywords:** NAFLD, caveolin-1, TGF- $\beta$ , insulin resistance, noninvasive tests

**Poster code:** B-9-73

## **POSTER TITLE: BIOLOGICAL, PSYCHOLOGICAL AND SOCIAL FACTORS AS DYSPNEA PREDICTORS AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASES**

**PhD candidate:** Latinka Basara Toromanović, Professor of Psychology

**Part of the thesis:** Biological, Psychological And Social Factors As Dyspnea Predictors Among Patients With Chronic Obstructive Pulmonary Diseases

**Mentor/s:** Sanja Popović Grle, MD,PhD; Nataša Jokić Begić, Professor of Psychology, PhD

**Affiliation:** University Hospital Centre Zagreb, Clinic for Pulmonary Diseases Jordanovac, Zagreb

**Introduction:** Dyspnea is a clinical term for shortness of breath, or breathlessness and because of its debilitating characteristics it is the most common complaint among patients with chronic obstructive pulmonary diseases. Although dyspnea is a result of a pathophysiologic process, it is likely to be influenced by factors as psychological state, bodily preoccupation, level of awareness, body weight, state of nutrition, and medications. Biopsychosocial model includes all of these factors into explaining symptoms and disease course.

**Hypothesis:** Psychosocial factors are more significant predictors of dyspnea in patients with asthma and chronic obstructive pulmonary disease (COPD) than biological factors.

**Aims:** The aim of the study is to evaluate the predictive value of biological, psychological and social characteristics when describing dyspnea in asthma and COPD patients.

**Materials and methods:** In order to gather data for biological variables we will use previous medical records, oxygen saturation data (puls oximeter) and usual materials in lung function testing. For psychological variables a battery of questionnaires and scales will be used: PANAS- Positive and Negative Affective Schedule, ASI - Anxiety Sensitivity Index, Locus of Control Scale, Coping Strategies Questionnaire, COPD Assessment Test, Asthma Control

Questionnaire. For assessing social variables we will use a demographic questionnaire constructed for the purpose of this study that will gather relevant sociodemographic data. To assess dyspnea - we will use Borg Scale. Methodology will consist of data collection from 200 outpatients (100 COPD and 100 asthma patients) from Clinic for Pulmonary Diseases Jordanovac that are currently in a stable phase of their disease. Standard measures and data will be taken from all participants: lung function testing, oxygen saturation, data for body mass index, duration and severity of disease, number of exacerbations, etc. All patients will fill out the battery of psychosocial tests, evaluate current subjective degree of their disease and give dyspnea rating. All patients will fill out an informed consent before participating in the study.

**Expected scientific contribution:** Scientific contribution will consist of describing specific and overall predictive contribution of biological, psychological and social factors to dyspnea ratings in COPD and asthma patients.

**Acknowledgments:**

**MeSH/Keywords:** dyspnea, chronic obstructive pulmonary disease, asthma, biopsychosocial model

**Poster code:** B-9-74

# POSTER TITLE: CORRELATION BETWEEN EXPRESSION OF RESISTIN IN SERUM AND IN CAROTID PLAQUE AND HISTOLOGICAL FEATURES OF ATHEROSCLEROTIC PLAQUE

**PhD candidate:** Ivana Šakić

**Part of the thesis:** Correlation between expression of resistin in serum and in carotid plaque and histological features of atherosclerotic plaque

**Mentor/s:** Marko Ajduk, MD PhD

**Affiliation:** Clinical medical science

**Introduction:** Carotid artery atherosclerotic disease is an important risk factor in developing stroke. Clinical manifestations of the disease depend on the degree of stenosis of the carotid artery and on the vulnerability of the atherosclerotic plaque which depends on its histologic composition. Inflammatory process is the most important pathogenetic mechanism of the atherosclerosis, and with the aim of clarifying it, numerous markers were studied. Several papers indicate correlation between resistin and the carotid artery intima media thickness, its association with other inflammatory factors in the development of carotid atherosclerotic process and the mechanism of its action in the pathogenesis of atherosclerosis.

**Hypothesis:** We expect that the expression of resistin levels in serum and atherosclerotic plaque of the carotid artery would be higher in plaques classified according to AHA classification as VI (complex plaque with a surface defect, hemorrhage or thrombus).

**Aims:** The main objective of this study is to evaluate the correlation between resistin expression in serum and carotid plaque and plaque histology. Specific aims include evaluation of resistin expression in different histological plaque types as well as correlation between serum resistin levels, resistin expression in carotid plaque and patient's symptoms, risk factors and inflammatory markers.

**Materials and methods:** This study will recruit 70 patients with indications for carotid endarterectomy. Carotid specimens will be excised by the vascular surgeon. Plaque morphology will be assessed by standard histological examination of hematoxylin and eosin-stained (HE) sections (4 µm) and screened for features indicative of plaque vulnerability. The plaques will be classified according to AHA classification. Immunohistochemistry will be performed using primary antibody to human resistin (Resistin/RETN antibody, polyclonal antibody BMS RETN2040, eBioscience following the manufacturer's instructions). The expression of resistin will be evaluated on a semi-quantitative scale and the scoring will be arbitrary. Blood samples for laboratory assays will be obtained before surgery. Serum concentration of resistin will be measured using ELISA method.

**Expected scientific contribution:** If our study confirms correlation between resistin serum concentrations, resistin expression in carotid plaque and plaque histology, the results of this research could classify resistin as a new biomarker of atherosclerotic carotid artery disease.

**Acknowledgments:**

**MeSH/Keywords:** atherosclerosis, carotid artery, inflammatory marker, resistin

**Poster code:** B-9-77

## POSTER TITLE: EFFECT OF PROLONGED WORKING TIME ON ACTIVATION OF HEMOSTATIC SYSTEM

**PhD candidate:** Hana Mažibrada, MD

**Part of the thesis:** Prolonged working time activates hemostatic system resulting with hypercoagulability of the blood

**Mentor/s:** Petar Gaćina, MD, PhD, assistant professor

**Affiliation:** KBC Sestre milosrdnice

**Introduction:** The stress on working place and prolonged working time have affect on hemostatic system what is confirmed by previos studies. A few information is known about the mechanisam of activation of the hemostatic system an circadian variation of the coagulation factors and fibrinolysis. This fact is important because the activation of hemostatic system and hypercoagulability of the blood increase risk of morbidity and mortality.

**Hypothesis:** Prolonged working time in health workers whose job is occasionally organised through twentyfour hours shifts affects hemostatic system resulting with hypecoagulability of the blood.

**Aims:** The aim of this research is to explore coagulation parameters and fybrinolisis in health workers who have prolonged working time in comparison with control group. The specific aims are to measure the concentrations of fibrinogen, D-dimers, TAT, PAP complexes, factor VIII, activity of von Willebrand factor, PV, INR, APTV, TV, fibrinolysis, CRP and also see the dynamic of these measurements. The aim is also to answer the question wheather there is more variations in circadian rhytm of these measurments comparing the study and control group of health workers.

**Materials and methods:** The study group includes thirty physicians age 25-35 who are on

education and whose work is occasionally organised as twentyfour hours labour. The control group are physicians matched for ethnicity and age, with same education. Participants excluded from the study are pregnant women, users of hormonal contraception, physicians with positive anamnesis of thromboembolic events, nicotinisam, acute infectios disease, BMI <18.5 and >25 kg/m<sup>2</sup>, and those who had last twentyfour hours labor before more than five days. The samples of the vein blood will be collected 15 minutes before 24h labor, 12h and 24 hours after the beginning of the 24h labor. We will measure the concentrations of fibrinogen, D-dimers, TAT, PAP complexes, factor VIII, activity of vWF, PV, INR, APTV, TV, fibrinolysis and CRP.

**Expected scientific contribution:** The better knowing of hemostatic system through variations of coagulation parameters and fibrinolysis in circadian rhytm of the health workers occasionally exposed to shift and 24h work would help us to better understand potential danger of prolonged working time on coagulation system.

**Acknowledgments:** mentor, colleagues and personnel in laboratory in which measurments would be done

**MeSH/Keywords:** prolonged working time, hypercoagulability, fibrinolysis

**Poster code:** B-9-90

## POSTER TITLE: PROGNOSTIC SIGNIFICANCE OF FAS, FASL AND C-FLIP EXPRESSION IN CLASSIC HODGKIN LYMPHOMA

**PhD candidate:** Željko Prka, dr.med.

**Part of the thesis:** Prognostic significance of Fas, FasL and c-FLIP expression in classic Hodgkin lymphoma

**Mentor/s:** Prof. Vlatko Pejša, MD, PhD, Čedna Tomasović Lončarić, MD, PhD

**Affiliation:** University hospital Dubrava

**Introduction:** Hodgkin/Reed Sternberg cell (H/RS) is cell of lymphocyte B origin and with complex interactions with its microenvironment is responsible for biological and clinical effects of Hodgkin lymphoma. RS cells usually lack B-cell receptor (BcR). Normal lymph node cells without BcR undergo Fas-mediated apoptosis. It is believed that c-FLIP mediates resistance of HRS to Fas-mediated apoptosis. Pathogenesis of Hodgkin disease and mechanisms of RS cell survival have been explored for a long period of time but there is lack of relevant papers about its influence on disease presentation and prognosis.

**Hypothesis:** Stronger expression of c-FLIP protein on Hodgkin/Reed-Sternberg cell is associated with larger number of negative prognostic parameters incorporated in standardized prognostic indexes in classic Hodgkin lymphoma (cHL).

**Aims:** 1. To determine prognostic significance of Fas, FasL and c-FLIP expression in cHL to show in indirect way importance of activation and inhibition of CD95 dependent apoptotic pathway in pathogenesis of cHL. 2. to explore relationship between expression of aforementioned proteins with groups of patients with good and poor prognosis and standard histological types. 3. to explore eventual overall survival differences due to different expression of c-FLIP and relationship of Fas, FasL and c-FLIP expression with clinical stage and relevant laboratory parameters.

**Materials and methods:** We will use paraffin embedded lymph node tissue of patients with diagnosis of cHL who were diagnosed and treated in our hospital from 01.01.2007 till 31.12.2012. For expression of investigated proteins we will use Fas c-20, Fas-L q-20 and FLIP S/L H-202 antibodies. Detection of expression will be semiquantitative. For every patient clinical parameters from standardized prognostic indexes (GHSG, EORTC, IPS) at time of diagnosis will be determined and divided accordingly in good and poor prognosis group. With minimal 50 patients and  $p < 0.05$  expected statistical power is 81%. Appropriate statistical analysis will be conducted by professional statistician.

**Expected scientific contribution:** Research of association between Fas, FasL and c-FLIP expression and relevant prognostic parameters could show real value of CD95 apoptotic pathway in cHL and whether different expression of these proteins has clinical/prognostic significance. Furthermore, association of expression of any of these proteins with poorer prognosis could, in era of monoclonal antibodies, have additional impact in therapy.

**Acknowledgments:** Thanks to both of my mentors for unreserved assistance and help in every part of my doctoral research.

**MeSH/Keywords:** Hodgkin disease, CD95, c-FLIP, prognosis

**Poster code:** B-9-93



## **POSTER TITLE: THE ROLE OF CHEMOPROPHYLAXIS IN IMMUNOCOMPROMISED PATIENTS' WITH POSITIVE QUANTIFERON TEST BEFORE INTRODUCTION OF BIOLOGICAL TREATMENT**

**PhD candidate:** Denis Baričević

**Part of the thesis:** The role of Quantiferon test in detection of latent and active tuberculosis in patients' with rheumatoid arthritis and inflammatory bowel disease during treatment with TNF- $\alpha$  inhibitors

**Mentor/s:** Assist. Prof. Sanja Popović Grle, MD, PhD, pulmonologist

**Affiliation:** University hospital center Zagreb, Department for pulmonary diseases Jordanovac

**Introduction:** When TNF- $\alpha$  inhibitors are used for the treatment of chronic non-infectious diseases severe side effects can occur. Among them, tuberculosis is one of the most common. Therefore, it is of utmost importance to screen every patient for latent tuberculosis, because identifying latent tuberculosis aims at identifying patients who would benefit from the chemoprophylaxis before initiating biological therapy. This is an important step to decrease number of patients with active tuberculosis. So far published literature showed no stratified results regarding the use of IGRA test in diagnosis of latent or active tuberculosis.

**Hypothesis:** Patients' with positive QuantiFERON test can benefit from chemoprophylaxis to prevent disease manifestation.

**Aims:** to identify the diagnostic accuracy of IGRA test, its positive and negative predictive value, as well as its phenotype in for these purpose chosen group of immunocompromised patients with an indication for the treatment with biological therapy.

**Materials and methods:** The study will comprised 100 patients' with rheumatoid arthritis, Mb Chron, chronic ulcerative colitis, while the incidence of the disease varies according the gender (RA and Chron affects women more frequently than men, while chronic ulcerative colitis affects more man than women). In all patients' clinical examination will be per-

formed and medical history will assess the following issues: co-morbidities, exposure history, family history of tuberculosis, occupational and environmental exposures, current and concomitant treatment, social status while BCG vaccination status will be assessed by examination for the presence of BCG scar. From each participant blood samples will be drawn for QTG test and in all patients' sputum test for BK 2X, ppd skin test, chest and heart radiography will be performed. The control group will comprised 100 patients' with rheumatoid arthritis, Mb Chron, chronic ulcerative colitis with the incidence of the disease that varies according the gender and who were not diagnosed with latent tuberculosis (Quantiferon negative). Before the introduction of the biological therapy all patients will be examined and ppd skin test, chest and heart radiography will be performed.

**Expected scientific contribution:** Results of this study should be of great importance in developing guidelines for the use of the QuantiFERON test in diagnosis of latent and active tuberculosis in patients with rheumatoid arthritis and inflammatory bowel disease.

**Acknowledgments:**

**MeSH/Keywords:** QuantiFERON test, latent and active tuberculosis, immunocompromised patients, rheumatoid arthritis, Mb Chron, chronic ulcerative colitis

**Poster code:** B-9-94

## POSTER TITLE: CALPROTECTIN IN ASSESMENT OF ACTIVITY OF ULCERATIVE COLITIS AND CROHN'S DISEASE

**PhD candidate:** Dora Grgić, MD

**Part of the thesis:** Calprotectin in assesment of activity of ulcerative colitis and Crohn's disease

**Mentor/s:** Associate Professor Željko Krznarić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre-Zagreb

**Introduction:** Inflammatory bowel diseases (IBD) (Crohn's disease and ulcerative colitis) are chronic conditions characterized with recurrent episodes of inflammation in the gastrointestinal tract. The diagnostic grounds for IBD are endoscopic methods, but due to minimized invasiveness, new diagnostic markers have been implemented into clinical practice. Calprotectin is a calcium-binding protein, very stable and resistant to proteolytic degradation in stool, found in abundance in neutrophils. In inflammatory and infectious conditions calprotectin's concentration rises up to 100 fold. Recent studies have suggested calprotectin as a good marker in distinguishing inflammatory bowel diseases from similar irritable bowel syndrome. However, intensity of endoscopic lesions and fecal calprotectin haven't been compared yet.

**Hypothesis:** Positive correlation exists between concentration of calprotectin in stool and Crohn's disease activity index in patients with Crohn's disease. Positive correlation exists between concentration of calprotectin in stool and Truelove Witts index in patients with ulcerative colitis.

**Aims:** 1. Analyze correlation of fecal calprotectin concentration in patients with IBD with disease activity 2. Determine concentration of fecal cal-

protectin in patients with ulcerative colitis 3. Determine concentration of fecal calprotectin in patients with Crohn's disease 4. Determine values of fecal calprotectin and correlation with different stages of disease activity 5. Analyze correlation of fecal calprotectin with laboratory parameters and indexes of activity of IBD.

**Materials and methods:** 164 patients with diagnosis of IBD ( 82 patients with Crohn's disease, 82 patients with ulcerative colitis) either hospitalized in Department of Gastroenterology either as outpatients will be included in our study. After agreement and written consent to be part of a study 5 grams of stool and 5 ml of blood will be taken for analysis. Elisa method will be used for quantitative measurement of fecal calprotectin

**Expected scientific contribution:** This research will explore the relationship between fecal calprotectin in IBD with the degree of inflammatory activity and also evaluate diagnostic value of fecal calprotectin in active IBD.

**Acknowledgments:**

**MeSH/Keywords:** calprotectin, inflammatory bowel disease, faecal markers

**Poster code:** B-9-102

## **POSTER TITLE: DO BIOMARKERS LEPTIN AND ADIPONECTIN HAVE IMPORTANT ROLE IN COPD?**

**PhD candidate:** Mirsala Solak, MD

**Part of the thesis:** Prognostic and predictive value of biomarkers leptin and adiponectin in patients with chronic obstructive lung disease

**Mentor/s:** Miroslav Samaržija, MD PhD

**Affiliation:** UHC Zagreb

**Introduction:** Chronic obstructive pulmonary disease (COPD) is multisystem disease in which inflammatory biomarkers have important role. Studies have shown that biomarkers leptin and adiponectin may have a role in this disease, but the results are contradictory and controversial.

**Hypothesis:** The hypothesis of this study is that values of leptin and adiponectin are different in patients with stable COPD compared to healthy individuals and acute exacerbation, and that they correlate with body mass index (BMI).

**Aims:** The aim of this study is to determine the correlation between leptin and adiponectin with severity of acute exacerbation of COPD, and to compare it to stable disease and healthy individuals, as well as to determine the frequency of COPD exacerbations. We will determine the number of exacerbations of COPD during one year of follow up and the time to first exacerbation, as well as correlation of these biomarkers with morbidity and mortality during this period. We will analyze the correlation between leptin and adiponectin and BMI during exacerbation,

compared to stable disease and healthy individuals, and determine whether these biomarkers affect quality of life.

**Materials and methods:** This study will include 50 male smokers in acute exacerbation of COPD, aged 40-75. They will be evaluated ER on first day of exacerbation, after one month and one year according to planned protocol. The study will include 50 healthy matching individuals (smokers and non-smokers). All participants will sign informed consent before entering the study. For statistical analysis programme STATISTICA, ver. 8,0 (StatSoft. Inc.) will be used.

**Expected scientific contribution:** We believe that this study will reveal whether these biomarkers have prognostic and predictive value in COPD.

**Acknowledgments:**

**MeSH/Keywords:** chronic obstructive lung disease, biomarkers, inflammation

**Poster code:** B-9-123

## POSTER TITLE: IMPACT OF STRESS HYPERGLYCEMIA ON HOSPITAL OUTCOME OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

**PhD candidate:** Marija Zlojtro, MD

**Part of the thesis:** Stress hyperglycemia is negative prognostic factor for AECOPD

**Mentor/s:** Associate Professor Marko Jakopović, MD, PhD

**Affiliation:** General Hospital Zabok

**Introduction:** Stress hyperglycemia is transient hyperglycaemia during acute illness and was thought to be harmless or even advantageous. However, results of previous studies showed that hyperglycaemia is associated with poor outcomes from pneumonia, myocardial infarction and stroke, but the effect of blood glucose on outcomes from acute exacerbations of chronic obstructive pulmonary disease (AECOPD) has not been established. Current guidelines do not comment on measurement or control of blood glucose in AECOPD. A study was therefore undertaken to determine the relationship between stress hyperglycemia, clinical outcomes and mortality in patients admitted with AECOPD.

**Hypothesis:** Stress hyperglycemia is negative prognostic factor for clinical outcomes and intrahospital mortality for AECOPD patients.

**Aims:** to determine whether stress hyperglycemia has negative prognostic impact on clinical outcome and mortality in patients admitted for AECOPD and to research the association to duration of hospitalization, variables of lung function, sputum culture results, acid base arterial blood gases, radiologic finding of pneumonia and need for mechanical ventilation. Specific aim of this study is also to determine the impact of corticosteroid-related stress hyperglycemia which was disregarded in previous studies.

**Materials and methods:** prospective study with 300 AECOPD patients in one year period, in two

groups (AECOPD with stress hyperglycemia with blood glucose > 7,8 mmol/L and without stress hyperglycemia). In both groups, subjects will be treated with daily recommended dose of 40 mg of metilprednisolon iv. Blood glucose will then be followed after 24 and 48 hours and on the day of hospital discharge and according to these values subjects will be stratified in 4 subgroups. Beside age, sex, BMI, smoking history, lipid status, CRP, HbA1C, arterial ABS and cardiovascular morbidity, in all subjects standard variables of lung function, need for mechanical ventilation, sputum culture results and radiological pneumonia finding will be evaluated and examined with measurements of blood glucose.

**Expected scientific contribution:** acquiring new knowledge about influence of stress hyperglycemia (before and after corticosteroid therapy) on clinical outcome and intrahospital mortality in AECOPD patients. We hope that our findings will support inclusion of blood glucose assessment in future recommendations and stimulate further studies about stricter glycemetic control that could possibly contribute to a better treatment outcome of these patients.

**Acknowledgments:**

**MeSH/Keywords:** COPD, stress hyperglycemia

**Poster code:** B-9-128

## POSTER TITLE: ASSOCIATION BETWEEN THE MEASURES OF ARTERIAL STIFFNESS AND SERUM LEVELS OF PROINFLAMMATORY CYTOKINE IN ARTERIAL HYPERTENSION

**PhD candidate:** Tina Katić, MD

**Part of the thesis:** Association Between the Measures of Arterial Stiffness and Serum Levels of Tumor necrosis factor-alpha in Arterial Hypertension

**Mentor/s:** Professor Krešimir Galešić, MD, PhD

**Affiliation:** University Hospital Dubrava, Zagreb

**Introduction:** Activation of renin-angiotensin-aldosterone system (RAAS) is connected to induction of proinflammatory and immunoregulatory cytokine Tumor necrosis factor-alpha (TNF-alpha). It is also connected to arterial hypertension and its repercussions on physiological and structural changes in the vascular wall.

**Hypothesis:** Raised measures of arterial stiffness (Pulse wave velocity- PWV and Augmentation index- Aix) are statistically correlated to elevated levels of TNF-alpha, both in examined group of patients with arterial hypertension and control group of individuals without arterial hypertension. In patients suffering from arterial hypertension who are treated with RAAS blockers there is a statistical trend of lowering the serum levels of TNF-alpha.

**Aims:** The aim of this research is to investigate the possible association between the levels of TNF-alpha and the measures of arterial stiffness in arterial hypertension. Thus, our goal is to explore indirectly the connection between immunological activation and inflammation which are related to activation of RAAS, and by that account to arterial hypertension and changes in the vascular wall. This relation indicates the inflammatory basis of hypertension. We will also examine possible effects of antihypertensive medication on inflammation and functional and structural changes in the vascular wall.

**Materials and methods:** Both examined and control group will consist of 47 individuals (according to statistical requirements). In both

groups PWV and Aix will be measured and serum levels of TNF-alpha determined. The correlation between the measures of arterial stiffness and serum levels of TNF-alpha will be statistically evaluated. The same method will be repeated after 12 months, primarily to evaluate the possible effects of antihypertensive medication in examined group of patients with arterial hypertension.

**Expected scientific contribution:** Previous research suggests that endothelial dysfunction and changes in the structure of vascular wall in some forms of hypertension is mediated by proinflammatory factors. We expect that our results might complement previous research on arterial hypertension and atherosclerosis, major causes of morbidity and mortality in developed world.

**Acknowledgments:** I would like to thank the members of the scientific board assigned for the thesis: Prof. Ljiljana Banfić, Prof. Danka Grčević, Prof. Bojan Jelaković, and also the mentor of thesis Prof. Krešimir Galešić. I thank these extraordinary people for their useful instructions and advice, based on their professional experience, extensive knowledge and generosity. Their excellence along with their humanity is a true example for every student of medicine and every PhD candidate.

**MeSH/Keywords:** cytokines, arterial stiffness, hypertension

**Poster code:** B-9-147

# POSTER TITLE: THERMAL CHANGES DURING HEALING OF DISTAL RADIUS FRACTURES

**PhD candidate:** Damir Halužan, MD

**Part of the thesis:** Thermal changes during healing of distal radius fractures

**Mentor/s:** Prof. Slavko Davila, MD, PhD

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** Simplified, bone is healing in three basic steps, inflammation phase, repair phase and remodeling phase. There are studies that show significant vascular response during fracture healing, and suggest that the blood flow and fracture healing are closely linked. Infrared thermography is a method of measuring body temperature that is not invasive and harmful.

**Hypothesis:** During fracture healing there is an increase in temperature at the site of the fracture and in the surrounding area.

**Aims:** General aim of this research is to confirm the existence of thermal changes in limb fracture site and in the surrounding area, and to determine the temperature difference between a healthy and a broken arm. Specific aims are to determine the dynamics of thermal changes during time of healing and to investigate correlation between the degree of thermal changes and speed of bone healing.

**Materials and methods:** A prospective study will be conducted. Study will included 50 patients between 50 and 80 years of age with distal radius fracture treated conservatively. Flir ThermaCAM B2 infrared teletermografic camera will be used. Both healthy and broken arm will be recorded on one image in order to compare them. Healthy arm will be a control for the broken arm. During immobilization time

temperature of the fingers of both hands will be measured, and after immobilization removal temperature will be measured at both wrists. Each patient will be measured 6 times during 6 months at a precise time interval after fracture. A group of 30 healthy volunteers aged between 50 and 80 years of age will examine the impact of plaster of Paris, which is used during immobilization, on thermal changes of fingers. Both arms will be recorded on one image. Each participant will make two measurements, first before plaster setting and another 24 hours later, just before removing the plaster. All of the gathered data will be processed and presented using appropriate statistical methods.

**Expected scientific contribution:** This research is to determine the difference, dynamics and time presence of thermal changes during fracture healing, which was not systematically investigated. Value of infrared thermography in clinical practice and whether this method can predict the course of bone healing are to be determined.

**Acknowledgments:**

**MeSH/Keywords:** thermal changes, fracture healing, distal radius, infrared thermography

**Poster code:** B-10-10

## **POSTER TITLE: FOREARM ULTRASOUND AS A PRIMARY DIAGNOSTIC METHOD OF CHOICE FOR BLUNT FOREARM TRAUMA IN CHILDREN**

**PhD candidate:** Mateja Marčec, MD, pediatric surgery resident

**Part of the thesis:** Diagnostic algorithm for blunt forearm trauma in children-the value of combined sonographic and clinical examination findings as basis for further diagnostic and therapeutic approach in emergency department

**Mentor/s:** Tomislav Đapić, MD, PhD, ortopedic surgeon

**Affiliation:** General Hospital Sisak

**Introduction:** Blunt forearm trauma is among the commonest types of injuries in children, most often acquired in play or sporting activities by a fall onto an outstretched hand or a direct blow. When evaluating forearm trauma at an emergency surgical ward, a clinical examination is typically followed by a two way x-ray in order to confirm or exclude an underlying fracture. Recently, the value of a forearm ultrasound (US) in diagnosing long bone fractures has been demonstrated.

**Hypothesis:** The PhD hypothesis is that one can develop a clinically reliable, applicable algorithm that favors US as a first in line diagnostic method for forearm fracture diagnosis in children. The algorithm could effectively reduce the number of classical radiographs needed to make a reliable definite emergency department decision on treatment of blunt forearm trauma in children presenting with maximal tenderness above distal and middle thirds of radius and ulna.

**Aims:** The general aim is to determine when to replace radiogram with an US exam, reducing the total number of radiograms taken in children for blunt trauma, thus reducing the exposure of pediatric population to ionizing radiation. Specific goals are to define combination of specific clinical signs and positive or negative US findings when antebrachial x-ray may safely be omitted and specific management started.

**Materials and methods:** The thesis will be performed as a two-step research. Phase 1 will be

performed on 30 consecutive patients (aged 0-16 years, signed Consent Form by a parent) presenting to the surgical emergency ward at General Hospital Sisak with blunt trauma to the forearm. The group will be evaluated clinically for signs of bone fracture, followed by an US and X-ray. Results obtained will help to formulate a clinically applicable algorithm demonstrating when to safely omit an X-ray based on the clinical and US findings. During Phase 2 the algorithm will be tested on 40 consecutive patients and further modified if necessary. Multiple regression, as well as descriptive statistical analysis will be performed.

**Expected scientific contribution:** No research so far has analyzed the value of clinical findings conjoined with US examination for blunt forearm trauma in children and no algorithm for pediatric antebrachial trauma implementing US findings has yet been developed and questioned in a clinical setting. No research in which US is the only examination performed when diagnosing some cases of blunt forearm trauma has been published.

**Acknowledgments:** General hospital Dr. Ivo Pedišić, Sisak, Marcel Gorup, MD.

**MeSH/Keywords:** child, forearm injury, radius fractures, ulna fractures, fracture diagnosis, ultrasonography, radiation, ionizing

**Poster code:** B-10-17

# POSTER TITLE: NEUROSURGICAL IMPORTANCE OF SPHENOID AND CLIVUS-TENTORIUM ANGLE IN ANATOMICAL VARIATIONS OF SUBTENTORIAL SPACE

**PhD candidate:** Jakob Nemir, dr.med.

**Part of the thesis:** Correlation between sphenoid angle (skull base flexion) and clivus-tentorium angle

**Mentor/s:** Prof.dr.sc. Josip Paladino, dr.med.

**Affiliation:** Department of Neurosurgery, University hospital center Zagreb

**Introduction:** The anatomical variations of skull base structures have a huge influence on making decisions for the best neurosurgical approach. Complex anatomical structures originate from development of neuro- and endocranium. Due to neuroimaging improvement, especially magnetic resonance (MR) certain structures are more precisely visible

**Hypothesis:** Measurement and analysis of topographic anatomical relationships variations in subtentorial space using magnetic resonance (MR) provides the most convenient access to the pathological lesions located in the posterior part of the skull base, brain stem and base of the brain.

**Aims:** In this dissertation we will point out the importance of sphenoid and clivus-tentorium angle for the definite development of infratentorial anatomy.

**Materials and methods:** The investigation includes patients diagnosed and treated in University hospital centre Zagreb in which MR of endocranium and skull base was indicated. Mediosagittal sections taken in different sequences (T1 and T2) will be analysed.

**Expected scientific contribution:** Analysis of the sphenoid angle and clivus-tentorium angle together with anatomical structures of subtentorial space using MR will further clarify micro-anatomy of specified regions and their variability. We expect the development of new guidelines for best neurosurgical approaches for each individual.

**Acknowledgments:**

**MeSH/Keywords:** posterior fossa, sphenoid angle, skull base, tentorium, clivus-tentorium angle, MR

**Poster code:** B-10-125



## **POSTER TITLE: EFFECT OF ELEVATED PREOPERATIVE HEMOGLOBIN A1C ON OUTCOMES IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING AND COMPARISON WITH THE STANDARDIZED METHOD OF ASSESSMENT OF OPERATIVE RISK**

**PhD candidate:** Martina Zrno Mihaljević, MD

**Part of the thesis:** Effect of elevated preoperative hemoglobin A1c on outcomes in patients undergoing coronary artery bypass grafting and comparison with the standardized method of assessment of operative risk

**Mentor/s:** Vedran Ćorić, MD, PhD

**Affiliation:** Department of cardiac surgery, University Hospital Center Zagreb, Croatia

**Introduction:** Results of a number of previous studies showed that diabetes mellitus has been associated with an increased risk of adverse outcomes in patients undergoing coronary artery bypass grafting (CABG). Glycosylated hemoglobin, also known as hemoglobin A1c (HbA1c), is a reliable measure of long-term glucose control. To date, it is not completely known whether adequacy of diabetic control, measured by hemoglobin A1c, is a predictor of adverse outcomes after coronary artery bypass grafting.

**Hypothesis:** Elevate preoperative hemoglobin A1c level is a predictor of adverse events in patients undergoing coronary artery bypass grafting

**Aims:** To assess whether elevated level of hemoglobin A1c is associated with adverse outcomes in patients undergoing coronary artery bypass grafting and whether the same is in correlation with the standardized method of cardiac operative risk evaluation (EuroSCORE II). To determine whether patients with well-controlled diabetes preoperatively (HbA1c < 7%) have better outcomes compared with patients with poorly controlled diabetes preoperatively (HbA1c ≥ 7%). To assess whether patients with well-controlled diabetes (HbA1c < 7%) have outcomes comparable to those without a history of diabetes.

**Materials and methods:** The study will be performing at Department of Cardiac Surgery of

University Hospital Center Zagreb. It will be prospective study. In the same will be included consecutive sample of patients undergoing isolated primary coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB). Immediately after admission to the Department, for all patients will be obtained preoperative HbA1c, that will represent an independent continuous variable. A multivariable logistic regression model will be used to determine association of the independent continuous variable (HbA1c) with 30-day mortality, level of troponin T, length of mechanical ventilation, necessity for insertion of mechanical circulatory support devices, occurrence of arrhythmias, renal failure, cerebrovascular accident, deep sternal wound infection and length of stay after coronary artery bypass grafting. Results obtained from these analysis will be compared with values of calculated EuroSCORE II, that will be reevaluated for all patients immediately after admission to the Department.

**Expected scientific contribution:** Joining of hemoglobin A1c to cardiac operative risk evaluation (EuroSCORE II).

**Acknowledgments:** We thank Stjepan Ivanković and Jakov Vojković for their assistance with data collection

**MeSH/Keywords:** hemoglobin A1c, coronary artery bypass grafting, relative risk

**Poster code:** B-10-70

## POSTER TITLE: PROGNOSTIC VALUE OF RIBOSOMAL PROTEIN S6-PS240 IN INVASIVE DUCTAL BREAST CANCER

**PhD candidate:** Frederik Cuperjani, MD

**Part of the thesis:** Prognostic value of ribosomal protein S6-Ps240 in invasive ductal breast cancer

**Mentor/s:** Mentor: Prof. Dr. Božena Šarčević. Comentor: Prof. Ass. Dr. Lumturije Gashi-Luci

**Affiliation:** University of Zagreb School of Medicine, University Clinical Centre of Kosova

**Introduction:** Breast cancer still remains one of the most common malignancies and a major cause of cancer-related deaths among women worldwide. The main causes of cancer-related death are progression of noninvasive to invasive carcinoma with subsequent metastatic spread. The S6 Kinases have been linked to diverse cellular processes, including protein synthesis, mRNA processing, glucose homeostasis, cell growth and survival. Human ribosomal protein S6 phosphorylation correlates with an increase in translation of mRNAs that encodes for proteins involved in cell cycle progression and proteins that are associated with the protein synthesis machinery such as ribosomal proteins and elongation factors. Synthesis of these proteins is an important early event in controlling mammalian cell growth and proliferation.

**Hypothesis:** Immunohistochemical analysis of ribosomal protein S6-pS240 in invasive ductal carcinoma of the breast may be additional prognostic parameter in the biology of individual cases. By this parameter we can identify groups of patients with possible adverse prognosis that requires more aggressive treatment at the onset. This would particularly be of benefit for the groups of patients with intermediate grade invasive ductal carcinoma of the breast.

**Aims:** To establish the possibility of immunohistochemical analysis of ribosomal protein S6-pS240 in invasive ductal carcinoma of the

breast. To compare its expression with other established prognostic histopathological indicators of the carcinoma of breast. On the basis of the gathered results, establish its value as prognostic marker in invasive ductal carcinoma of the breast.

**Materials and methods:** The study will involve archive paraffin blocks of the tissue samples from 200 patients operated in the Department of Thoracic Surgery at the University Clinical Center of Kosova. Besides histopathology examination, the study will include the results of the ER/PgR expression, Her-2/neu amplification and proliferation index (Ki-67). The cases without these parameters will be excluded from the study.

**Expected scientific contribution:** Results of this study could contribute to the assessment of correlation of ribosomal protein S6-pS240 with other prognostic parameters especially in intermediate grade carcinoma. This would offer new perspectives for better individual treatment of patients within the intermediate grade group but with a possible more aggressive behavior.

**Acknowledgments:** I would like to thank School of Medicine, University of Zagreb and University Clinical Centre of Kosova for support.

**MeSH/Keywords:** Ribosomal protein S6-Ps240, breast cancer

**Poster code:** B-10-116

## **POSTER TITLE: EFFECTS OF COMBINED TOPICAL HYALURONIC ACID AND SYSTEMIC DICLOFENAC SODIUM ON FORMATION OF ADHESIONS ON INJURED FLEXOR TENDONS IN CHICKENS**

**PhD candidate:** Ylber Zejnullahu MD, Plastic Surgeon

**Part of the thesis:** Effects of combined topical hyaluronic acid and systemic diclofenac sodium on formation of adhesions on injured flexor tendons in chickens

**Mentor/s:** Assoc. Prof. Rado Zic, MD, PhD. Asst. Prof. Hysni Arifi, MD, PhD.

**Affiliation:** University Clinical Centre, Prishtina. Laboratory of the Pathophysiology Department.

**Introduction:** Even today no real and exact response to eliminate the adhesions especially flexors. Countless techniques, materials and substances have been used to decrease the level of adhesions after injured or repaired tendons. This study hyaluronic acid (HA) topically and diclofenac sodium systemically will be applied. HA is an anionic, nonsulfated glycosaminoglycan distributed widely throughout connective tissues and one of the chief components of the extracellular matrix. The second agent in this study is diclofenac sodium as NSAID where primary mechanism is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX).

**Hypothesis:** Topically applied hyaluronic acid is more effective in decreasing the adhesions on flexor tendons if combined with systemically applied diclofenac sodium.

**Aims:** To determine if the combination of hyaluronic acid applied topically and diclofenac sodium applied sistemically would decrease the amount of adhesions.

**Materials and methods:** 24 chickens with a total of 48 profundus flexor tendons are divided into four major groups. Two toes from one chicken foot will be operated on (flexor tendons), making a total of six flexor tendons from each subgroup. On the third and fourth toes (zone II) of

the same foot will be intentional harming will undergo two different manners. the first manner involves a perpendicular sharp cut of the flexor profundus tendon, which will be immediately sutured by a modified Kessler technique with 5/0 polypropylene core and 7/0 circular sutures and as second manner the crushing of the forth toe by applying the pressure on a 1-cm wide area under force of 10 Newton units for 20 seconds. Each subgroups, the same procedures will be performed but the implication of hyaluronic acid sodium (HA) 0.5 ml injected locally in exposed tendon and diclofenac sodium (DS) 5 mg i.m. injection intraoperatively and two days in a row after the surgery will be different, as well as the presence or absence of immobilization. Intraoperatively ceftriaxon 50 mg/kg/bw i.m. single dose.

**Expected scientific contribution:** To prove that the combination locally HA and Sistemically Diclofenac sodium may provide a better solution on future for decreasing the adhesions in humans too.

**Acknowledgments:** To my family, Mentors and the staf of Pathophysiology Laboratory.

**MeSH/Keywords:** Hyaluroinic acid, diclofenac sodium, adhesions, flexor tendon, chickens.

**Poster code:** B-10-106

## POSTER TITLE: APOPTOSIS IN NATIVE VEIN WALL IN FAILURE OF HEMODIALYSIS ARTERIOVENOUS FISTULAS

**PhD candidate:** Laura Leci Tahiri

**Part of the thesis:** Thesis proposal

**Mentor/s:** Prof. Ivo Lovrićević, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Clinical Centre of Kosova

**Introduction:** Failure of the arteriovenous fistula (AVF) is a common problem in hemodialysis patients and remains a major cause of morbidity and hospitalization. Puncture of a vein will leave a scar. When a fistula is created, such scars interfere with harmonious dilation and remodeling, cause turbulent flow, and predispose to stenosis.

**Hypothesis:** Apoptosis is to correlate positively with previous venepuncture and failure of AVF.

**Aims:** To evaluate apoptotic markers in the native vein wall of patients who will undergo an surgery for AVF for dialysis access.

**Materials and methods:** Comparison between veins punctured before and those that were not punctured before will be carried out and evaluation of apoptosis influence on failure of AVF will be done. Vein specimens will be obtained from at least 50 patients with chronic renal disease, divided in two groups, who will undergo an AVF surgery for the first time. Patients in whom the vein which will be used to create the AVF has been previously punctured will present Group I and Group II will present patients in whom the vein has not been previously punctured (control). For each patient, data related to gender,

age, duration of renal failure, duration on dialysis, site, type and duration of fistula, Doppler sonographic data before creation of fistula will be noted. Presence of comorbid conditions, use of other drugs, prior central catheter placement, HbAs antigen, HCV, HIV, history of intravenous drug abuse and smoking will be included for analysis. Before creation of AVF, 1cm vein segment will be excised from distal part of the vein for immunohistochemical analysis of markers involved in process of apoptosis (e.g. caspase 3, p53, Bcl-2 and Bax). For statistical analysis will be used: X2-test or Fisher exact test, Mann-Whitney U-test, Kruskal-Wallis test, student t-test or ANOVA test. The level  $P < 0.05$  will be considered as the cut-off value for statistical significance.

**Expected scientific contribution:** Because apoptosis has not yet been investigated in veins prepared for AVF, an original scientific contribution is expected of importance for the practical clinical problem of AVF failure in hemodialysed patients.

**Acknowledgments:**

**MeSH/Keywords:** venepuncture, apoptosis, hemodialysis, arteriovenous fistula

**Poster code:** B-10-127

## POSTER TITLE: USE OF BLOOD AS A QUALITY INDICATOR IN VASCULAR SURGERY

**PhD candidate:** Lidija Erdelez, MD

**Part of the thesis:** Outcome evaluation of aortoiliacal procedures by standardised quality indicator use of blood

**Mentor/s:** Jasna Mesarić, MD, PhD

**Affiliation:** Medical School University of Zagreb

**Introduction:** Surgery of infrarenal aortoiliac disease is combined with blood loss. Transfusion is associated with increased mortality and morbidity and blood supply is limited and costly. In our literature, there are no reports on the quality of transfusion and surgical practice, and on blood transfusion correlation with surgical treatment outcome. There are open questions: indications for perioperative blood transfusion, indications for cell-saver, great variety in transfusion practice which may require reevaluation and standardization. Utilization of blood and blood components is the part of Croatian accreditation standards (By law of hospital accreditation standards NN 33/11). The Performance Assessment Tools for Hospital (PATH) program of the World Health Organization Regional Office for Europe provide a quality indicator Use of blood as a tool for quality measurement of transfusion practice in different fields of surgery. This indicator was modified for vascular surgery and aortoiliacal procedures.

**Hypothesis:** Quality indicator Use of blood as a tool for evaluating outcome of elective infrarenal aortoiliacal procedures, will define areas of surgical and transfusion practice that require improvement in preoperative patient set-up, ordering and use of blood pre-, intra- and postoperatively.

**Aims:** To analyze current surgical and transfusion practice in elective aortoiliacal procedures, define areas for improvement, compare transfu-

sion practice between hospitals involved, justify allogenic transfusion and to analyze correlation between transfusion and postoperative complications including local infection, pneumonia and sepsis.

**Materials and methods:** This prospective, cohort, multicentric study will include at least 100 patients undergoing elective aortoiliacal procedures at 4 hospitals. Patients with coagulation abnormalities, prothrombin time  $<0,35$ , platelet count  $<50000/\mu\text{l}$ , those with reoperation for the same diagnosis and those submitted to more than one surgical procedure during the same hospital episode, were excluded from investigation. Demographic and clinical data, data of transfusion and surgical therapy were gathered prospectively using Excel list as a collection data tool designed for indicator Use of blood in the frame of PATH program supported by WHO for Europe.

**Expected scientific contribution:** This research will evaluate the role of quality indicator Use of blood in quality assessment of transfusion and surgical practice with aim to improve it, and contribute to standardization of transfusion practice in aortoiliacal procedures.

**Acknowledgments:**

**MeSH/Keywords:** infrarenal aortoiliac procedures, AAA, indicators, transfusion practice

**Poster code:** B-10-130

## **POSTER TITLE: IMPACT OF EXTRACORPOREAL LIFE SUPPORT ON BLOOD CLOT VISCOELASTIC PROPERTIES AND PLATELET AGGREGATION**

**PhD candidate:** Lucija Svetina

**Part of the thesis:** Impact of extracorporeal life support on blood clot viscoelastic properties and platelet aggregation

**Mentor/s:** Professor Bojan Biocina, MD, PhD

**Affiliation:** Department of Cardiac Surgery, University Hospital Centre Rebro, Zagreb, Croatia

**Introduction:** Extracorporeal life support (ECLS) therapy based on extracorporeal membrane oxygenation (ECMO) is used to temporarily support heart or lung function during cardiopulmonary failure, until organ recovery or replacement. Most thromboembolic and hemorrhagic complications occur despite conventional coagulation test values being within the targeted range. Conventional coagulation tests cannot identify thromboembolic and hemorrhagic complications that occur due to qualitative platelet aggregation disturbance, hyper/hypofibrinolysis, hypercoagulability due to tissue factor hyperactivity or increased clot firmness. Whole blood viscoelastic tests (rotational thromboelastometry) and platelet function tests (thrombocyte aggregation tests) reflect in detail the hemostasis of patients undergoing ECLS therapy and the efficacy of their anticoagulation therapy.

**Hypothesis:** Hemorrhagic and ischemic adverse outcomes can be assessed through testing thrombocyte function and viscoelastic blood clot properties in patients treated with extracorporeal life support therapy.

**Aims:** The goal of this study is to specifically address the issue of viscoelastic properties of blood clot and platelet function using point of care tests (POC). The results will be correlated with ischemic and hemorrhagic events during postoperative recovery.

**Materials and methods:** This prospective observational study will encompass patients treated with ECLS/ECMO due to onset of cardiogenic shock, CPR, bridge-to-decision, bridge-to-transplant or bridge-to-recovery treatment. Demographic data will be collected prior to treatment and subsequent laboratory tests will be done every 24 hours until recovery, transplant or death, taking into account biochemistry, CBC, conventional coagulation parameters and results of POC tests (rotational thromboelastometry using the ROTEM Delta device and thrombocyte aggregation tests using the Multiplate device). Hemodynamic parameters and incidence of hemorrhagic and/or ischemic incidents will also be noted and analyzed.

**Expected scientific contribution:** These principal questions are of interest: 1) do non-standard thrombocyte aggregation and rotational thromboelastometry tests provide novel information on the coagulation status of patients on ECLS/ECMO, 2) do the test results correlate with adverse outcomes (hemorrhagic and ischemic incidents) in patients on ECLS/ECMO, 3) do the test results provide practical information valuable in real-time patient therapy modifications.

**Acknowledgments:**

**MeSH/Keywords:** Extracorporeal life support, aggregation, coagulation, ROTEM Delta, Multiplate

**Poster code:** B-10-169

## **POSTER TITLE: THE INFLUENCE OF THE BADLY CONTROLLED BONE DRILLING ON THE HEAT BUILDUP IN THE DRILLING ZONE**

**PhD candidate:** Tin Ehrenfreund, MD

**Part of the thesis:** The Influence of the Badly Controlled Bone Drilling on the Heat Buildup in the Drilling Zone

**Mentor/s:** Prof. Slavko Davila, MD, PhD

**Affiliation:** KBC Zagreb, Department of Surgery, Kišpatičeva 12, Zagreb

**Introduction:** The principal operative fracture treatment is open reduction and internal fixation during which the plate is fixed to the bone by screws placed into predrilled holes. The highest increase in temperature occurs around the drill hole. The temperature decreases as the distance from the drill hole increases. One minute of exposure to the temperature of 47°C causes irreversible damage to the bone. Previous research has been based on the linear motion of the drill exclusively. In the clinical environment the direction of the drilling depends on the surgeon so it is not always possible to maintain the direction constantly.

**Hypothesis:** Hand driven bone drill produces more temperature at the drilling site comparing to machine driven drill

**Aims:** 1. To establish by changing the parameters of drilling whether the hand driven drill produces more temperature at the drilling site

than the machine driven one. 2. To establish differences in temperature at the drilling site in relation to drilling parameters and experience of the operator. 3. To establish differences in temperature between machine and hand driven drilling in relation to examined parameters.

**Materials and methods:** Hand drilling and machine drilling of fresh cadaver porcine femur according to previously determined protocols.

**Expected scientific contribution:** The research wants to investigate the justification of the introduction of automatic bone drilling systems into operative fracture treatment.

**Acknowledgments:**

**MeSH/Keywords:** thermal osteonecrosis, bone drilling

**Poster code:** B-10-161

## POSTER TITLE: IMMUNOGLOBULIN G GLYCOSYLATION IN PATIENTS WITH COLORECTAL CANCER

**PhD candidate:** Kujtim Thaci, Mr.Ph.

**Part of the thesis:** Immunoglobulin G Glycosylation in Patients with Colorectal Cancer

**Mentor/s:** Gordan Lauc, Prof.dr.sc.

**Affiliation:** Glycobiology laboratory of Genos-Zagreb.

**Introduction:** Because the Colorectal Cancer (CRC) develops slowly from removable precancerous lesions, detection of the disease at an early stage during regular health examination can reduce both the incidence and mortality of the disease. There have been previous reports that IgG antibodies can act as independent CRC prognostic factors. Glycosylation is an important regulator of IgG function with levels of „core“ fucose influencing Fc effector functions.

**Hypothesis:** 1) N-glycomic analysis could reveal significant inter-individual differences and identify several specific glycan biomarkers which are associated with CRC prognosis. 2) Population variation in N-glycans levels may influence cancer prognosis, through variation in immune system capacity to recognize and destroy cancer cells and through variation in the metastatic potential of colorectal cancer cells.

**Aims:** General aim: To identify IgG N-glycans biomarkers with discriminative power to predict survival in patients with CRC and so help treatment. Specific aims: 1) To investigate the association between plasma IgG N-glycans and CRC survival and evaluate their potential role as clinical biomarkers for CRC prognosis. 2) To investigate the relationship between plasma levels of IgG N-glycans and CRC mortality. 3) To investigate the discriminative power of specific plasma IgG N-glycans as clinical biomarkers of CRC prognosis.

**Materials and methods:** Samples for the analyses were assembled by prof. Malcolm Dunlop. In this research will be included 2000 CRC cases and matching controls from the University of Edinburg, with detailed clinical data for each patient's CRC episode, which include: clinical and imaging data, date of diagnosis, presence /date of recurrence, new cancer occurrence data, date of death, cause of death. I will isolate IgG proteins from the plasma samples using immobilized protein G. To quantify whole plasma IgG N-glycans, I will use high throughput UPLC analysis of fluorescently labelled glycans. I will apply proportional hazards regression models. I will use stpower Cox command in Stata.

**Expected scientific contribution:** A biomarker with high discriminative power to predict cancer survival outcome would help tailor the most appropriate surgical and chemotherapy regimens to individual patients thereby improving patient outcomes and this would reduce overall treatment toxicity and improve cost effectiveness.

**Acknowledgments:** A special note of thanks to Professor Gordan Lauc for his gold advises regarding this project.

**MeSH/Keywords:** Glycosylation, IgG, CRC.

**Poster code:** B-11-105



## **POSTER TITLE: INFLUENCE OF COMBINATION OF CYP2C9, VKORC1 AND MDR1 GENE POLYMORPHISMS ON INDIVIDUALIZATION OF WARFARIN THERAPY**

**PhD candidate:** Ksenija Makar Aušperger

**Part of the thesis:** Influence of combination of CYP2C9, VKORC1 and MDR1 gene polymorphisms on individualization of warfarin therapy

**Mentor/s:** Professor Nada Božina, MD, PhD

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** Warfarin is usually prescribed for treatment and prevention of thrombotic disorders. Despite that warfarin has been used as anticoagulant for many years its dosing presents a challenging task owing to its narrow therapeutic range and large variability in dose-response relationship. Therapy usually starts after assessment of clinical characteristics (age, body size, race), vitamin K intake and use of concomitant medications. The drug is often dosed empirically: an initial dose is prescribed, typically followed by at least weekly measurement of the INR and subsequent dose adjustment. Despite that, inappropriate dosing continues to contribute to significant morbidity and mortality due to thrombotic disease and bleeding complications. So far genetic variations in the cytochrome P450 (CYP2C9) and vitamin K epoxide reductase (VKORC1) have been identified as the most important enzymes in the warfarin pharmacological pathway. But MDR1/ABCB1 gene which encodes the efflux transporter P-glycoprotein (Pgp) and its C3435T polymorphism is associated with altered pharmacokinetics of many drugs. Warfarin was identified as one of the Pgp substrates.

**Hypothesis:** Applying pharmacogenetic testing to individualize dosing of warfarin stable maintenance dose could be achieved earlier with fewer side effects in the beginning of the therapy.

**Aims:** The aim of the present study is to investigate the influence of combination of CYP2C9,

VKORC1 and MDR1 gene polymorphisms on individualization of warfarin therapy.

**Materials and methods:** In this study 100 patients with clinical indication for warfarin therapy who will be treated in our Hospital will be included. Indications are atrial fibrillation, pulmonary embolism and deep vein thrombosis and before initiation of warfarin therapy pharmacogenetic testing will be performed. On the basis of the pharmacogenetic and clinical parameters warfarin dose will be calculated. Control group will include 100 patients for which warfarin dose will be calculated according to clinical characteristics of patients only (age, BMI, gender).

**Expected scientific contribution:** This study will be the first study to evaluate the significance of CYP2C9, VKORC1 and MDR1 gene polymorphisms for warfarin therapy individualisation. These three genes are involved in pharmacokinetics and pharmacodynamics of warfarin and if they have significant influence on the prediction, of warfarin dose it will be very important not only for science but for clinical practice as well.

**Acknowledgments:** I would like to express my gratitude to my mentor professor Nada Božina for her support and encouragement during this project.

**MeSH/Keywords:** warfarin, pharmacogenetics, gene polymorphism, individualization of therapy

**Poster code:** B-13-103

## POSTER TITLE: DETECTION OF CAG PATHOGENICITY ISLAND VIRULENCE GENES AND DUPA GENES OF HELICOBACTER PYLORI ISOLATES AFTER FAILED ERADICATION THERAPY

**PhD candidate:** Dijana Varda Brkić, MD

**Part of the thesis:** Detection of cag pathogenicity island virulence genes and dupA genes of *Helicobacter pylori* isolates after failed eradication therapy

**Mentor/s:** Professor Vanda Plečko, MD, PhD, School of Medicine, University of Zagreb, Zagreb

**Affiliation:** Department of Clinical and Molecular Microbiology, Clinical Hospital Center Zagreb, Zagreb, School of Medicine, University of Zagreb, Zagreb

**Introduction:** *Helicobacter pylori* is a spiral, microaerophilic, gram-negative bacteria. It plays an important role in the development of chronic gastritis, peptic ulcer, gastric cancer and MALT lymphoma. Several *Helicobacter pylori* genes, including cagA, are located in cagPAI (cytotoxin pathogenicity island) associated with gastroduodenal diseases and hence the variations in gene structure cagPAI may be responsible for different clinical outcomes. According to some research, the dupA gene, located in the *H. pylori* plasticity region, is associated with the development of duodenal ulcers and plays a protective role in the development of atrophy and intestinal metaplasia.

**Hypothesis:** 1. The presence of the virulence gene of cagPAI islands is related to higher degrees of chronic active gastritis and precancerous lesions of the gastric mucosa. 2. The presence of dupA genes is higher in patients suffering from antrum predominant gastritis, as opposed to patients suffering from diffuse- or corpus-predominant gastritis.

**Aims:** Detection of virulence genes of cagPAI islands and dupA genes of *Helicobacter pylori* strains in patients after multiple failed eradication treatments, and the comparison with pathohistological changes of the gastric mucosa.

**Materials and methods:** The research samples used in the study are *Helicobacter pylori*

strains from gastric mucosal biopsy specimens, obtained during routine, clinically indicated gastroduodenoscopies. The research includes clinical *H. Pylori* strains from patients after multiple failed eradication treatments. Conducted research methods shall include: 1. Basic microbiological diagnostics, 2. Molecular microbiological diagnostics, PCR

**Expected scientific contribution:** 1. Characterization of *Helicobacter pylori* strains present in patients in northwest Croatia, which have not been successfully eradicated after multiple treatment attempts, and their relation to the virulence factors of cagPAI islands, dupA genes and pathohistological diagnosis. 2. Extraction of those groups of patients who are at higher risk of developing premalignant and malignant lesions of the gastric mucosa, and with which it is obligatory to insist on eradicating the *H. pylori* infection. 3. Supplementation of the national diagnostics algorithm with molecular methods. 4. Contribution to future research related to the molecular epidemiology of *H. pylori* (human migration, clonal grouping specific to a particular ethnic group).

**Acknowledgments:** professor V. Plečko, MD, PhD, and professor M. Katičić, MD, PhD.

**MeSH/Keywords:** *Helicobacter pylori*, genotyping, cag pathogenicity island, dupA gene

**Poster code:** B-16-39

## POSTER TITLE: (99M)TC HYNIC-TOC SOMATOSTATIN RECEPTOR SCINTIGRAPHY

**PhD candidate:** Mate Trogrlić, MD

**Part of the thesis:** Added value of SPECT/CT in Nuclear Medicine

**Mentor/s:** Stanko Težak, MD, PhD

**Affiliation:** University Hospital Centre Zagreb, CROATIA.

**Introduction:** Neuroendocrine tumours (NETs) are relatively rare tumours overexpressing somatostatin receptors. The diagnosis of neuroendocrine tumours (NETs) and monitoring of therapy relied mainly on morphological imaging techniques such as computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI). In the last decade, strong efforts have been undertaken to establish radiopeptides in nuclear oncology for targeted tumour diagnosis and therapy. Radiolabeled somatostatin analogs have proved very useful in localization of somatostatin receptor expressing tumours. Technetium 99m hydrazinonicotinyl-Tyr(3)-octreotide (99mTc HYNIC-TOC) is increasingly gaining acceptance as a new radiopharmaceutical for the diagnosis of pathologic lesions overexpressing somatostatin receptors.

**Hypothesis:** 99mTc HYNIC-TOC SPECT/CT (Single photon emission computed tomography/computed, x-ray tomography) is an excellent imaging modality for evaluation of NET-s in terms of sensitivity, specificity and diagnostic accuracy.

**Aims:** To evaluate the potential usefulness of 99mTc HYNIC-TOC SPECT/CT in patients with metastatic NETs and in patients with suspected

NET and to evaluate the value of SRS in daily clinical practice compared to conventional imaging methods (CT, MR, EUS) and histology.

**Materials and methods:** This is a prospective study of 60 patients with known or suspected NET with at least one year follow up. Whole Body and tomographic acquisition were taken 2 and 4 hours after administration of 666 MBq of 99mTc HYNIC-TOC. All the patients underwent SPECT/CT 4 hours after injection of the tracer. Results will be compared with conventional imaging methods (CT, MRI, EUS), clinical follow up of at least one year and histology.

**Expected scientific contribution:** Implementation of 99mTc HYNIC-Tyr3-octreotide(TOC) SPECT/CT in daily clinical practice as a method of choice for evaluation of patients with neuroendocrine tumours.

**Acknowledgments:** I would like to thank my mentor for the support.

**MeSH/Keywords:** Neuroendocrine tumours, receptors somatostatin, tomography, emission-computed, single-photon, technetium Tc 99m hydrazinonicotinyl-Tyr(3)-octreotide

**Poster code:** B-17-48

## POSTER TITLE: HYBRID SPECT/CT WITH RADIOLABELED LEUKOCYTES IN PATIENTS WITH PAINFUL ARTHROPLASTY

**PhD candidate:** Margareta Dobrenić

**Part of the thesis:** Hybrid SPECT/CT with radiolabeled leukocytes in patients with osteoporosis

**Mentor/s:** Zlatko Giljević, MD, PhD

**Affiliation:** Clinical Department of Nuclear Medicine and Radiation Protection, Clinical Hospital Centre Zagreb, School of Medicine, University of Zagreb, Croatia

**Introduction:** Combined planar leukocytes (or white blood cells, WBCs) and colloid bone marrow scans are presently radionuclide imaging modality of choice for diagnosing periprosthetic bone infection. In addition to planar imaging, acquisition of SPECT/CT improves accuracy of scintigraphic technique. CT data are used for attenuation correction of SPECT images and for creating fused SPECT/CT scans for anatomical localization. Therefore, hybrid SPECT/CT imaging provides both functional and anatomical information in single scan.

**Hypothesis:** Hybrid SPECT/low-dose CT with radiolabeled leukocytes improves specificity and sensitivity of detection of periprosthetic bone infection in patients with painful arthroplasty.

**Aims:** To improve radionuclide imaging of periprosthetic bone infection in patients with painful arthroplasty.

**Materials and methods:** Patients with painful arthroplasty and suspected periprosthetic bone infection will be included in this prospective study. Planar images of region of interest and SPECT/low-dose CT of the same region will be made with autologous WBCs labeled with  $^{99m}\text{Tc}$  - HMPAO. Also, bone marrow imaging of region of interest will be performed with  $^{99m}\text{Tc}$ -nanocolloid. In case of absent accumulation of WBCs in the region of interest, colloid bone marrow imaging will not be performed. Furthermore, if the accumulation of WBCs seen on SPECT/CT is in the soft tissue, colloid study

will also not be acquired. Combined leukocytes and colloid images will be assumed positive for periprosthetic bone infection when there is accumulation on leukocytes scans without congruent uptake on colloid bone marrow images, regardless of the intensity of WBCs accumulation. Findings on planar WBCs images and leukocytes SPECT/CT scans will be analysed and any difference in number of foci or extension of WBCs accumulation will be documented. Clinical follow-up or/and bacteriological data obtained from the tissue biopsy will be used as a standard for proving periprosthetic bone infection.

**Expected scientific contribution:** SPECT/CT gives exact anatomical data of focal WBCs uptake around prostheses making location and extent of periprosthetic bone infection very precise. Furthermore, although metallic implants produce artefacts on CT scan, leukocytes SPECT/CT together with bone marrow imaging using colloid help in distinction between WBCs accumulation in bone marrow versus that in periprosthetic soft tissue.

**Acknowledgments:** I would like to thank Professor Dražen Huić for his support and constructive advices.

**MeSH/Keywords:** periprosthetic infection, SPECT/CT, hybrid imaging, radiolabeled leukocytes, bone marrow scan

**Poster code:** B-17-165

## **POSTER TITLE: DO CONVERGENCE INSUFFICIENCY PLAYS AN IMPROTANT ROLE IN CHILDREN DIAGNOSED WITH ADHD SYNDROME?**

**PhD candidate:** Barbara Dawidowsky

**Part of the thesis:** The relation of convergence insufficiency and ADHD syndrome

**Mentor/s:** Prof dr Branimir Cerovski

**Affiliation:** KDB Zagreb

**Introduction:** ADHD syndrome (attention deficit/hyperactivity disorder) is a developmental disorder of a self control. It consists of problems with attention span, impulse control and activity level. One of the symptoms is a disturbance in reading and writing, as well as a nonspecific visual disturbance that a child or a parent cannot precisely describe. That state is often recognized in preschool and school age as the expectation of abilities that consist of longer concentration and better attention arise. In Children's Hospital Zagreb, at the Department of ophthalmology, all of the children with diagnosis of ADHD syndrome had a complete ophthalmologic exam. We noticed that children diagnosed with ADHD had a high incidence of convergence insufficiency (CI). The symptoms of these two conditions can overlap and both can interfere with reading and learning abilities.

**Hypothesis:** Ophthalmologic exercises which improve CI and binocularity lead to concentration and attention enhancement in children with ADHD syndrome.

**Aims:** to demonstrate that ophthalmologic exercises which improve convergence insufficiency and binocularity (those are regularly used to help patients with same pathology without ADHD syndrome) can improve concentration and attention in children with ADHD syndrome.

**Materials and methods:** Children between 6 and 12 years diagnosed with ADHD syndrome

will have complete ophthalmologic examination (visual acuity measured with Snellen optotips, convergence measured in cm, stereovision measured with synoptophore, Lang test I and II Titmus test) to establish ophthalmologic status. In collaboration with pediatric psychologists all of the patients will be tested for concentration and attention degree with D2 Test of Attention (a psychodiagnostic test for measuring processing speed, compliance, and quality of performance allowing for a neuropsychological estimation of individual attention and concentration performance) Furthermore, the exercises for improving their CI and stereovision will be performed. After the period of three and six months, the ophthalmologic examination as well as psychology testing will be made in order to verify children's psychological status

**Expected scientific contribution:** We expect that the results of psychology testing will show improvement in concentration and attention after ophthalmologic exercises, and the enhancement of CI and binocular vision will help reduce symptoms of ADHD syndrome.

**Acknowledgments:** Prof dr Branimir Cerovski, dr Aleksandra Klobučar

**MeSH/Keywords:** Convergence insufficiency, binocular vision, ADHD syndrome

**Poster code:** B-18-154

## **POSTER TITLE: CYTOKERATIN-20 POSITIVE CELLS IN BLOOD OF COLORECTAL CANCER PATIENTS AS A PROGNOSTIC MARKER**

**PhD candidate:** Davor Kust, MD

**Part of the thesis:** Circulating colorectal cancer cells detected by cytokeratin-20 expression analysis as a specific marker

**Mentor/s:** Ivan Šamija, PhD

**Affiliation:** Clinical Hospital Center „Sestre milosrdnice“, Department of Oncology and Nuclear Medicine

**Introduction:** Detection of circulating cancer cells by reverse transcription-PCR (RT-PCR) was studied as prognostic marker in colorectal cancer patients but so far with conflicting results regarding specificity and prognostic value. In this study, cytokeratin-20 (CK20) will be evaluated as a marker for circulating colorectal cancer cells detection, and also influence of surgical tumor resection on the presence of circulating colorectal cancer cells will be analyzed.

**Hypothesis:** Presence of circulating colorectal cancer cells detected by cytokeratin-20 expression analysis as a specific marker is correlated with shorter overall and disease-free survival in patients with colorectal cancer.

**Aims:** Primary aim of this study is to determine the prognostic value of circulating cancer cells detected by RT-PCR in patients with colorectal cancer. Additional aim is to analyze the influence of surgical tumor resection on the presence of circulating colorectal cancer cells. For that purpose blood samples obtained before and after surgery will be analyzed.

**Materials and methods:** RNA was isolated from mononuclear cell fraction of blood samples taken from 95 colorectal cancer patients before and after tumor resection and from 23 healthy volunteers and assayed by real-time RT-PCR for CK20 expression.

**Expected scientific contribution:** Regarding contrary results of former similar studies, this research will help to evaluate prognostic value of cytokeratin-20 as a marker for circulating cancer cells detection in patients with colorectal cancer. This research could besides scientific also have clinical value, in the sense of introducing new marker which could improve treatment of these patients.

**Acknowledgments:** I would like to thank my mentor and all employees of Department of Oncology and Nuclear medicine of Clinical hospital center "Sisters of charity" on support.

**MeSH/Keywords:** biological tumor markers, circulating neoplastic cells, colorectal neoplasms, keratin-20, reverse transcriptase polymerase chain reaction

**Poster code:** B-19-63

## POSTER TITLE: PROGNOSTIC AND PREDICTIVE SIGNIFICANCE OF 25OH D IN COLORECTAL CANCER PATIENTS

**PhD candidate:** Zrna Antunac Golubić

**Part of the thesis:** Prognostic and Predictive Significance of 25OH D in Colorectal Cancer Patients

**Mentor/s:** Professor Stjepko Pleština, MD, PhD

**Affiliation:** University Hospital Centre Zagreb

**Introduction:** There is growing evidence that vitamin D exerts anticarcinogenic effects. Recent studies have largely shown that low 25-hydroxy-vitamin D levels, which are considered to be the best indicator of vitamin D status, are a significant risk factor for cancer mortality. Our aim is to examine the association between 25OHD levels and survival or relapse in colorectal cancer patients.

**Hypothesis:** Colorectal cancer patients with 25OHD levels higher than 75 nmol/l have an improved two-year survival and lower recurrence rate. Daily supplementation with vitamin D 2000 IU will improve survival and reduce the recurrence rate.

**Aims:** The purpose of this study is to examine the association between 25(OH)D levels and two-year survival and relapse in patients with colorectal cancer. Our goals are to determine the prevalence of vitamin D deficiency in colorectal cancer patients and to investigate the influence of vitamin D supplementation on prognosis and response to therapy.

**Materials and methods:** 224 patients with colorectal cancer (stages I-IV) will be enrolled in

our study. Blood samples will be collected after surgery but before initiation of chemotherapy. Concentration of 25OHD will be measured at recruitment and every three to six months. Patients with 25OHD levels lower than 75nmol/l will be randomised in two groups. Patients in the first group will be prescribed vitamin D3 (cholecalciferol) 2000 IU and patients in the second group will be observed.

**Expected scientific contribution:** Few prospective studies showed that low vitamin D levels were associated with increased mortality of patients with colorectal cancer. No study has yet examined whether vitamin D supplementation improves outcome or response to therapy. Our findings may stimulate further research directed at investigating the effects of vitamin D supplementation on colorectal cancer prognosis.

**Acknowledgments:**

**MeSH/Keywords:** vitamin D, colorectal carcinoma, survival

**Poster code:** B-19-49

## **POSTER TITLE: PREDICTIVE SIGNIFICANCE OF NONSPECIFIC LABORATORY PARAMETERS TO THE RESPONSE TO FIRST LINE CHEMOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED AND METASTATIC NON-SMALL CELL LUNG CANCER**

**PhD candidate:** Sonja Badovinac

**Part of the thesis:** Predictive significance of nonspecific laboratory parameters in patients with locally advanced and metastatic non-small cell lung cancer treated with chemotherapy

**Mentor/s:** Marko Jakopović

**Affiliation:** University Hospital Centre Zagreb, Clinic for Lung Diseases Jordanovac

**Introduction:** Lung cancer is the leading cause of cancer death worldwide and Croatia is among the countries with the highest lung cancer incidence and mortality rate. Non-small-cell lung cancer represents 80% of all lung cancers. Most of the patients are diagnosed with locally advanced or metastatic stage of the disease (stage IIIB and IV) and chemotherapy is the standard therapeutic strategy. The main goal of the treatment is to slow down disease progression. Lung cancer has heterogenic biology with wide range of prognostic and predictive variability therefore the search for adequate predictive factors for defining patients with better or worse response to the therapy is still in progress.

**Hypothesis:** Pretreatment level of inflammation reactants has predictive value to the chemotherapy response in patients with locally advanced or metastatic non-small cell lung cancer.

**Aims:** To evaluate connection between pretreatment level of inflammation reactants and chemotherapy response

**Materials and methods:** The data will be collected from medical documentation of the patients with locally advanced or metastatic non-small-cell lung cancer treated on oncology department at Jordanovac pulmonology Clinic during 2011. All patients with diagnosed stage IIIB and IV non-small cell lung cancer will be identified and included in the patients' reg-

istry. A retrospective analysis of the complete medical documentation and laboratory data will be performed. For this study following demographic and clinical data will be collected: age, gender, histologic and cytologic type of tumor, stage of the disease, chemotherapy type. Routine laboratory results prior chemotherapy will be collected: CRP, leucocyte count, fibrinogen, hemoglobin level. Chemotherapy start date and response at reevaluation of disease will be documented. Time to progression after first line chemotherapy as well as overall time to treatment end will be analyzed. Data will be analyzed by using appropriate parametric and non parametric statistical tests. Results will be shown in graphs and tables.

**Expected scientific contribution:** Results from the study will contribute to understand connection between inflammation and tumor proliferation and to define nonspecific laboratory parameters that can be used as surrogate measure of tumor activity and independent predictors of disease.

**Acknowledgments:** financial support to be defined

**MeSH/Keywords:** non-small-cell lung cancer, C-reactive protein, fibrinogen, leucocyte count, haemoglobin

**Poster code:** B-19-54



## **POSTER TITLE: METABOLIC SYNDROME, CHARACTERISTICS OF BREAST CANCER AND 25-HYDROXYVITAMIN D STATUS AT DIAGNOSIS**

**PhD candidate:** Katarina Vučić, MD

**Part of the thesis:** Relation of Metabolic Syndrome Factors and Characteristics of Newly Diagnosed Breast Cancer to 25-Hydroxyvitamin D Status

**Mentor/s:** Associate Professor Stjepko Pleština, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre Zagreb

**Introduction:** Few studies performed in women with newly diagnosed breast cancer showed poorer prognostic characteristics in women with 25-hydroxyvitamin D deficiency and in those with metabolic syndrome (MetS), investigating them separately.

**Hypothesis:** Poorer prognostic characteristics of newly diagnosed breast cancer (BCa) have women with both 25(OH)D deficiency and metabolic syndrome compared to women with only MetS.

**Aims:** To compare BCa characteristics in women with both 25(OH)D deficiency and MetS vs. women having only MetS.

**Materials and methods:** Cross-sectional study. Two groups of female patients with newly diagnosed BCa will be formed - one from those with 25(OH)D deficiency (< 50 nmol/l) and one from patients with  $\geq 50$  nmol/l 25(OH)D (i.e. group

with 'normal' concentration). All clinical findings related to MetS and BCa characteristics will be compared between these two groups of patients.

**Expected scientific contribution:** Prevalence of 25(OH)D deficiency and MetS in women with newly diagnosed BCa - possible comparison with general population in Croatia for overweight, central overweight, hypertension and diabetes. Data on characteristics of newly diagnosed BCa in women with both 25(OH)D deficiency and MetS in comparison with women having only MetS - association with 25(OH)D deficiency. Data source for future studies.

**Acknowledgments:**

**MeSH/Keywords:** breast cancer, vitamin D deficiency, metabolic syndrome

**Poster code:** B-19-78

# POSTER TITLE: COMPARISON OF DIRECT AND INDIRECT COST AND OUTCOME OF OPERATIVE TREATMENT OF SUBACROMIAL IMPINGEMENT SYNDROME, BY OPEN AND ARTHROSCOPIC TECHNIQUES

**PhD candidate:** Danijel Matek, MD

**Part of the thesis:**

**Mentor/s:** Prof. Domagoj Delimar, MD, PhD

**Affiliation:** n/a

**Introduction:** In clinical orthopaedic practice patients suffering of subacromial impingement syndrome are rather common. By recent literature incidence of patients with shoulder pain is 29.3 in 1000 patient years, with prevalence of 41.2-48.4 patient years. Out of those patients some 70% have difficulties originating from disorders and damage to the rotator cuff. Although it is common pathology, by this day there are no studies which would define and compare total costs of operative treatment and postoperative rehabilitation until return to work in the system of the Croatian institute for health insurance. Conservative and operative treatments as well as different operative techniques were compared, but in recent literature we did not find any survey that would compare total costs of arthroscopic and open operative techniques.

**Hypothesis:** The patients who are operated by arthroscopic technique will reach full functional and working capability before than those operated by open technique and due to less analgesics used and shorter time period spent on sick leave will ultimately reach less total cost of treatment.

**Aims:** GENERAL AIMS - To compare efficiency and cost-benefit ratio for arthroscopic and open technique in operative treatment of subacromial impingement syndrome. SPECIFIC AIMS - 1) Comparison of efficiency of two operative

techniques based upon several parameters (duration of postoperative hospital stay, pain intensity during postoperative period, analgesics spent, time needed for full functional and working capability). 2) Determining and comparison of treatment costs - direct, indirect and total.

**Materials and methods:** In recent literature we found no valid data concerning outcomes which could help determine a number of patients needed for power analysis (i.e. average time needed for full functional capability and measures of variability of that outcome). By insight in recent orthopaedic literature we found the number of 60 (1:1) consecutive patients of both sexes aged 18-65 would be sufficient to adequately estimate cost and benefit ratio of those two operative techniques.

**Expected scientific contribution:** The proposed research is the first to compare direct and indirect costs and efficiency of operative treatment of subacromial impingement syndrome by arthroscopic and open techniques. If arthroscopic technique shows less total costs with comparable efficiency, the procedure could be proposed as preferable for future use.

**Acknowledgments:**

**MeSH/Keywords:** subacromial impingement syndrome, arthroscopy, open surgery, cost

**Poster code:** B-20-45

## POSTER TITLE: CEFAZOLIN PROPHYLAXIS - GOLDEN STANDARD OR STANDARD MISTAKE?

**PhD candidate:** Krešimir Crnogaća

**Part of the thesis:** True cefazolin inhibition strength on *Staphylococcus epidermidis* growth as antibiotic prophylaxis for total knee arthroplasty

**Mentor/s:** Professor Domagoj Delimar, MD, PhD

**Affiliation:** Department of Orthopaedic surgery, Clinical Hospital Centre Zagreb, University of Zagreb

**Introduction:** Total joint arthroplasty is a safe and effective procedure improving the quality of life and restoring function to patients with arthritis of the hip and knee. Increasing number of joint replacement procedures is made every year. Large numbers of implanted prostheses mean that there is an increasing number of complications to deal with. Infections of the joint are regarded as one of the most feared complications following total arthroplasty and develop in 0.4 to 2% of the patients. The most common organisms identified are *Staphylococcus aureus* and *Staphylococcus epidermidis* which are credited for more than half of all infections. Because of the economic and psychologic burden of this complication, strategies to minimize or prevent it are needed. Strategies include pre-operative patient optimization, body exhaust system, laminar air flow during operation, scrubbing of the operative field, sterile draping, and the use of antibiotic prophylaxis which we believe is the cornerstone in struggle against infection. Cefazolin has been used for many years to treat bone and joint infection and now is the most commonly used antibiotic drug in arthroplasty prophylaxis worldwide and in our Department as well.

**Hypothesis:** Our hypothesis is that bone concentration of cefazolin during primary knee arthroplasty is not high enough to have inhibitory effect on *Staphylococcus epidermidis*

**Aims:** To analyze effectiveness of different regiments of cefazolin antibiotic prophylaxis by

measuring inhibitory capacity of cefazolin on *Staphylococcus epidermidis* growth in cancellous and cortical bone obtained during surgery.

**Materials and methods:** Patients with normal renal function which will have elective primary total knee arthroplasty will be included in our study. Patients receiving antimicrobial therapy prior to surgery and patients with evidence of avascularity seen on plain radiographs will be excluded. In this double blind prospective study patients will be randomized in two groups with different regiments of antibiotic prophylaxis with cefazolin. During the operation uniform specimens of cancellous and cortical bone will be obtained and planted to a agar plate streaked evenly with the standardized broth suspension of *Staphylococcus epidermidis*. Zones of inhibition will be measured after 24 hours of incubation at 37 degrees, interpreted and presented using appropriate statistical methods

**Expected scientific contribution:** To define the optimal algorithm for cefazolin antibiotic prophylaxis in primary total knee arthroplasty.

**Acknowledgments:** I would like to sincerely thank my colleague Goran Bićanić, MD, PhD for his invaluable help in making this thesis proposal.

**MeSH/Keywords:** Antibiotic prophylaxis, Knee, Endoprosthesis, Periprosthetic infection

**Poster code:** B-20-167

# POSTER TITLE: COMPARISON OF BIOMECHANICAL PROPERTIES OF THE PLANTARIS AND GRACILIS TENDONS FOR MEDIAL PATELLOFEMORAL LIGAMENT RECONSTRUCTION

**PhD candidate:** Josip Vlaić, MD

**Part of the thesis:** Comparison of biomechanical properties of the plantaris and gracilis tendons for medial patellofemoral ligament reconstruction

**Mentor/s:** Assistant Professor Mislav Jelić, MD, PhD

**Affiliation:** Division of Pediatric Orthopedic Surgery, Children's Hospital Zagreb Department of Orthopaedic surgery, Clinical Hospital Centre Zagreb, University of Zagreb Medical

**Introduction:** Patellar luxation comprises 2-3% of all knee injuries. After patellar dislocation in more than 90% of cases there is damage to the medial patellofemoral ligament (MPFL). MPFL injury disrupts a complex of passive medial patellar stabilizers and subsequently comes to instability of the patella in a number of patients. Patellar instability causes much discomfort, and it is necessary to do a reconstruction of the MPFL. Reconstructive techniques utilizing gracilis tendon graft are mostly used. Gracilis tendon is harvested from structures that have important role in biomechanics of the knee, thus additionally impairing stability of the injured knee.

**Hypothesis:** The plantaris tendon is suitable as a graft for MPFL reconstruction, and the plantaris tendon graft has comparable biomechanical properties with gracilis tendon graft, which is now commonly used for this procedure.

**Aims:** To compare the biomechanical properties of the graft made up of double-folded plantaris tendon, to be used for substitute a damaged MPFL, with biomechanical properties of double-folded gracilis tendon graft whose biomechanical properties are adequate for the MPFL reconstruction.

**Materials and methods:** Gracilis and plantaris tendons will be procured from 20 cadavers in a way as already described in the literature. Each tendon will be double-folded and grafts will be

made, not less than 9 cm long. Double-folded tendon grafts will be than caught in specially designed tendon clamp. Clamps will be placed in tensile testing machine and strength and tension parameters will be measured. Biomechanical properties of the plantaris tendon graft will be compared with biomechanical properties of the gracilis tendon graft, which is currently commonly used for MPFL reconstruction. Depending on type of distribution data will be analyzed using parametric or nonparametric statistical tests.

**Expected scientific contribution:** To get adequate tendon graft for MPFL reconstruction made of plantaris tendon, without additional distortion of biomechanical relations in the injured knee, and extend graft choice for knee ligaments reconstructive procedures.

**Acknowledgments:** Authors would like to thank following institutions and their staff: Department of Orthopedic Surgery University Hospital Centre Zagreb, Department of Forensic Medicine School of Medicine University of Zagreb, Department of Pathology and Cytology University Hospital Centre Zagreb, Faculty of Mechanical Engineering and Naval Architecture University of Zagreb

**MeSH/Keywords:** medial patellofemoral ligament reconstruction, plantaris tendon graft

**Poster code:** B-20-131

## POSTER TITLE: CHARACTERIZATION OF IMMUNOSUPPRESSIVE PROPERTIES OF MESENCHYMAL STEM CELLS DERIVED FROM HUMAN PALATINE TONSILS

**PhD candidate:** Antun Bačić, MD

**Part of the thesis:** Characterization of immunosuppressive properties of mesenchymal stem cells derived from human palatine tonsils

**Mentor/s:** Prof. Drago Prgomet, MD, PhD

**Affiliation:** University Hospital Center - Zagreb, Merkur Clinical Hospital

**Introduction:** There is supporting evidence for the therapeutic use of allogeneic mesenchymal stem cells (MSCs) due to their hypoinflammatory and immunosuppressive properties. At present, bone marrow is considered the most accessible source of MSCs (BM-MSCs). However, BM-MSCs derivation has significant complications and risks. Recently it has been shown that palatine tonsils are an attractive alternative source of young, easily accessible and rapidly proliferating MSCs.

**Hypothesis:** Mesenchymal stem cells derived from human palatine tonsils (T-MSCs) will demonstrate immunosuppressive properties over T-lymphocytes. T-MSCs will inhibit division and growth of T-lymphocytes and suppress secretion of T-lymphocyte specific cytokines.

**Aims:** It has been demonstrated that T-MSCs possess similar surface epitope profiles, characteristics, and differentiation potential as BM-MSCs. Therefore, we speculate that they could also share similar immunosuppressive properties. In a present work, we want to determine and compare the immunomodulatory activities of T-MSCs to activities of the well-characterized population of BM-MSCs, in order to facilitate further experiments and possible therapeutic use of T-MSCs.

**Materials and methods:** Isolation and expansion of T-MSCs and control BM-MSCs in a tissue culture, epitope characterization on surface of T-MSCs and BM-MSCs by immunophenotypization, mixed lymphocyte reaction of MSCs and T-cells and analysis of T-lymphocyte proliferation, mixed cultures of MSCs and T-lymphocytes induced to Th1 and Th2 cells, cytokine secretion analysis (IFN- $\gamma$  in Th1 mixed cultures and IL-4 in Th2 mixed cultures).

**Expected scientific contribution:** Growing evidence on immunomodulatory characteristics of BM-MSCs have led to experimental introduction of allogeneic BM-MSCs in the treatment of numerous different diseases, such as GvHD, diabetes, RA or SLE. Human tonsils are proven, newly discovered source of young, rapidly dividing MSCs. Tonsillectomy is the most common surgical procedure in children, therefore, tonsils are plentiful tissue banking source containing MSCs. Favorable results of our research could lead to numerous novel therapeutic applications of T-MSCs.

**Acknowledgments:**

**MeSH/Keywords:** mesenchymal stem cells, MSC, palatine tonsils, immunosuppression, T-cells

**Poster code:** B-21-71

## POSTER TITLE: IMMUNOHISTOCHEMICAL EXPRESSION OF ESTROGEN RECEPTORS BETA IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

**PhD candidate:** Krešimir Gršić, MD

**Part of the thesis:** Immunohistochemical expression of estrogen receptors beta in head and neck squamous cell carcinoma

**Mentor/s:** Professor Božena Šarčević, MD, PhD

**Affiliation:** University hospital for tumors University hospital center „Sister of Mercy“, Zagreb

**Introduction:** Squamous cell carcinoma of the head and neck (HNSCC) is the fifth most common cancer in people worldwide. Emerging on the mucosa of the upper respiratory and digestive systems HNSCC is strongly influenced by the exposure to carcinogens in tobacco and alcohol, virus contacts (such as human papilloma virus), and genetic predisposition. Although modern principles of multimodal therapy were introduced in therapeutic procedures, survival of patients with HNSCC has not been significantly altered in the last 30 years. New researches are required to discover specific genetic and molecular changes responsible for the onset and development of HNSCC metastatic potential. Recent studies emphasize the important role of nuclear estrogen receptor beta (ER $\beta$ ) in HNSCC carcinogenesis.

**Hypothesis:** Determination of estrogen receptor beta (ER $\beta$ ), which is supposed to have a protective role in the development of squamous cell carcinoma of head and neck, would provide extracting the group of patients with better prognosis.

**Aims:** The survey aims to determine the immunohistochemical expression of estrogen receptor beta in squamous cell carcinomas of head and neck with respect to the site of the primary process (oral cavity, oropharynx, hypopharynx, larynx), disease stage, degree of tumor differentiation, and survival of patients.

**Materials and methods:** This retrospective study will be including patients with squamous cell carcinoma of head and neck who have been treated in the interval from 2000 to 2006 in our institution and have been monitored for at least 5 years. A total of about 200 patients with location of primary tumors in the oral cavity, oropharynx, hypopharynx and larynx will be enrolled in the research. Biopsy analysis from patients with known prognostic factors (TNM stage and tumor differentiation), and known course of the disease (local recurrence, regional recurrence, dissemination, survival) will reveal the immunohistochemical expression of estrogen receptor beta (ER $\beta$ ).

**Expected scientific contribution:** The study will define the importance of estrogen receptor beta (ER $\beta$ ) as possible predictors of locoregional aggressiveness. This would open the opportunity for potent drugs innovation, development and application. Moreover, the existing multimodal procedures (surgery, chemotherapy and irradiation) will be revised in order to better efficiency.

**Acknowledgments:** I would like to thank Professor Božena Šarčević for her support and encouragement during this project.

**MeSH/Keywords:** squamous cell carcinoma of the head and neck, estrogen receptor beta, neoplastic cell transformation, survival

**Poster code:** B-21-82

## POSTER TITLE: PITUITARY-THYROID FEEDBACK CONTROL IN HYPOTHYROID AND ATHYREOTIC PATIENTS

**PhD candidate:** Darko Solter, MD

**Part of the thesis:** Altered metabolism of triiodothyronine (T3) is the cause of impaired pituitary-thyroid feedback control in hypothyroid and athyreotic patients.

**Mentor/s:** Prof. Vladimir Bedeković, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Sestre milosrdnice University Hospital Center, Department of Otorhinolaryngology - Head

**Introduction:** Hypothyroidism is the most frequent endocrine dysfunction and is found in 2-10% of the population. It presents numerous symptoms and appears as clinical or subclinical disease. Hypothyroidism treatment is connected to the following dilemmas: 1) which is the normal thyrotropine (TSH) level, 2) which TSH target value is to be achieved by substitution therapy and 3) is the combined levothyroxine (LT4)-levotriiodothyronine (LT3) treatment superior to LT4 monotherapy alone. The objectives of hypothyroidism substitution therapy are: 1) ensure a complete physical and psychological capacity and 2) attain a normal value of the thyroid hormones, in particular the TSH. Normal TSH serum values are the major indicator of well treated hypothyroidism. The optimal TSH target value to be achieved has not been clearly established and vastly depends on the patient's age group. The role of T4 in the suppression of TSH release and the regulation of pituitary-thyroid feedback is well defined. Whether this mechanism functions equally in hypothyroidism/athyreosis as in healthy people is not entirely certain.

**Hypothesis:** Pituitary-thyroid feedback control is impaired in hypothyroid and athyreotic patients.

**Aims:** 1) Test the efficacy of T4 in suppressing the release of TSH in hypothyroidism and athyreosis. 2) Assess the impact of the altered metabolism of T3 on pituitary-thyroid feedback

control. 3) Establish the differences in the pituitary-thyroid feedback control between hypothyroid and athyreotic patients.

**Materials and methods:** This retrospective study will encompass 250 hypothyroid and 110 athyreotic patients selected by random choice. All selected patients were treated with T4 over a minimum of 12 months. Normal TSH serum concentration was considered as the main parameter of successful treatment. The control group will cover 210 healthy persons. A T4/TSH (TSH Suppressibility Index -TSI) will be calculated in all examinees, showing T4 capacity in inducing suppression of TSH. The T3/TSH ratio (parameter of the contribution of T3 in TSH suppression) will be calculated as well as the T4/T3 ratio (parameter of T3 converting from exogenous LT4). Statistical analysis will be performed with licenced software STATISTICA 10.0 ([www.statsoft.com](http://www.statsoft.com)).

**Expected scientific contribution:** This study will analyse pituitary-thyroid feedback control and define the role of T3 in TSH suppression in hypothyroid and athyreotic patients, indicating possible benefits of the combined application of LT4 and LT3 in substitution therapy.

**Acknowledgments:**

**MeSH/Keywords:** Pituitary, Thyroid, Hypothyroidism, Athyreosis, TSH, T3, T4, Levothyroxine, Levotriiodothyronine

**Poster code:** B-21-113

## POSTER TITLE: IMMUNOHISTOCHEMICAL EXPRESSION OF PROTEIN NEDD9 IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

**PhD candidate:** Iva Ledinsky

**Part of the thesis:** Immunohistochemical expression of protein NEDD9 in head and neck squamous cell carcinoma

**Mentor/s:** Professor Božena Šarčević, MD, PhD, Marija Pastorčić Grgić, MD, PhD

**Affiliation:** University hospital for tumors University hospital center „Sister of Mercy“, Zagreb

**Introduction:** Head and neck squamous cell carcinoma (HNSCC) is the fifth most common cancer worldwide and the most common cancer of the mucosa of the upper respiratory and digestive system. Patients with HNSCC have significantly impaired quality of life. Although treatment techniques were improved, survival of patients with HNSCC has not been significantly altered in recent decades. New researches are required to discover specific genetic and molecular changes responsible for the onset and development of HNSCC metastatic potential. One of the possible important control points in HNSCC carcinogenesis could be the protein NEDD9. It belongs to a group of CAS proteins, so far the most researched in migration and invasion of cancer. Increased expression of the NEDD9 in breast cancer, melanoma and glioblastoma results in increased metastatic potential and poor patient prognosis. Previous research on the protein NEDD9 are not sufficient to explain its impact on the HNSCC carcinogenesis.

**Hypothesis:** Increased expression of protein NEDD9 in patients with head and neck squamous cell carcinoma is an indicator of poor survival.

**Aims:** The aims of this study are to determine the immunohistochemical expression of protein NEDD9 in HNSCC and regional metastases (neck lymph nodes) and to examine its relationship to the site of the primary process (oral cavity, oropharynx, hypopharynx, larynx), disease stage,

degree of tumor differentiation as well as overall survival.

**Materials and methods:** In the proposed retrospective research, the expression of NEDD9 will be analyzed in patients with HNSCC who have been treated in the period from 2000 to 2006 in our institution. A minimum of 120 patients with primary tumors located in the oral cavity, oropharynx, hypopharynx and larynx and who have been followed up for at least 5 years will be included in the research. Two groups of patients will be compared: group of patients with and without regional metastases. The material used in the study was processed by standard histological methods. One additional cut from each tumor will be immunohistochemically processed with monoclonal antibody for protein NEDD9.

**Expected scientific contribution:** The proposed research will contribute to knowledge on the role of protein NEDD9 in HNSCC carcinogenesis. The comparison of two groups of patients will explain the influence of NEDD9 on metastatic potential. The prognostic value of protein NEDD9 will be determined on patients' five-year survival rate.

**Acknowledgments:** I would like to thank Professor Božena Šarčević and Marija Pastorčić Grgić for their support during this project.

**MeSH/Keywords:** squamous cell carcinoma of the head and neck, NEDD9, survival

**Poster code:** B-21-132



## POSTER TITLE: THYROTROPIN RECEPTOR MRNA (TSHR MRNA) AS A NOVEL MARKER FOR THYROID CANCER

**PhD candidate:** Tomislav Novosel, dr. med

**Part of the thesis:** Thyroid cancer cells in peripheral circulation present normal thyrotropin receptor. Detecting mRNA of the thyrotropin receptor in peripheral circulation indicates thyroid cancer presence.

**Mentor/s:** Prof. Dr. Sc. Vladimir Bedekovic

**Affiliation:** The Cleveland Clinic, Cleveland, Ohio, USA

**Introduction:** Thyroid cancer incidence has been rising in the last 30 years. Early thyroid malignancy diagnosis and early recurrence detection improves patients' survival rate. New thyroid cancer tumor marker for thyroid cancer identification or thyroid cancer recurrence would improve patient care and position it to the higher level. Existing thyroid cancer tumor marker, thyroglobulin, is overall good tumor marker for recurrence detection but it has limits.

**Hypothesis:** Detection of the thyrotropin receptor mRNA (TSHR mRNA) in peripheral circulation is correlated with differentiated thyroid cancer diagnosis.

**Aims:** The aim of this study is to investigate presence of the TSHR mRNA in patients with differentiated thyroid cancer, measure TSHR mRNA concentration in peripheral circulation and correlate TSHR mRNA concentration with thyroid cancer presence.

**Materials and methods:** In this institutional review board approved retrospective study thyrotropin receptor messenger RNA (TSHR mRNA) will be analyzed in patients with thyroid nodules, as well as thyroid cancer characteristics (tumor size, multifocality, specimen weight, lymph node status, histologic subtype, thyroglobulin level). TSHR mRNA measurements were performed using quantitative real-time reverse transcriptase polymerase chain reaction. This method extracts total RNA from the cellular fraction of a peripheral blood sample, and then amplifies

mRNA specific for the TSHR using specifically designed primers. Approximately 10 cancer cells per milliliter of blood can be detected. Optimum sensitivity and specificity performance have been defined when TSHR mRNA levels  $>1$  ng/ug are interpreted to signify the presence of thyroid cancer. Statistical analysis will be performed using JMP 7.0 (SAS Institute) software. The Chi-square test for association will be used to study the relationship between TSHR mRNA, tumor size, multifocality and lymph node status. The 2-sample t test will be used to examine differences in positive and negative TSHR mRNA values as a function of tumor size, specimen weight, preoperative thyroglobulin, tumor size and multifocality. The level of statistical significance for this study will be defined as  $P < 0.05$ .

**Expected scientific contribution:** In this study will be investigated the presence of available tumor markers for differentiated thyroid cancer in peripheral circulation, the presence of novel tumor marker for thyroid cancer and impact of available and novel tumor markers for thyroid cancer treatment as well as diagnostic and prognostic value of new thyroid cancer tumor marker.

**Acknowledgments:** This study was performed during research fellowship at endocrine surgery department at The Cleveland Clinic.

**MeSH/Keywords:** neoplasm, circulating cell, receptor, RNA, thyroglobulin, thyroid cancer, tumor marker

**Poster code:** B-21-136

# POSTER TITLE: ROLE OF MATRIX METALLOPROTEINASES AND THEIR INHIBITORS IN THE DEVELOPMENT OF CERVICAL METASTASES IN PAPILLARY THYROID CARCINOMA

**PhD candidate:** Boris Bumber, MD

**Part of the thesis:** Matrix Metalloproteinases And Their Inhibitors In Papillary Thyroid Carcinoma

**Mentor/s:** Associate Professor Drago Prgomet, MD, PhD

**Affiliation:** University Hospital Centre - Zagreb

**Introduction:** Matrix metalloproteinases (MMPs) are zinc-dependent endopeptidases, enzymes capable of degrading all kinds of extracellular matrix proteins. MMPs also thought to play a major role on cell behaviors such as cell proliferation, migration, differentiation, angiogenesis, apoptosis. A number of MMPs have been strongly implicated in multiple stages of cancer progression including the acquisition of invasive and metastatic properties. In particular, MMP-1 (Interstitial Collagenase), MMP-2 (Gelatinase A), and MMP-9 (Gelatinase B) have strongly been implicated in the induction of the local invasiveness, angiogenic switch and metastasis of certain tumors. TIMPs are the major endogenous regulators of MMP activities in the tissue, and four homologous TIMPs (TIMPs-1 to -4) have been identified to date capable of inhibiting the activities of all known matrix metalloproteinases (MMPs) and as such play a key role in maintaining the balance between extracellular matrix (ECM) deposition and degradation in different physiological processes. TIMP-1 and TIMP-2 can inhibit tumor growth, invasion, and metastasis in experimental models which has been associated with their MMP inhibitory activity. TIMP-1 and TIMP-2 have mitogenic activities on a number of cell types, whereas overexpression of these inhibitors reduces tumor cell growth.

**Hypothesis:** MMPs (MMP-1, MMP-2, MMP-9) and TIMPs (TIMP-1 and TIMP-2) may play a role in

pattern of metastatic process in papillary thyroid cancer

**Aims:** Aim of the study is to explore the connection between MMPs and TIMPs with the pattern of metastatic process in metastatic papillary thyroid carcinoma and to define biomarkers for prognosis and progression of metastatic process in papillary thyroid cancer.

**Materials and methods:** Tissue samples of papillary thyroid carcinoma and metastatic papillary thyroid carcinoma will be collected. All patients were operated by the same surgeon. 100 samples of papillary metastatic thyroid cancer (study group) and 50 samples of papillary thyroid carcinoma without metastases will be analyzed. Resected specimens fixed with formalin and embedded in paraffin will be subjected to immunohistochemistry analysis.

**Expected scientific contribution:** Exploring potential biomarkers for prediction of the development of malignant disease can have a significant impact on the understanding of the physiology of malignant tumors.

**Acknowledgments:**

**MeSH/Keywords:** MMP, TIMP, papillary thyroid cancer, metastasis

**Poster code:** B-21-174

## POSTER TITLE: ROLE OF RHO/RHO-KINASE SIGNALING PATHWAYS IN DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN THE EXPERIMENTAL RAT MODEL

**PhD candidate:** Qendresa Beqiraj MD

**Part of the thesis:** Role of Rho/Rho-kinase signaling pathways in development of bronchopulmonary dysplasia in the experimental rat model

**Mentor/s:** Prof.Dr.Muharrem Jakupaj, Prof.Dr.sc. Zdenko Kovač

**Affiliation:** University of Prishtina Faculty of Medicine, University Clinical Centre of Kosovo

**Introduction:** In the rat model of bronchopulmonary dysplasia induced by hyperoxia we plan to test a contribution of kinase pathways to the development of disease. Basic hypothesis of the research assumes that Rho/Rho kinase and MAPK kinase may be contributing factors in development of hypercontractile state and the delayed relaxations of muscles. The expression of Rho and MAPK kinase may contribute to disorder of tissue morphogenesis. Using the pharmacological inhibitors in vivo and in vitro will enable us to test a potential contribution of those pathways to disease development. Experimental and control groups of animals will consist of 10 rats per group and data will be statistically analyzed.

**Hypothesis:** Hyperoxia contributes to the BPD by upregulation of the Rho/Rho-kinase pathway.

**Aims:** The study of ethiopathogenetic pathways, using animal BPD model may contribute to better treatment and prevention of the diseases in patients.

**Materials and methods:** On day 5th of the life, Sprague Dawley rat pups will be exposed to hyperoxia or room air for seven days. Then the animals will be sacrificed, trachea and lungs will be taken, placed in Krebs-Henseleit (KH) solution, pH=7.4 and serve for in vitro studies.

Segments of trachea will be placed in the organ baths, filled with KH solution continuously aerated with the mixture of gases 95% O<sub>2</sub> and 5% CO<sub>2</sub>. They will connect to the isometric force displacement transducer and responses will be recorded digitally via power lab and chart program included in the four channel tissue organ bath system. For contraction studies, tissues will be stimulated with methacholine or with growth factors such as insulin-like growth factor-1, in absence or presence of Rho-kinase inhibitors, 30 min prior induce of contraction. In another set of experiments, Rho-kinase inhibitors daily will be injected in vivo to the rat pups during hyperoxic or room air exposure, then the effect will be tested under in vitro conditions.

**Expected scientific contribution:** Evaluation of the role of Rho/Rho-kinase and MAPK-kinase pathway in the BPD in the rat model may useful model for investigation and prevention of BPD as well as hyperoxia effects.

**Acknowledgments:** I would like to thank Professor Muharrem Jakupi and Professor Zdenko Kovač, providing me with much needed advice regarding this research.

**MeSH/Keywords:** Bronchopulmonary dysplasia, hyperoxia, kinase-inhibitors

**Poster code:** B-22-156

## POSTER TITLE: COMPARISON OF CLASSICAL AND ADVANCED DIAGNOSTIC TOOLS IN BONE TUMORS

**PhD candidate:** Ardita Qerimi MD

**Part of the thesis:** Comparison of classical and advanced diagnostic tools in bone tumors

**Mentor/s:** Professor Sven Seiwerth, MD, PhD, Professor Vesna Janevska MD, PhD

**Affiliation:** University of Zagreb, School of Medicine, Institute of Pathology

**Introduction:** Bone tumor diagnosis still mainly relies on the classical combination of clinical data and radiological -pathological correlation. However just recently some breakthrough in molecular diagnostics add new light into this diagnostic field. Combination of immunohistochemical and molecular methods can improve the diagnostic capacity in thesis changing also the therapeutic approach to a given patient.

**Hypothesis:** Application of advanced diagnostic techniques will give additional value to the diagnostic procedure of a selected group of bone tumors.

**Aims:** Reclassify a group of bone tumours using standard diagnostic protocol and compare the results with the results obtained using advanced diagnostic techniques.

**Materials and methods:** Samples from 60 patients with bone tumours will be included in the study. Paraffin blocks containing tumor tissue will be retrieved from the archives of Institute of pathology University of Zagreb School of Medicine and Institute of Pathology University of Skopje. The tumours included in the study will be Langerhans cell histiocytosis (Eosynophilic granuloma), Ewing sarcoma, Giant cell tumour of bone and Aneurysmal bone cyst. Additional fifteen giant cell lesions (non-ossifying fibroma, osteosarcoma and MFH) will be included as

controls. Tumors will be reclassified using histological review and additional methods - both immunohistochemical and molecular. In Ewing sarcoma EWS/FLI1 fusion will be demonstrated using RT-PCR in addition to immunohistochemical demonstration of FLI1 and CD99 in order to differentiate from other small cell neoplasms, Giant cell tumours will be stained immunohistochemically for CD 68 and p63 in order to differentiate them from other giant cell lesions Langerhans cell histiocytosis the demonstration of CD1a positive cell will be performed and in Aneurysmal bone cysts a characteristic USP6 Break apart demonstrable with FISH will serve for determination whether the lesion is a primary or a secondary one. Clinical (size, site, radiological appearance, therapeutic procedure) and demographic data will also be included in the study as well as survival.

**Expected scientific contribution:** Proposed research will contribute in revealing the usefulness of advanced diagnostic techniques in bone tumor diagnosis.

**Acknowledgments:** Proposed research will contribute in revealing the usefulness of advanced diagnostic techniques in bone tumor diagnosis.

**MeSH/Keywords:** Giant cell tumor, Aneurysmal bone cyst, Ewing sarcoma

**Poster code:** B-23-163

## POSTER TITLE: COMPARISON OF PLEURAL LESIONS USING VIBRATIONAL SPECTROSCOPY

**PhD candidate:** Fatlinda Sadiku Zehri MD

**Part of the thesis:** Comparison of pleural lesions using vibrational spectroscopy

**Mentor/s:** Prof. Dr. Sven Seiwerth and Doc. Dr. Ozren Gamulin

**Affiliation:** University of Zagreb, School of Medicine, Department of Pathology and Department of Physics and Biophysics

**Introduction:** Vibrational spectroscopy can provide information on biological materials. Any changes leading to disease are due to some biochemical changes in components that it is composed of. The vibrational spectra are sensitive to the structure of these components, so they can change with the diseased state. The aim of this study is to compare the vibrational spectra of normal pleura, pleura with inflammatory changes, with primary neoplastic disease and with metastatic disease. This way we can add vibrational spectroscopy as a possible additional tool in differential diagnosis of pleural lesions.

**Hypothesis:** Vibrational spectra of normal pleura, pleura with inflammatory changes, with primary neoplastic disease and with metastatic disease will be different and in this constitute a potentially useful tool in the differential diagnosis of pleural pathology.

**Aims:** Correlation between morphological entities and vibrational spectra achieved with vibrational spectroscopy. Comparison of vibration spectra of normal pleura, pleura with inflammatory changes, with primary neoplastic disease and metastatic disease.

**Materials and methods:** We will choose the data for 10 patients who have had a resection of mesothelioma of the pleura, 10 patients with pleuritis, 10 patients with metastatic tumours in pleura and 10 normal pleura. Then, take the paraffin blocks from the archive, from which we will cut and prepare 20 new tissue sections

5 micrometers thick, from each block. New tissue sections will be put on optical grade silicon windows and paraffin will be removed following standard histology protocols. At the end samples will be placed in vacuum for 10 minutes to extract remaining water. Vibrational spectra of prepared samples will be recorded with PERKIN-Elmer SPECTRUM GX spectrometer. Vibrational spectra of each of tissue type will be recorded for more than 10 spectra for later statistical analysis. Vibrational spectra of each type of lesion will be compared with vibrational spectra of the normal pleura. Statistical methods which we will use to report the results are multivariate methods (PCA, STT, standard deviation) and descriptive statistics.

**Expected scientific contribution:** This study is the first in using these methods in tissue sections of pleura and pleural lesions. It is expected that this research will confirm the correlation between different types of lesions and their vibrational spectra. This approach will contribute in better determination and differentiation of specific pleural lesions.

**Acknowledgments:** I would like to thank Prof. Dr. Sven Seiwerth and Doc. Dr. Ozren Gamulin for great support, advice and help.

**MeSH/Keywords:** Pleura, Pleuritis, Mesothelioma, metastatic tumours, vibrational spectroscopy

**Poster code:** B-23-86

## **POSTER TITLE: NEDD9 AS A PANCREATIC ADENOCARCINOMA METASTASIS GENE**

**PhD candidate:** Petra Radulović, dr.med.

**Part of the thesis:** Expression of NEDD9, gamma-catenin and e-cadherin in pancreatic adenocarcinoma

**Mentor/s:** Professor Božo Krušlin, MD, PhD

**Affiliation:** University Hospital Centre

**Introduction:** Early metastasis is a hallmark of pancreatic ductal adenocarcinoma and responsible for more than 90% of pancreatic cancer death. Since patient outcome is not reliably predicted using pathological factors (tumor stage, differentiation, resection margin status) alone, markers of tumor behaviour are needed. One among candidates is NEDD 9 (HEF-1/CAS-L), recently identified as a key protein in tumor cell proliferation and migration. There are no studies so far that investigate the role of this protein in pancreatic adenocarcinoma.

**Hypothesis:** Overexpression of NEDD9 negatively regulates e-cadherin and gamma-catenin expression thus promoting epithelial-mesenchymal transition, tumor progression and invasion.

**Aims:** To investigate the expression of NEDD9, gamma-catenin and e-cadherin in pancreatic carcinoma and its relationship with the clinicopathologic characteristics.

**Materials and methods:** Expression of NEDD9, gamma-catenin and e-cadherin will be analysed

in 50 cases of pancreatic adenocarcinoma and 50 samples of normal pancreatic tissue measuring the intensity of immunohistochemical staining as well as the percent of positive tumor cells in tissue sample. Before mentioned markers will be correlated with the clinicopathologic parameters (age, gender, tumor size, histological grade, lymphovascular and perineural invasion, lymph node status, resection margins).

**Expected scientific contribution:** Differences among NEDD9, gamma-catenin, and e-cadherin expression in pancreatic adenocarcinoma and normal pancreatic tissue could give new insight in differential diagnostics between pancreatic carcinoma and non-neoplastic lesions, as well as reveal new targeting molecules for treatment of pancreatic adenocarcinoma.

**Acknowledgments:**

**MeSH/Keywords:** pancreatic adenocarcinoma, nedd9, e-cadherin, gamma-catenin

**Poster code:** B-23-64

## POSTER TITLE: EXPRESSION OF PIWIL2 AND HMGA2 IN PAPILLARY THYROID CARCINOMA

**PhD candidate:** Sandra Moslavac MD

**Part of the thesis:** The level of expression of Piwil2 and HMGA2 in papillary thyroid carcinoma

**Mentor/s:** Professor Hrvoje Čupić, MD, PhD

**Affiliation:** University Hospital Centre 'Sestre milosrdnice', Polyclinic 'Sunce'

**Introduction:** Recent studies have demonstrated that Piwil2 and HMGA2 are expressed in various types of human cancers with the lack of expression in the normal tissue. Unlike HMGA2 expression, Piwil2 expression in thyroid has not been investigated. The aim of this study is immunohistochemical analysis of Piwil2 and HMGA2 expression in papillary thyroid carcinomas (PTC) with and without regional lymph node (RLN) metastases, follicular adenomas, hyperplastic nodules and normal thyroid tissue.

**Hypothesis:** The level of expression of Piwil2 and HMGA2 is significantly higher in papillary carcinomas with metastases by comparison to papillary thyroid carcinomas without metastases.

**Aims:** To analyse Piwil2 and HMGA2 expression in PTC with and without RLN metastases and in follicular adenomas, hyperplastic nodules and normal thyroid tissue. To compare Piwil2 and HMGA2 expression in PTC with RLN metastases with the expression in PTC without RLN metastases and in PTC with and without RLN metastases with the expression in follicular adenomas and hyperplastic nodules. To compare Piwil2 and HMGA2 expression with histological grade and clinical parameters including age, gender and tumour size.

**Materials and methods:** Immunohistochemical expression of before mentioned markers in analysed groups will be compared and correlated with the histological grade and clinical parameters. The archival paraffin blocks of at least 30 patients with PTC and RLN metastases, 30 patients with PTC without RLN metastases, 30 patients with follicular adenomas and 30 patients with hyperplastic nodules will be used in the study.

**Expected scientific contribution:** The subgroup of patients with PTC and higher risk of more aggressive biological behaviour could be identified based on the expression of Piwil2 and HMGA2. Hypothetical results would allow less extensive therapy approach in patients with prospect of advantageous clinical course as well as adequate therapy in patients with more aggressive biological behaviour regarding the expression of analysed tumor markers.

**Acknowledgments:** I would like to thank to all those who gave me the possibility to complete this thesis, especially to my mentor, professor Hrvoje Čupić, MD, PhD.

**MeSH/Keywords:** papillary thyroid carcinoma, Piwil2, HMGA2

**Poster code:** B-23-76

## **POSTER TITLE: THE FREQUENCY AND TREND OF FACTOR CONCENTRATES' USAGE IN CHILDREN DIAGNOSED WITH HAEMOPHILIA IN CROATIA FROM 2008 TO 2012**

**PhD candidate:** Petra Jurčić, MD

**Part of the thesis:** The frequency and trend of factor concentrates' usage in children diagnosed with haemophilia in Croatia from 2008 to 2012

**Mentor/s:** Ernest Bilić, MD, Associate Professor

**Affiliation:** Department of Haematology and Oncology, Pediatric Clinic, Zagreb University Hospital Center, Zagreb

**Introduction:** Haemophilia is a rare hereditary disorder that impairs blood clotting. Haemophilia A is caused by a functional factor VIII deficiency and is present in about 1 in 10,000 male births while haemophilia B is caused by a factor IX deficiency which occurs in one per 60000 male births. It is a hereditary X-linked recessive disorder. In 30% of haemophilia patients, the disorder appears as a result of new mutations. Haemophilia cannot be clinically distinguished and it is usually manifested by the end of the first year of a child's life by means of excessive bleeding in different parts of the body. Depending on the level of active clotting factor deficiency in blood plasma, haemophilia is classified as severe ( $F < 1\%$ ), moderate ( $F 1-5\%$ ) and mild ( $F > 5\%$ ). The haemophilia diagnosis is set by determining the level of active factors.

**Hypothesis:** The incidence and prevalence of various forms of haemophilia will match the data from developed countries and, while we believe the average and total reported annual consumption of factor concentrates to be lower than that reported in developed countries, we also expect a noticeable consumption growth trend when comparing the data from 2008 to those from 2012.

**Aims:** Our objectives are to demonstrate the incidence of haemophilia A and B in children, to determine the prevalence of haemophilia A and

B among other hereditary blood clotting disorders, according to the severity of the disease, and also to determine which treatment is most commonly used and how many children are undergoing prophylactic treatment.

**Materials and methods:** The examinees in this study were children with haemophilia treated in the period from January 1, 2008 to December 31, 2012 in the Reference Centre for Paediatric Haematology and Oncology of the Republic of Croatia which is located at the Department of Paediatrics in the University Hospital Centre Zagreb. Treatment data were collected after reviewing medical records, outpatient records and medical history. IBM SPSS software, version 19.0.0. will be used for a statistical analysis of the data.  $p < 0,05$  was defined as the limit of significance for all tests.

**Expected scientific contribution:** Due to the fact that there is no registry of people suffering from haemophilia in the Republic of Croatia, the results of this study will contribute to a better understanding of the treatment and of the disease at a young age.

**Acknowledgments:**

**MeSH/Keywords:** haemophilia, factor VIII, factor IX

**Poster code:** B-24-43



## POSTER TITLE: THE CORRELATION OF ANTISTREPTOLYSIN O LEVEL WITH CHILDHOOD ATTENTION DEFICIT, HYPERACTIVITY AND IMPULSIVITY DISORDER

**PhD candidate:** Tamara Žigman, MD

**Part of the thesis:** The Correlation of Antistreptolysin O level with Childhood Attention Deficit, Hyperactivity and Impulsivity Disorder

**Mentor/s:** Professor Ljerka Cvitanović- Šojat, MD, PhD

**Affiliation:** Pediatric Clinic, University Hospital Centre Sisters of Charity

**Introduction:** In the mid 20th century, rheumatic fever was described as an acute, non-suppurative sequel of acute streptococcal infection. In 10-15% of patients it manifested as Sydenham chorea, sometimes after a very long latency period. In 1998, Swedo et al. described the first 50 patients with PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder associated with streptococcal infections) and set the clinical diagnostic criteria. In May 2012, it was proposed by Swedo herself to change the term PANDAS to PANS/CANS (Pediatric Acute-onset Neuropsychiatric Syndrome/Childhood Acute Neuropsychiatric Symptoms). PANS/CANS includes the simultaneous presence of additional neuropsychiatric disorders, beside obsessive-compulsive activities and tics that were the primary characteristics of PANDAS. ADHD was described for the first time way back in 1902. It is characterized by attention deficit and developmentally inappropriate hyperactivity and impulsivity, and as such may constitute PANS/CANS. Antistreptolysin O titer (ASO titer) is the most widely used antibody to streptococcal antigen (streptolysin O).

**Hypothesis:** Elevated level of antistreptolysin O titer is associated with childhood attention deficit, hyperactivity and impulsivity disorder.

**Aims:** The main goal of this study is to determine whether there is association of elevated antistreptolysin O titer with childhood attention deficit, hyperactivity and impulsivity disorder.

der. Some additional goals will result from the study.

**Materials and methods:** The study group will consist of 75 children of both sexes, age range 5-15 years, who have symptoms of ADHD. The control group will consist of 150 children without symptoms of ADHD that will be strictly matched with the study group according to age and gender. ADHD will be diagnosed with ADHD-test, standardized test translated to Croatian language. To evaluate the influence of predictor variable (ASO titer) on dependant variables (ADHD quotient, subtest standardized values), the method of multiple linear regression will be used.

**Expected scientific contribution:** After the research, we will be able to answer two very important questions that represent the current scientific debate, as pointed out in the introduction. 1. Whether and to what extent are ADHD symptoms associated with acute streptococcal infections? 2. Can we include the ADHD spectrum disorders in the spectrum of PANS/CANS triggered with acute streptococcal infection?

**Acknowledgments:** I thank to my menthor, Professor Ljerka Cvitanović- Šojat for her comprehensive support in all aspects of life

**MeSH/Keywords:** attention deficit, hyperactivity and impulsivity disorder, antistreptolysin O titer, children

**Poster code:** B-24-62

## **POSTER TITLE: DETERMINATION OF EARLY ATHEROSCLEROTIC CHANGES IN CHILDREN WHO SUFFER FROM JUVENILE IDIOPATHIC ARTHRITIS**

**PhD candidate:** Iva Rukavina, MD

**Part of the thesis:** Children who suffer from juvenile idiopathic arthritis have early atherosclerotic changes

**Mentor/s:** Assistant of Professor Marija Jelušić Dražić, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** Atherosclerosis commences in childhood but manifests clinically later in life. Besides usual risk factors, nowadays more attention has been given to its inflammatory etiology, what actually makes atherosclerosis an inflammatory disease. Similarity between atherosclerotic process and inflammatory changes in the course of systemic connective tissue disease (included juvenile idiopathic arthritis (JIA)) has been noticed. JIA is arthritis started at child's age, before age of 16. In order to prevent disease progression it is important to look for signs of premature atherosclerosis. Like good and non-invasive methods that can be used in this purpose are determination of intima media thickness of carotid arteries and measuring of arterial stiffness. Usage of this methods in everyday clinical practice could contribute to identification of signs of premature atherosclerosis and starting action for slowing down its development.

**Hypothesis:** Children who suffer from juvenile idiopathic arthritis have early atherosclerotic changes.

**Aims:** Determine whether children who suffer from juvenile idiopathic arthritis have early atherosclerotic changes.

**Materials and methods:** The study design is a case - control trial including 60 JIA patients di-

vided into two groups - early JIA patients and patients who suffer from disease 5-7 years, and 30 age and sex matched healthy controls. Intima - media thickness of common carotid artery and determination of parameters of arterial stiffness were measured by high - resolution ultrasonography. Laboratory investigations include total cholesterol, HDL, LDL, triglycerides, lipoprotein (a), C - reactive protein, fibrinogen, factor VIII, aggregation of platelets, MTHFR analysis, homocysteine and vitamin D. Disease activity indexes will be measured by JADAS 10, JAFS and PRQL score. Normality of data distribution will be analysed using the Kolmogorov - Smirnov test. Depending on results, adequate parametric and/or non-parametric statistical analyses will be done.

**Expected scientific contribution:** Implementation of this methods in everyday clinical practice could contribute to identification of signs of premature atherosclerosis at JIA patients and starting action for slowing down its development on time.

**Acknowledgments:**

**MeSH/Keywords:** atherosclerosis, juvenile idiopathic arthritis, intima media thickness, arterial stiffness

**Poster code:** B-24-173

## **POSTER TITLE: VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN SERUM AND BASIC FIBROBLAST GROWTH FACTOR (bFGF) IN URINE IN CHILDREN WITH HEMANGIOMAS**

**PhD candidate:** Arnes Rešić, MD

**Part of the thesis:** Importance of determining vascular endothelial growth factor (VEGF) in serum and basic fibroblast growth factor (bFGF) in urine in children with hemangiomas.

**Mentor/s:** Assistant professor Ante Čizmić, MD, PhD

**Affiliation:** Children's Hospital Zagreb

**Introduction:** Hemangiomas are the most common benign vascular tumors of infancy, with an incidence of 5 to 10%. They are characterized by rapid growth in infancy (proliferative phase), followed by slow regression occurring between the age of 2 to 7 years, often leading to complete involution with different clinical outcomes. Pathogenesis of hemangioma is not yet fully understood. Dysregulation of angiogenesis represents a possible mechanism in the pathogenesis of hemangioma. In addition to hypoxia, the most important inducers of angiogenesis, that is associated with the growth of hemangiomas, are vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF).

**Hypothesis:** In the proliferative phase are expected elevated levels of vascular endothelial growth factor (VEGF) in the serum and basic fibroblast growth factor (bFGF) in the urine as compared to involutive phase values and in healthy controls.

**Aims:** The aim of this study is to investigate the importance of determining VEGF in serum and bFGF in urine in various stages of growth of hemangiomas in children.

**Materials and methods:** This is a prospective study of research pairs (case-control study), which will include fifty patients (N = 50) with hemangiomas in the stage of proliferation and

fifty patients (N = 50) with hemangiomas in the involution phase and hundred healthy patients (N = 100) as a control group of comparable age and sex of the patient group. Immunoassay (ELISA) shall be determined by the value of VEGF and bFGF in serum and urine in the proliferative phase of hemangioma growth and involution phase of the hemangioma. The results will be compared with the results of the analysis of the control group of children of comparable age and sex, by analyzing data such as age and gender of the child, occurrence of solitary or multiple hemangioma, places of origin hemangioma, type of hemangioma, extracutaneous manifestations, complications and association with other anomalies in the syndromes, as well as the results of the treatment procedures.

**Expected scientific contribution:** The results of this study will contribute to a better understanding of the pathogenesis of hemangioma, the course of disease, and to more accurate predictions of outcomes and planning of therapeutic interventions.

**Acknowledgments:**

**MeSH/Keywords:** hemangiomas, angiogenesis, vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF)

**Poster code:** B-24-81

## POSTER TITLE: MYOTONIC DISCHARGES IN CHILDREN WITH RADICULOPATHY

**PhD candidate:** Ivan Lehman, MD

**Part of the thesis:** Myotonia in children due to radiculopathy

**Mentor/s:** Nina Barišić

**Affiliation:** University of Zagreb, School of Medicine, University Hospital Centre Zagreb, Department of Paediatrics

**Introduction:** Peripheral nerves' hyperexcitability (neuromyotonia) is a disorder that is present not only in muscle dystrophies and congenital myotonia but also in a heterogeneous group of disorders including myositis, myasthenia gravis and other non specific disorders with myopathic changes. Myotonia is also connected with autoimmune diseases, especially in disorders involving humoral immunity, some of them involving central nervous system. In contrast to myotonic dystrophy, myotonia in other disorders is present due to changed cell membrane excitability because of ion channels dysfunction (primarily sodium and chloride channels). Myotonia is detected by electrophysiological studies as a spontaneous activity and can be easily recognized. Myotonia has not been previously described in patients with radiculopathy. In our preliminary study 36% of patients with neuromyotonia had signs of radiculopathy.

**Hypothesis:** Neuromyotonia in patients with excluded myotonic dystrophy and congenital myotonia can be a sign of radiculopathy.

**Aims:** The aim of the study is to select a group of patients (children) with neuromyotonia and signs of radiculopathy and negative to myotonic dystrophy and congenital myotonia and to determine the connection with these two entities. Secondly, to propose the possible mechanisms

of motor nerves' hyperexcitability including congenital (genetic) disorders of ion channels.

**Materials and methods:** Children with signs of peripheral nervous system disorder will be electrophysiologically tested (electromyoneurography). In children with neuromyotonia and signs of radiculopathy genetic testing will be performed to exclude myotonic dystrophy and congenital myotonia. Testing for possible causes of radiculopathy (X rays, MRI, and lumbar tap) will be performed in others. Statistical analysis will be performed to confirm connection between radiculopathy and myotonia. All patients or their parents will sign informed content.

**Expected scientific contribution:** Expected scientific contribution is to confirm myotonia as easily recognisable electrophysiological sign that can be present in patients with radiculopathy and to confirm genetic predisposition (ion channels mutations) as a possible factor of peripheral motor nerves hyperexcitability in patients with radiculopathy.

**Acknowledgments:**

**MeSH/Keywords:** radiculopathy, electrophysiology, myotonia, child,

**Poster code:** B-24-129

## POSTER TITLE: CLINICAL, BIOCHEMICAL AND GENETICAL CHARACTERISTICS OF ALBANIAN PEDIATRIC CELIAC DISEASE PATIENTS FROM KOSOVO

**PhD candidate:** Atifete Ramosaj Morina

**Part of the thesis:** Clinical, biochemical and genetical characteristics of Albanian pediatric celiac disease patients from Kosovo

**Mentor/s:** Ass. Prof. Renata Žunec, Prof. Mehmedali Azemi, MD

**Affiliation:** Department of Transfusion Medicine and transplantation biology, Tissue Typing Centre, Clinical Hospital Centre Zagreb1, Pediatric Clinic, Department of Gastroenterology, University Clinical Centre of K

**Introduction:** CD is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations, CD-specific antibodies, HLA-DQ2 or HLA-DQ8 haplotypes, and enteropathy.

**Hypothesis:** An increasing incidence of CD in Albanian children from Kosovo can be expected, as it is the case in other European countries. Autoantibody testing results, intestinal biopsy findings and HLA typing will provide data for the future cost effective and efficient diagnostic algorithm appropriate for the primary care setting in Kosovo. Additionally, some specific HLA haplotypes may be expected, especially in non DQ2/DQ8 patients. Genetic testing may be introduced in at-risk relatives of patients

**Aims:** General: provide data about clinical and pathological spectrum of CD in this population. Specific: 1. Obtain results about sensitivity and specificity of serum EMA, anti-TG2, anti-DGP tests. 2. Analyse HLA-DRB1, DQA1 and DQB1 class II polymorphisms. 3. Determine HLA predisposing factors. 4. Compare the HLA gene and haplotype frequency data with other European populations. 5. Determine population specific HLA genes and haplotypes involved in disease predisposition.

**Materials and methods:** Forty children, treated in Pediatric Clinic, University Clinical Centre of Kosova, 9 months to 18 years old will be involved in this study as Participants. Data on personal (name, age), family (diseases with familiar predispositions) and medical data (signs and symptoms) will be recorded through individual interviews. All patients doubted to have CD will be tested for specific anti-bodies included anti-TG2, anti-DGP and EMA, class A immunoglobulin. In IgA-deficient patients with CD, IgG class of antibodies will be tested. To investigate genetic predisposition to CD, patients positive for specific antibodies will be tested for HLA-Dr, DQA1 and DQB1 allele polymorphisms. All patients admitting the conditions will undergo for upper endoscopy and biopsies.

**Expected scientific contribution:** This will be the first systematic research of celiac disease in Albanian children from Kosovo. It will provide data about prevalence, clinical presentation and serum celiac disease-related antibody profile. The study of HLA polymorphism will reveal predisposing and population specific genes and haplotypes in this population.

**Acknowledgments:**

**MeSH/Keywords:** Celiac disease, Kosovo, children, HLA heterodimer, antibodies

**Poster code:** B-24-126

## POSTER TITLE: THE IMPACT OF RISK FACTORS IN EARLY LIFE ON DEVELOPMENT OF ALLERGIC SENSITIZATION

**PhD candidate:** Helena Tesari Crnković

**Part of the thesis:** The Impact of Risk factors in Early Life on Development of Allergic Sensitization in Newborns whose Parents Have Asthma and/or Hay Fever

**Mentor/s:** Professor Neda Aberle, MD, PhD and Krešo Bendelja, PhD

**Affiliation:** General County Hospital Požega, Institute of Immunology

**Introduction:** Atopic hypersensitivities are based on interaction between environmental influences and genetic predisposition. It is assumed that respiratory viral infections, especially by respiratory syncytial virus (RSV), play a promoting role in allergic sensitization in children at risk for developing allergy. RSV-specific immunoglobulin E (IgE) and immunoglobulin G4 (IgG4) antibodies are detected in some of the infected children. That group of children can be susceptible of post RSV-allergic sensitization due to present Th2 immune reaction initiated by RSV.

**Hypothesis:** RSV infection in infancy contributes to early allergic sensitization development together with other environmental risk factors and familiar anamnesis positive for atopy.

**Aims:** To determine presence and impact of prenatal and postnatal risk factors in neonates with familiar anamnesis positive for atopy and/or asthma, evaluate a role of RSV infection in infancy and presence of RSV-specific IgE and IgG4 antibodies on allergic sensitization development during the first two years of life.

**Materials and methods:** The prospective birth cohort study will include 270 children born in General County Hospital Požega. Anamnestic data and prenatal risk factors (exposure to environmental tobacco smoke, maternal age at menarche, uterine complications, previous oral contraceptive pill and paracetamol use) will be

assessed. The absolute eosinophil count and the level of total immunoglobulin E (IgE) will be determined in the cord blood. Gestational age, birth weight, head circumference, breastfeeding duration, time of solid food introduction, exposition to tobacco smoke, pet exposure, frequency of respiratory infections in the first two years of life, paracetamol and antibiotic use will also be registered. At one and two years of age absolute eosinophil count, total and allergen specific IgE (Dermatophagoides pteronyssinus, grass, tree and weed pollen, cat, dog, cow's milk, egg white, wheat and peanut), RSV-specific IgE, IgG and IgG4 will be determined. At two years of age in children with positive familiar anamnesis for atopy and wheezing episodes skin prick test will be performed.

**Expected scientific contribution:** Former studies have contradictory results. This study can contribute to better comprehension of genetic and environmental factors interaction on atopy development in early childhood which can contribute to early diagnosis, therapy and prevention of allergic diseases.

**Acknowledgments:** I would like to thank my mentors Professor Neda Aberle and Krešo Bendelja for guidance and General County Hospital Požega for financial support.

**MeSH/Keywords:** atopic hypersensitivity, respiratory syncytial virus, children, risk factors

**Poster code:** B-24-135

## POSTER TITLE: THE PREDICTIVE VALUE OF INITIAL SPINAL MRI FINDINGS FOR POST-THERAPEUTIC CLINICAL OUTCOME OF VERTEBRAL OSTEOMYELITIS

**PhD candidate:** Matej Mustapić, MD

**Part of the thesis:** MRI findings and clinical outcome of vertebral osteomyelitis

**Mentor/s:** Klaudija Višković, MD, PhD

**Affiliation:** University Hospital for Infectious Diseases, Zagreb, University Hospital Centre Sisters of Mercy, Zagreb

**Introduction:** Vertebral osteomyelitis accounts for about 1% of bone infections. The possible causes of vertebral infection are bacteria, fungi, or rarely, parasites. The most common bacterial pathogen is *Staphylococcus aureus*. Radiographs are still often used as the first diagnostic procedure, although the changes are observed within 2-8 weeks from the onset of symptoms. Magnetic resonance imaging (MRI) with a paramagnetic contrast agent and fat suppression techniques, shows a high sensitivity (96%), similar to scintigraphy, and specificity similar to computerized tomography (CT) (93%).

**Hypothesis:** The findings of the initial MRI of the spine affect the type of therapeutic treatment (conservative, surgical, or combined) and may predict the clinical outcome of vertebral osteomyelitis after treatment.

**Aims:** To determine the correlation of the initial spinal MRI findings with clinical outcome of vertebral osteomyelitis after treatment. To analyze the correlation of clinical and laboratory findings with clinical outcome of the disease. To analyze the correlation of the initial spinal MRI findings with clinical and laboratory findings. To analyze the correlation of the initial spinal MRI findings with conservative or surgical treatment.

**Materials and methods:** This is a retrospective analysis of data collected from patients treated at the University Hospital for Infectious Dis-

eases, Zagreb, in cooperation with the Clinical Department of Diagnostic and Interventional Radiology, University Hospital Centre Sisters of Mercy, Zagreb, in the period from 2006 to 2010. The study includes 110 participants of both gender, age 18 and over, diagnosed with pyogenic vertebral osteomyelitis by clinical, laboratory and MRI findings. Statistical analysis of demographic and clinical data, laboratory and diagnostic imaging findings, treatment and clinical outcome will be done.

**Expected scientific contribution:** This research provides new insights, because the studies, so far conducted, have not systematically evaluated the correlation of the initial spinal MRI findings at 1.5 T MRI scanners with treatment and clinical outcome of vertebral osteomyelitis. The results of this research may have a significant impact on planning of the treatment of vertebral osteomyelitis after the initial MRI. Systematic retrograde analysis of spinal MRI in patients with known clinical outcome of vertebral osteomyelitis may enable better radiological evaluation in the future and reduce the mistakes in interpretation.

**Acknowledgments:**

**MeSH/Keywords:** vertebral osteomyelitis, magnetic resonance imaging, treatment, clinical outcome

**Poster code:** B-25-18

## **POSTER TITLE: CLINICAL SIGNIFICANCE OF COMPUTED TOMOGRAPHY FINDINGS IN PATIENTS WITH CHRONIC RHINOSINUSITIS**

**PhD candidate:** Tomislav Gregurić, MD

**Part of the thesis:** Correlation of Clinical Symptoms and Radiological Findings in Patients with Chronic Rhinosinusitis

**Mentor/s:** Mentor: Professor Zvonimir Sučić, MD, PhD

**Affiliation:** University Hospital Centre „Sestre milosrdnice“, Zagreb

**Introduction:** The diagnosis of chronic rhinosinusitis is confirmed by the presence of symptoms characteristic for rhinosinusitis and objective findings on endoscopy or computed tomography (CT). Nasal polyposis is considered to be a subgroup of chronic rhinosinusitis. This study evaluates the correlation between the symptoms, quality-of-life questionnaire, and staging on CT in patients with chronic rhinosinusitis, compared to control group. The study will evaluate whether presence of the nasal cavity and paranasal sinus anatomic variations may contribute to severity of symptoms or CT score.

**Hypothesis:** Patients with chronic rhinosinusitis and nasal polyposis have correlation between subjective symptoms characteristic for rhinosinusitis and disease severity on CT imaging. Patients with chronic rhinosinusitis have correlation of symptoms with sinus anatomic variations compared with the control group of patients.

**Aims:** To evaluate correlation between symptom scores, computed tomography findings, and common anatomic variations in chronic rhinosinusitis with and without nasal polyps, comparing to control group. To examine the influence of nasal polyposis on the severity of subjective symptoms and extend of sinus opacification on CT scan. To determine frequency and types of sino-nasal anatomic variations in chronic

rhinosinusitis patients with and without nasal polyposis.

**Materials and methods:** A 100 patients with diagnosis of chronic rhinosinusitis by the EPOS criteria, will be included in the study. They will be classified into two groups depending on the presence of polyps: chronic rhinosinusitis without polyps and chronic rhinosinusitis with polyps. Study will include control group with 60 patients who do not have chronic rhinosinusitis by the EPOS criteria. Before CT scan, patients will complete questionnaire SNOT-22 and visual analog scale (VAS) symptom score. Mucosal changes will be analysed on CT imaging and scored according to Lund-MacKay staging system. Nasal cavity and paranasal sinus anatomic variation will be examined on the same CT imaging.

**Expected scientific contribution:** This study will evaluate correlation between subjective symptoms and objective CT scan findings in different subgroups of chronic rhinosinusitis, and find out whether patients with higher symptom scores are more likely to have more severe CT imaging findings of rhinosinusitis.

**Acknowledgments:**

**MeSH/Keywords:** chronic rhinosinusitis, nasal polyposis, SNOT-22, VAS

**Poster code:** B-25-38



## **POSTER TITLE: NGAL IN EARLY DIAGNOSIS OF CONTRAST INDUCED NEPHROPATHY (CIN)**

**PhD candidate:** Karlo Novačić, MD

**Part of the thesis:** NGAL is superior to serum creatinine in early diagnosis of CIN

**Mentor/s:** Mladen Knotek, MD, PhD

**Affiliation:** Clinical Hospital Merkur, Zagreb, Croatia

**Introduction:** Contrast induced nephropathy (CIN) is deterioration of kidney function following administration of radiographic contrast. It is determined by increase in the serum creatinine levels which is insensitive in reflecting early changes in renal function. NGAL (Neutrophil Gelatinase Associated Lipocalin) is a new biomarker which appears to be predictive for acute renal injury. The purpose of this investigation is to evaluate the effectiveness of NGAL compared to serum creatinine in early diagnosis of CIN (Contrast Induced Nephropathy).

**Hypothesis:** NGAL is new biomarker of acute kidney injury which enables earlier detection of Contrast Induced Nephropathy in comparison with standard serum creatinine.

**Aims:** Determine the clinical value of NGAL in detection of CIN in patients referred for diagnostic or interventional procedures. The specific aims are: 1. Determine the incidence of CIN in followed cohort of patients. 2. Determine the time frame in which NGAL value peaks after contrast administration. 3. Determine the correlation between degree of peripheral arterial disease stage and occurrence of CIN. 4. Determine the value of NGAL in detection of CIN in patients with chronic kidney disease.

**Materials and methods:** This prospective cohort study will include patients referred to diagnostic or interventional radiology procedures in our cath lab. Patients will have to sign an

informed consent and give their approval for participation in investigation. Patient inclusion criteria : male and female patients older than 18 years with symptoms of peripheral arterial disease and hepatocellular carcinoma. Exclusion criteria: patients with transplanted kidney, on dialysis, those who received contrast within 7 days or had PTA or PTCA within 30 days and patients who take nephrotoxic drugs. Baseline serum creatinine followed by 24 and 48 hours after contrast administration will be determined. Urine NGAL levels prior to contrast, followed by sequential 4, 8 and 24 hours after contrast will be determined. Statistical analysis with Student t-test, Mann-U-Whintey test, X-quadrat test and Kruskall Walis test will be done. Diagnostic performance of NGAL will be investigated with ROC (Receiver Operator Characteristic).

**Expected scientific contribution:** If hypothesis is correct, data from this study may help to implement urinary NGAL in routine clinical assessment of CIN. Early detection of CIN is essential for implementing supportive measures to prevent further deterioration of renal function and associated morbidity and mortality.

**Acknowledgments:** Mladen Knotek, management and employees of Clinical Hospital Merkur

**MeSH/Keywords:** NGAL, Contrast Induced Nephropathy

**Poster code:** B-25-40

## **POSTER TITLE: ELASTOGRAPHIC VALUES OF BREAST TISSUE IN WOMEN**

**PhD candidate:** Martina Džoić Dominković, MD

**Part of the thesis:** Characterisation Of Woman Breast Tissue With Elastography And Comparison To Estimated Mammographic Density

**Mentor/s:** Gordana Ivanac, MD, PhD

**Affiliation:** Clinical Institute for Diagnostic and Interventional Radiology, Clinical Hospital Dubrava - Department for Radiology, General Hospital Orašje

**Introduction:** Elastography is a new quantitative ultrasound technique for measuring tissue stiffness. Breast elasticity can be measured with elastography and it is possible to determine its association with certain parameters, also to determine the difference in elasticity in different breast tissue (fat and glandular). Many physiological changes of breast tissue depend on the age, menstrual cycle and many other parameters.

**Hypothesis:** Breast elastographic values of fat and glandular tissue are different, they are also different in each breast quadrant. Mammographic dense breasts have higher elastographic values measured by sonoelastography.

**Aims:** The aim of this study is to evaluate elastic properties of normal breast tissues in a large group of women, to search for factors which play a role in its mechanical properties, to determine the difference in elasticity in different breast tissues (glandular and fat) and also to compare elastographic value of different breast tissue with estimated mammographic breast density which is a risk factor for breast carcinoma.

**Materials and methods:** We will perform a prospective study with 200 women of different

age. Women aged > 40 years will have mammographic pictures attached with estimated density of breast parenchyma. B-mode ultrasound examination and real-time elastography will be performed. Each breast will be divided in 4 quadrants and elasticity of glandular and fat tissue in each quadrant will be measured. Elastographic value will be compared with estimated value of mammographic density.

**Expected scientific contribution:** This research will make contribution to better understanding of breast physiology and pathophysiology. Average elastographic values of fat and glandular tissue in breast will be defined and elastographic measurement will be better standardized. If our research shows positive relation between breast stiffness and density, than we will be able to place women in group of those with lower and higher risk for development breast carcinoma with method that is fast, cheap and without ionizing radiation.

**Acknowledgments:**

**MeSH/Keywords:** Breast, Elastography, Density of glandular parenchyma, Elasticity of glandular parenchyma, Elasticity of fat tissue

**Poster code:** B-25-75

## POSTER TITLE: ROLE OF DIGITAL TOMOSYNTHESIS IN DIAGNOSIS OF SACROILIITIS

**PhD candidate:** Luka Novosel, MD

**Part of the thesis:** Role of digital tomosynthesis in diagnosis of sacroiliitis

**Mentor/s:** Prof.dr.sc. Kristina Potočki

**Affiliation:** University Medical Centre Zagreb

**Introduction:** Seronegative spondyloarthropathies (SpA) are characterized by inflammation of the sacroiliac (SI) joints. Patients satisfy the classification criteria for SpA if they have certain radiologic changes on SI joints indicative of sacroiliitis. According to the criteria patients can be diagnosed with seronegative SpA if they have a radiologic confirmation of sacroiliitis. Conventional radiography is still the most available method to depict sacroiliitis, but the complex form of SI joints makes it difficult to detect pathologic changes. MRI is, according to the new ASAS criteria, now considered the method of choice because it lacks radiation and is able to depict early changes. The structural changes seen on MRI are not included in the ASAS criteria, however the importance of early detection of structural changes is essential since these are the lesions with the highest specificity for SpA. Digital tomosynthesis is an imaging technique using a flat panel detector to produce a series of slices at different depths. It can provide high resolution images with a considerably lower radiation dose than CT.

**Hypothesis:** Digital tomosynthesis is a more sensitive method than conventional radiography for detection of structural changes in SI joints that occur in sacroiliitis with a radiation dose to the patient being comparable to conventional radiography.

**Aims:** To determine whether digital tomosynthesis is more sensitive in depicting structural

changes on SI joints in patients with sacroiliitis compared to conventional radiography and compare the delivered radiation dose to the patient.

**Materials and methods:** The study will be conducted on a statistically relevant number of patients who have been referred to our department for radiologic analysis because of suspected sacroiliitis. We will include those patients who have at least four of the possible five clinical criteria for low back pain according to the ESSG criteria. Two experienced radiologists will analyze the imaging material without any insight into the identity or the clinical and laboratory findings. We will analyze the presence and severity of structural changes. The radiation dose will be measured with thermoluminescent dosimeters (TLD) which will be placed on the position of radiosensitive tissues and organs.

**Expected scientific contribution:** The results of this study will allow insight into the value of digital tomosynthesis in the diagnosis of sacroiliitis and set the ground for other studies involving the use of this method in musculoskeletal diseases.

**Acknowledgments:**

**MeSH/Keywords:** digital tomosynthesis, sacroiliitis, dosimetry

**Poster code:** B-25-137

## POSTER TITLE: MESIAL TEMPORAL SCLEROSIS: MRI AND HISTOPATHOLOGY CORRELATION

**PhD candidate:** Nataša Katavić, MD

**Part of the thesis:** Correlation of MRI and histopathology findings in mesial temporal lobe sclerosis improves diagnostic capacity

**Mentor/s:** Dijana Zadravec, MD PhD

**Affiliation:** Clinical Center Osijek

**Introduction:** Mesial temporal sclerosis (MTS) is a specific pattern of hippocampal neuronal loss accompanied by gliosis and atrophy. MTS is the most common cause of partial complex epilepsy in adults. MRI became the method of choice for presurgical detection of mesial temporal sclerosis.

**Hypothesis:** In patients with refractory epilepsy volume of temporal lobe assessed by MR is in correlation with degree of pathologically-confirmed sclerosis (neuronal loss and gliosis) and MR signal intensity in T2WI and FLAIR sequence.

**Aims:** The purpose of this study is to assess MRI accuracy in evaluation of temporal lobe patomorfologic changes rates in patients with clinically proven refractory epilepsy. With MRI analysis of hippocampal patomorfologic changes using T1, T2 and FLAIR sequences and based on statistical analysis establish degree of mesial temporal sclerosis and extent of temporal lobe resection. A better understanding of this correlation may help enhance management of patients with pharmaco-resistant temporal lobe epilepsy.

**Materials and methods:** Thirty patients from one clinical center in Croatia with the diagnosis of pharmaco-resistant epilepsy of temporal lobe origin underwent hippocampal resection and preoperatively and postoperatively serial magnetic resonance imaging assessments. MR

studies were acquired on 1,5T Magnetom Avanto using correct MRI temporal lobe protocol. Slice thicknesses used was 1 and 3mm. Volumetric measurements will be performed with an interactive semiautomated software package developed by Faculty of Electrical Engineering Osijek. MR signal intensity studies will be performed by 3 neuroradiologists who will independently evaluate MR images. Resected hippocampus will be sent to histopathology examination to assess degree of sclerosis (low, moderate or high). Statistical analyses will be performed to test the correlation of the resection volume of hippocampus and the extent of hippocampal sclerosis on MRI and histopathologic findings with surgical outcome.

**Expected scientific contribution:** Results of this study will bring significant contribution in establishment of criteria for the most accurate diagnostic imaging method and positioning of MRI parameters in diagnostic algorithm for resection of epileptic hippocampus suggesting their predictive value in postsurgical seizure outcome in patients with pharmaco-resistant mesial temporal lobe epilepsy.

**Acknowledgments:**

**MeSH/Keywords:** mesial temporal sclerosis, magnetic resonance, volumetry, histopathology findings

**Poster code:** B-25-115

## POSTER TITLE: DEMORALIZATION AND LUNG CANCER

**PhD candidate:** Lea Galunić Bilić, MD

**Part of the thesis:** Demoralization and Quality of life in lung cancer patient receiving palliative radiotherapy

**Mentor/s:** Professor Antonio Juretić, MD, PhD, Docent Marijana Braš, MD, PhD

**Affiliation:** Department of oncology, University Hospital Centre Zagreb, Zagreb, Croatia

**Introduction:** Lung cancer has the highest mortality rate in the Western world in men and women. The overall prognosis remains poor, with 15% patients surviving 5 years. The majority of NSCLC patients present with locally advanced or metastatic disease at diagnosis with very poor rate of cure. Morbidity from lung cancer or lung metastases often presents as troublesome thoracic symptoms such as hemoptysis, cough, chest pain, and dyspnea. Palliative radiotherapy has been effective in ameliorating these symptoms and improves or preserves the quality of life. Patients experiencing more physical symptoms are at higher risk for psychological distress. The demoralization syndrome reflects a specified psychological state where loss of meaning is linked with its cognitive, motivational and affective implications.

**Hypothesis:** Demoralization in lung cancer patients is related with quality of life and duration of illness. Lung cancer patients that have lower quality of life will have higher prevalence of demoralization. There is a significant positive effect of physical problems on demoralization and quality of life.

**Aims:** 1. to explore characteristics of demoralization syndrome as well as the relationship between demoralization syndrome and quality of life. 2.) to assess the occurrence of demoraliza-

tion in sample of lung cancer patients on palliative radiotherapy treatment. 3.) to examine the impact of the quality of life on demoralization

**Materials and methods:** This is prospective study that will include 300 patients with locally advanced cancer and metastatic lung cancer (stages III and IV) patients treated in Clinical Unit for Radiotherapy, University Hospital Centre, Zagreb. Aspects of physical health and functioning will be measured using the Physical Functioning Scale of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 Items (QLQ-C30) and a visual analogue pain scale. Level of demoralization will be assessed by Demoralization Scale (Kissane et al. J Palliat Care. 2004).

**Expected scientific contribution:** This is original scientific paper that will associate quality of life and demoralization in lung cancer patients. Demoralized patients generally do not respond to antidepressants so the responsibility lies with physicians to restore meaning and hope.

**Acknowledgments:**

**MeSH/Keywords:** demoralization, lung cancer, quality of life, palliative radiotherapy

**Poster code:** B-26-44

## **POSTER TITLE: CARBOXYHAEMOGLOBIN HELPS TO IDENTIFY THE ENTRANCE GUNSHOT WOUND**

**PhD candidate:** Marija Baković

**Part of the thesis:** Evaluation of Carboxyhaemoglobin as an Indicator of Close Range Entrance Wound

**Mentor/s:** doc. dr. Davor Mayer

**Affiliation:** Department of Forensic Medicine, University of Zagreb School of Medicine

**Introduction:** Establishing the entrance wound is one of the essential tasks in forensic autopsy of individuals with lethal firearm injuries. Assessment is based on the morphology of the wound, which is not always typical. In close range shots, propellant gases are blown into the tissues around the bullet tract which produces carboxyhaemoglobin (CO-Hb).

**Hypothesis:** Carboxyhaemoglobin levels in blood samples from close range entrance wounds are significantly higher than levels of CO-Hb in associated exit wounds.

**Aims:** The aim of this research is to investigate the concentrations of CO-Hb in blood samples from close entrance wounds and associated exit wounds by determining CO-Hb levels in blood sample from every entrance and exit wound, by defining the relationship between CO-Hb concentrations in blood samples from entrance and exit wounds and by evaluating the correlation of CO-Hb concentrations and different parameters

of shooting (type of weapon involved and length of the bullet track).

**Materials and methods:** Blood samples from the entrance and exit wound and a control sample from femoral artery will be collected during the autopsy. The samples will be analyzed by quantitative spectrophotometry according to Heilmeyer.

**Expected scientific contribution:** Differences in CO-Hb levels could help distinguishing the entrance from exit wound in close range shots. This research will evaluate usefulness of this finding and, possibly, establish a new method for identification of entrance wound which would be of great diagnostic value in routine work of forensic pathologist.

**Acknowledgments:**

**MeSH/Keywords:** Gunshot Wounds, shooting deaths, carboxyhaemoglobin, entrance wound

**Poster code:** B-27-100

## POSTER TITLE: FORENSIC ROLE OF mtDNA SNPs

**PhD candidate:** Marijana Mašić, BSc.

**Part of the thesis:** Mitochondrial DNA control region SNPs in Croatian population

**Mentor/s:** Mentor: Professor Milovan Kubat, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, Department of forensic medicine and criminology, DNA laboratory

**Introduction:** Determination of mitochondrial DNA (mtDNA) frequencies that occur in a given population is important for the application of mitochondrial markers in forensic studies. High copy number of mtDNA molecules per cell, maternal inheritance, lack of recombination and the high mutation rate of mitochondrial DNA are the main reasons for the use of mtDNA analysis in forensic medicine, population studies, molecular evolution, anthropology and archaeology. In order to identify polymorphic positions and to determine their frequency, the mitochondrial DNA control region of 200 unrelated individuals from Croatia will be amplified and directly sequenced.

**Hypothesis:** This research is to acknowledge SNP analysis of control region of mtDNA as useful method in identification cases, forensic cases and other studies.

**Aims:** 1. Analyse mtDNA control region and find SNPs location. 2. Determine SNPs with higher level of discrimination that could be useful for forensic cases. 3. Determine frequency of such SNPs in Croatian population. 4. Compare results with literature data.

**Materials and methods:** Blood samples from 200 unrelated Croatians will be analysed. DNA

will be extracted from bloodspots on FTA cards with Instagene matrix (BIO-RAD). PCR amplification of HV1 region combines F15971 and R16410 primers, HV2 region combines F15 and R484 primers and the region in between F16190 and R270 primers. Amplification is carried out on PCR Thermocycler 9700 (Applied Biosystems). Purified PCR products are sequenced using BigDye Terminator v 1.1 kit (Applied Biosystems). Sequencing analysis is performed by capillary electrophoresis on 3100-Avant Genetic Analyzer (Applied Biosystems). Results will be analysed with Sequencing Analysis v5.2 software (Applied Biosystems).

**Expected scientific contribution:** In some cases of identification process mtDNA analysis of HV1 and HV2 regions doesn't provide enough information. Using SNPs of mtDNA control region could provide additional discrimination which improves identification process, especially in cases where nuclear DNA analysis (analysis of STR loci) is impossible.

**Acknowledgments:** DNA laboratory, Zagreb

**MeSH/Keywords:** DNA typing, mitochondrial DNA, PCR, population study

**Poster code:** B-27-104

## POSTER TITLE: POLYMORPHISM OF FOLLICULE-STIMULATING HORMONE GENE RECEPTOR IN ALBANIAN MALE POPULATION

**PhD candidate:** Shkelzen Elezaj dr.med-urolog

**Part of the thesis:** The ultimate goal is to apply a genetic marker as a routine diagnostic test, which can be used in the evaluation of therapy success rate or in the introduction of new procedures for the treatment of male infertility.

**Mentor/s:** Tamara Nikuševa Martić, Assist Prof., Feodora Stipoljev, Assist Prof.

**Affiliation:** Clinic of Urology, General Hospital Peja, Kosovo

**Introduction:** Follicle stimulating hormone (FSH) plays a key role in maintaining the normal reproductive male function. There are several polymorphisms of FSH receptor gene (FSHR), which modulate the response to FSH. Clinically very significant, are two polymorphisms: Ala307Thr and Asn680Ser, which result in two variant alleles: Thr307/Asn680 Ala307/Ser680, respectively.

**Hypothesis:** We expect that the investigated FSHR polymorphism would affect spermatogenesis in infertile man and also influences on the difference in concentration level of FSH, in both fertile and infertile men in Albanian population.

**Aims:** The aim of this study is to genotype Asn680/Ser680 polymorphisms in FSHR gene and to determine the frequency of these two variant alleles in Albanian male population, and its possible clinical impact on investigated group of infertile males.

**Materials and methods:** Genotyping from the peripheral blood samples will be performed, us-

ing allelic discrimination real-time PCR, in the group of 120 infertile and 100 normally fertile man. Biochemical parameters of seminal fluid, FSH, LH, prolactin and body mass index value will be correlated with the FSHR variant alleles in the infertility group.

**Expected scientific contribution:** We expect that the results of this study will show that Asn680/Ser680 allelic variant in FSHR gene in a combination with other parameters (spermogram, hormones, BMI) could be used as a predictive test to assess an individualized approach to the patients in the dosage of responding drugs, and for the improvement of spermatogenesis.

**Acknowledgments:** This study was financially supported by Polyclinic Biolab Zafi. I would like to thank both of my mentor's and Regional Hospital in Peja.

**MeSH/Keywords:** Infertility, Polymorphisms, FSHR, FSH, PCR.

**Poster code:** B-28-141



## POSTER TITLE: THE IMPACT OF UGT1A9 POLYMORPHISM ON MYCOPHENOLIC ACID PHARMACOKINETIC PARAMETERS IN KIDNEY ALLOGRAFT RECIPIENTS

**PhD candidate:** Sandra Nad Škegro, MD

**Part of the thesis:** The Impact of UGT1A9 Polymorphism on Mycophenolic Acid Pharmacokinetic Parameters in Kidney Allograft Recipients

**Mentor/s:** Professor Nada Božina, MD, PhD, Professor Josip Pasini, MD, PhD

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** Mycophenolic acid (MPA) is immunosuppressive agent widely used in kidney allograft recipients to prevent graft rejection. After ingestion, Mycophenolate mophetil (MMF) or enteric-coated mycophenolic acid sodium salt (EC-MPA) are hydrolyzed to the active metabolite mycophenolic acid (MPA) which is extensively glucuronidated by UDP-glucuronosyltransferases (predominantly UGT1A9) to glucuronide metabolite. It undergoes extensive enterohepatic circulation. MPA displays variable pharmacokinetics, which can be partly explained by presence of genetic polymorphisms in key enzymes and patients concomitant therapy with calcineurin inhibitors. UGT1A9 is highly polymorphic and polymorphism frequencies are significantly different among populations and ethnic groups. Main goal of immunosuppression therapy is to prevent graft rejection without compromising recipients health, and balance between these objectives is important for outcome.

**Hypothesis:** Polymorphism UGT1A9 98T>C in combination with concomitant immunosuppressive therapy with cyclosporine or tacrolimus can differently modulate MPA pharmacokinetic in Croatian kidney allograft recipients.

**Aims:** The aim of proposed study is to assess the impact of UGT1A9 98T>C polymorphism on MPA pharmacokinetic parameters in kidney

transplant recipients with stable graft function receiving concomitantly cyclosporin or tacrolimus.

**Materials and methods:** In the study 65 kidney transplant patients with stable graft function, on a standard immunosuppressant treatment including MPA, corticosteroides and a calcineurin inhibitor (cyclosporine or tacrolimus) will be enrolled. Steady-state pharmacokinetics of MPA during one dosing interval (12h) will be analyzed. Blood samples will be drawn at 0, 0.5, 1, 2, 3, 8 and 12h after the morning dose. Plasma concentrations of MPA will be detected using validated HPLC method. DNA will be isolated from peripheral blood, and all patients will be genotyped for UGT1A9 98T>C polymorphism by means of Real-time PCR method.

**Expected scientific contribution:** We expect that obtained results can improve individual approach for dosage regimens of MPA which can decrease adverse effects of immunosuppressive agents and prevent graft rejection.

**Acknowledgments:**

**MeSH/Keywords:** mycophenolic acid, UGT1A9 polymorphism, kidney transplantation, immunosuppressive therapy

**Poster code:** B-28-158

# POSTER TITLE: ATTACHMENT STYLE AND EMOTIONAL REGULATION IN ADOLESCENT PATIENTS WITH ANOREXIA NERVOSA

**PhD candidate:** Maja Crnković, psychologist

**Part of the thesis:** Attachment Style and Emotional Regulation in Adolescent Patients with Anorexia Nervosa

**Mentor/s:** Ivan Begovac, MD, PhD

**Affiliation:** Department of Paediatrics, University Hospital Centre Sisters of Charity, Gymnasium Lucijan Vranjanin Zagreb

**Introduction:** Anorexia nervosa is associated with serious biological, psychological, and sociological morbidity and significant mortality. Emotional regulation and attachment style form a key part of conceptual model of anorexia nervosa (AN), but the experimental findings to support this are limited.

**Hypothesis:** Factors of emotional regulation and attachment style contribute significantly to the prediction of the anorexia nervosa.

**Aims:** The main objective is to examine the extent to which attachment style and emotional regulation contribute to the prediction of the development of anorexia nervosa in adolescent population.

**Materials and methods:** The Questionnaire of general data, Eating Disorders Inventory (EDI-3), Questionnaire Difficulties in emotional regulation (DERS), and Experiences in close relationships-revised (ECR-R) will be administered to 140 woman adolescents aged 14-18 (70 with AN, 70 healthy controls) (HCs). Statistical com-

parison of the results and logistic regression will confirm and explain the significant differences between the two groups of subjects relating to the overall psychological adjustment, with an emphasis on style attachment and emotional regulation, with consideration of the contribution of specific factors in the prediction of anorexia nervosa.

**Expected scientific contribution:** The data will provide support for conceptualizations of eating disorders that emphasize the role of emotion regulation and attachment in the development of anorexia nervosa. The importance of these results will be discussed, and directions for future research of anorexia nervosa will be indicated.

**Acknowledgments:** I would like to express my gratitude to my supervisor Ivan Begovac, MD, PhD

**MeSH/Keywords:** Anorexia nervosa, Emotional regulation, Attachment style, Adolescence

**Poster code:** B-29-15

## POSTER TITLE: ROLE OF TRAUMA IN CONDUCT DISORDER

**PhD candidate:** Ivana Maček

**Part of the thesis:** Early trauma in the etiology of conduct disorder

**Mentor/s:** Professor Vlasta Rudan, MD, PhD, psychiatrist and psychotherapist

**Affiliation:** University of Zagreb School of Medicine, University Hospital Centre - Zagreb

**Introduction:** There are many different theories of personality development and their interpretation of the importance of certain developmental stages. Traumatic events in early childhood (separation anxiety, abuse and pathological personality characteristics of parents) can interfere with the normal development of the child. When this strong relationship is violated with some traumatic event, it can have a strong influence on the further development of the child. Such traumatic experiences and delay in the normal development can lead to pathological patterns that can cause serious changes in behavior. Such behavior is often interpreted as a „bad upbringing“, and therefore a large number of such disorders remain unrecognized or very late discovers. Conduct disorder refers to a group of behavioral and emotional problems of children and youth. These disorders are the most common in adolescence when development process involves a degree of transient deviations to feelings and attitudes within itself and in relation to others. It is also important to note that children and young adolescents their internal states less verbalize and more show through behavior. Therefore, conduct disorder as a diagnostic entity can be classified only when symptoms persistent and are repeated over a period of one year.

**Hypothesis:** Early trauma in childhood will lead to attachment disorder that affects the development of conduct problems in adolescence.

**Aims:** The purpose of this study is to determine the association of early traumatic experiences, attachment disorders and behavioral problems in adolescents.

**Materials and methods:** The study will be conducted on 100 adolescent outpatients diagnosed as conduct disorder aged 14-18 years who were in treatment in Clinic of Psychological Medicine, University Hospital Center Zagreb. Results will be collected from questionnaires that measure attachment, early trauma and conduct disorder. PBI - Parental bonding instrument, ECR-R - Experience in close relationship, YSR - Youth Self Report, CBCL - Child behavior checklist, TSCC - Trauma Symptom Checklist for Children and SKID II - The structured clinical interview for personality disorders with Axis II of the DSM- IV.

**Expected scientific contribution:** This research will add the possibility of better differential diagnosis, early detection of the disorder and for indications of treatment and methods of approach to conduct disorder.

**Acknowledgments:** I would like to thank Professor Vlasta Rudan for her help and guidance that made this study possible.

**MeSH/Keywords:** childhood trauma, attachment, adolescence

**Poster code:** B-29-122

## POSTER TITLE: CLINICAL AND NEUROPHYSIOLOGICAL CHANGES IN PATIENTS WITH PINEAL REGION EXPANSIONS

**PhD candidate:** Sibila Nanković

**Part of the thesis:** Abstract

**Mentor/s:** Prof. Sanja Hajnšek, MD, PhD

**Affiliation:** School of medicine and Department of Neurology, University hospital Zagreb

**Introduction:** The pineal gland is located on the level of the diencephalon outside the blood-brain barrier. As a neuroendocrine transducer, it changes neural into endocrine signals and is known to be the main source of melatonin production. Melatonin as anticonvulsive agent is involved in the mechanisms of epileptogenesis, regulation of the circadian rhythm, thereby affecting several biological functions such as immune function, blood pressure regulation, retinal and ovarian physiology.

**Hypothesis:** The plan is to do a prospective study of patients with radiologically confirmed pineal cyst. Patients will be analyzed according to the following predictors: heredity, provocative factors, age, gender, EEG findings, MRI findings (classification according to the size of the cysts), the concentration of estrogen/testosterone, visual evoked potentials, the clinical outcome of the applied antiepileptic therapy. Based on the obtained parameters the candidates for neurosurgery will be recruited and the postoperative follow up will be performed.

**Aims:** The aim of the study is to explain the relationship between pineal cyst and headaches, or primary generalized epilepsy.

**Materials and methods:** In the last 20 years neurological and neurosurgical follow up of our patients with pineal region expansions (118 patients) pointed to certain clinical

and neurophysiological regularities. We performed retrospective study which included 84 patients with pineal region expansions. The study included 55 women and 29 men, mean age  $30.08 \pm 13.93$  years, with positive brain magnetic resonance imaging (MRI) - 70 patients (83.4%) had simple pineal gland cysts, and 14 patients (16.67%) had expansive process in pineal region with compressive effect. All patients had headache, while 32 patients (38%) had epileptic phenomena - typical absences, myoclonias and generalized tonic-clonic seizures. Patients had common electroencephalography (EEG) pattern with paroxysmal discharges of 3Hz (or more than 3 Hz) spike-and-wave complexes with or without lateralisation. This study points to often appearance of seizures that clinically and neurophysiologically present as primary generalized epilepsy in patients with pineal region expansions.

**Expected scientific contribution:** Proposed diagnostic and therapeutic protocol for patient with pineal cysts after evaluation of all criteria included in the research.

**Acknowledgments:** mentor Prof. Sanja Hajnšek, MD, PhD

**MeSH/Keywords:** pineal gland, expansions, epilepsy, headache

**Poster code:** B-30-110

**2.3.**  
**RESEARCH PROPOSALS**  
**- PUBLIC HEALTH AND HEALTH CARE**



## **POSTER TITLE: EXPLORING THE RISK FACTORS FOR THE DEVELOPMENT OF ALLERGIC RESPIRATORY DISEASES BY BAYESIAN NETWORKS BUILT ON MULTIPLE-SOURCE DATA**

**PhD candidate:** Jelena Kovačić, mag. math.

**Part of the thesis:** Exploring the risk factors for the development of allergic respiratory diseases by Bayesian networks built on multiple-source data

**Mentor/s:** Veda Marija Varnai, MD, PhD and Anamarija Jazbec, dipl. ing. math., PhD

**Affiliation:** Institute for Medical Research and Occupational Health

**Introduction:** Fusion of partially overlapping micro-data from multiple sources in the same model is an active research field in biomedicine. Nevertheless, in the available literature there is no published model that would describe not yet adequately explained role of risk factors for allergic respiratory diseases, as well as their complex interrelationship. Moreover, the methods for fusion of overlapping data from multiple sources are still under development.

**Hypothesis:** In the research of risk factors for allergic respiratory diseases, the analysis of overlapping data from multiple sources has a higher sensitivity, specificity and positive and negative predictive values than analysis of a single data source.

**Aims:** The aims of proposed dissertation are 1) to improve the methods for data fusion from multiple sources in the models of generalized Bayesian networks, and 2) to apply the improved method in the research of risk factors associated with allergic respiratory diseases.

**Materials and methods:** Research will be performed on four epidemiologic data sources comprising, in total, approximately 2500 subjects of various age, gender and profession. Existing

algorithm for multiple-source data fusion, Integration of overlapping datasets, will be complemented with parameter learning algorithm, such as expectation-maximization or multiple imputation. Algorithm validation will be performed on synthesized datasets. Models of logistic regression and Bayesian networks will be built on each single data source, as well as on all four data sources using validated algorithm. Created models will be compared in terms of specificity, sensitivity and predictive values.

**Expected scientific contribution:** This research proposal will complement existing knowledge on risk factors for allergic respiratory diseases and their interaction. Furthermore, contribution to statistical methodology is expected, as the proposal should result in improved algorithm for the analysis of partially overlapping datasets in the models of generalized Bayesian networks. Improved algorithm would increase usability of such analyses in other epidemiologic studies.

**Acknowledgments:**

**MeSH/Keywords:** allergic asthma, allergic rhinitis, epidemiology, Bayesian networks, partially overlapping data from multiple sources

**Poster code:** C-1-42

## **POSTER TITLE: CHARACTERISTICS OF INCIDENCE AND MORTALITY TRENDS OF MALIGNANT MELANOMA OF THE SKIN IN CROATIA AND SOUTH-EASTERN EUROPEAN COUNTRIES**

**PhD candidate:** Jelena Barbaric, MD, MSc

**Part of the thesis:** Characteristics of incidence and mortality trends of malignant melanoma of the skin in Croatia and South-Eastern European countries

**Mentor/s:** Ariana Znaor, MD, PhD

**Affiliation:** Croatian National Institute of Public Health, Zagreb, Croatia Andrija Štampar School of Public Health, University of Zagreb School of Medicine, Zagreb, Croatia

**Introduction:** Incidence of melanoma of the skin has been increasing in Europe over the past decades. Mortality seems to be stabilizing in some countries, but is still rising in many of them. Croatia and South-Eastern (SE) European countries have low to intermediate incidence, but high mortality rates.

**Hypothesis:** Malignant melanoma incidence and mortality trends in Croatia and SE European countries are increasing and vary by age, sex and birth cohort.

**Aims:** To analyse melanoma incidence and mortality trends in Croatia and SE European countries.

**Materials and methods:** Incidence data will be obtained from national or regional registries. Mortality data will be obtained from national or regional registries and World Health Organisation (WHO) mortality database. United Nations population estimates will be used for calculating the age-specific rates. Age-standardised melanoma incidence and mortality rates in Croatia

and SE European countries will be calculated and analysed by joinpoint regression method. Trends will be compared among the analysed populations and with trends in other European countries. Age-period-cohort models will be used for additional analysis of long-term incidence and mortality trends in Croatia. The effects of age, period and cohort on age-specific trends will be estimated and birth cohort specific risks for melanoma incidence and mortality will be calculated.

**Expected scientific contribution:** The results will contribute to better understanding of melanoma burden presence and dynamics in Croatia and SE Europe. Furthermore, they will help creating and evaluating melanoma cancer plans at both national and regional level.

**Acknowledgments:**

**MeSH/Keywords:** malignant melanoma, time trends, incidence, mortality, cancer registries, Croatia, South-Eastern Europe

**Poster code:** C-1-98



## **POSTER TITLE: CORRELATION OF FORMAL EDUCATION AND NURSING STUDENTS' ATTITUDES TOWARD NURSING AS A PROFESSION**

**PhD candidate:** Snježana Čukljek

**Part of the thesis:** Correlation of formal education and nursing students' attitudes toward nursing as a profession

**Mentor/s:** Professor Vesna Jureša, MD, PhD

**Affiliation:** University of Applied Health Studies, Department of Nursing

**Introduction:** Nurses constitute the largest group of health care professionals, they perform complicated and demanding tasks and even though the roles and responsibilities of nurses have significantly changed over the past twenty years they are still being stereotyped. Nursing is identified as caring for the patient and nurses are associated with the maternal role and feminized stereotypes. Previous studies have shown that the changes in nursing students' attitudes are expected to occur during the course of their study as a result of the educational content.

**Hypothesis:** Hypothesis of the research are: 1. full-time and part-time nursing students have different attitudes toward nursing as a profession at the beginning and at the end of their study, 2. attitudes of full-time students are influenced by formal education whereas this is not the case with part-time students of nursing.

**Aims:** The aim of the research is to determine the attitudes of students toward nursing at the University of Applied Health Studies and the validation of the Nursing image questionnaire.

**Materials and methods:** This prospective study will include 110 full-time and 150 part-time nursing students at the University of Applied Health Studies. An anonymous questionnaire including demographic data and a Nursing image ques-

tionnaire (Toth, 1998) will be used for research purposes. The demographic questionnaire will include questions about age, gender, professional qualifications, place of work, years of working experience and marital status. The Nursing Image Questionnaire will be used to assess the attitudes towards: nursing roles and responsibilities, professionalism, values, and nursing stereotypes in the society. The questionnaire will be given to students in their first year of study and during their third year of study as well.

**Expected scientific contribution:** The research will provide insight into attitudes toward nursing as a profession, it will determine in which way formal education influences the change in attitudes during the course of nursing study. Research results will be used for the improvement of the study programmes with the purpose of further developing the nursing profession. The research will validate the Nursing image questionnaire in Croatia. The acquired data will enable international comparison and ensure basic data for further research.

**Acknowledgments:**

**MeSH/Keywords:** nursing, profession, education, attitudes

**Poster code:** C-2-114

## POSTER TITLE: PRIORITIES FOR NATIONAL MEDICINES POLICY IN THE EUROPEAN UNION

**PhD candidate:** Hilarije Baričević

**Part of the thesis:** National Medicines Policy in the European Union

**Mentor/s:** Professor Stjepan Orešković, PhD

**Affiliation:** University of Zagreb School of Medicine, Krka-Farma d.o.o.

**Introduction:** The primary role of EU pharmaceutical legislation is to safeguard public health while encouraging development of industry through creation of single market for pharmaceuticals. On the other hand, division of competences within EU ensures that member states have responsibility for organization of their health care systems. Result is shared competences space between national and EU level where evidence on effectiveness and transferability of most policy interventions is very limited. In this setting Croatia needs to formulate set of new, coherent policies in order to achieve an adequate balance between cost-containment, innovation, patients' access to medicines and health outcomes. Moreover, these policies need to be well aligned with EU objectives while bearing in mind their feasibility in light of recent economic crisis and negative demographic trends. This research will apply systematic, consensus based approach through nationwide expert panel in order to define and prioritize policy components that will meet challenges of the next decade.

**Hypothesis:** Croatian long-term policy priorities are well aligned by content and rank with main EU objectives.

**Aims:** To define content of long-term policy components and rank them. To measure consensus regarding feasibility of implementing these components as policy measures.

**Materials and methods:** Research process will include literature review and primary research using two-round Delphi survey with a panel comprising of key experts in pharmaceutical sector. Components will be organized in topics and voted on ten-point Likert scale regarding two main measures, their importance and feasibility.

**Expected scientific contribution:** This research will for the first time, through nationwide expert panel define, rank and analyse long-term priorities for medicines policy in new EU setting, in order to accomplish main objectives regarding cost-containment, innovation, patients' access to medicines and better health outcomes. In addition, it opens space for further research regarding benchmarking of best practices between countries in order to facilitate accession process in this policy area.

**Acknowledgments:**

**MeSH/Keywords:** Croatia, European Union, pharmaceutical policy, priorities

**Poster code:** C-2-124

## POSTER TITLE: THE HEALTH BURDEN AND ECONOMIC COSTS OF MELANOMA IN CROATIA

**PhD candidate:** Goran Benčina, MPharm, M.Econ.

**Part of the thesis:** The health burden and economic costs of melanoma in Croatia

**Mentor/s:** Ranko Stevanović, PhD, MD

**Affiliation:** Croatian National Institute of Public Health

**Introduction:** The rapidly increasing incidence of melanoma occurs at the same time as an increase in general healthcare costs, particularly the expenses associated with cancer care. Information provided by cost-of-illness (CoI) studies are used in policy making and are particularly useful for measuring the potential savings from averting a case of disease. Although most cases are caught early, melanoma is devastating when diagnosed at a later stage. Moreover, the median age at diagnosis is between 45 to 55 years, coinciding with peak professional productivity and family responsibility.

**Hypothesis:** There is a greater cost for patients presenting with melanoma in more advanced stages, with the largest component of cost for the treatment of metastatic disease.

**Aims:** The purpose of this study was to estimate the direct and indirect cost of treating melanoma disease in Croatia.

**Materials and methods:** We will design a comprehensive model of expenses in melanoma that

considers the dynamic costs generated by the natural progression of the disease, which produces costs associated with treatment, surveillance and terminal care. The complete range of initial clinical (TNM) stages of the disease and initial tumor stages will be analyzed in this model and the total healthcare costs for the 3 years following melanoma presentation at each particular stage will be calculated.

**Expected scientific contribution:** The growing cost of melanoma continues to highlight the medical need to find cost-effective means of prevention and reduce the economic burden of malignant melanoma. We expect to quantify and prioritize between areas—recurrence, early stage disease, and palliative care—where efforts to innovate and refine practice could derive significant clinical and cost benefit.

**Acknowledgments:**

**MeSH/Keywords:** melanoma, cost of illness, pharmacoeconomics

**Poster code:** C-2-143

# POSTER TITLE: PSYCHOLOGICAL PREDICTORS OF SPORT INJURIES AMONG PROFESSIONAL SOCCER, HANDBALL AND BASKETBALL PLAYERS

**PhD candidate:** Tomislav Madžar

**Part of the thesis:** Psychological predictors of sport injuries among professional soccer, handball and basketball players

**Mentor/s:** Professor Neven Henigsberg, MD, PhD and Milan Milosevic, MD, PhD

**Affiliation:** MD

**Introduction:** In order to plan preventive measures to be as accurate as possible it is necessary to know information why an athlete in a particular situation risking injury and how a particular injury occurs. For efficient prevention of sports injuries is necessary to take into account psychological characteristics of athletes.

**Hypothesis:** Some psychological characteristics of professional football players, handball and basketball players such as reduced motivation, increased anxiety, depression and poor coping with stressful events significantly increase the likelihood of sports injuries.

**Aims:** The aim of the dissertation is to make the best methodology in prevention of sports injuries for professional football, handball and basketball athletes in relation to their psychological characteristics.

**Materials and methods:** The study is a prospective cohort study that will be conducted during a one sports season and will include all professional players with the first team contract in the first Croatian football, handball and basketball league. Athletes who are acutely injured and who are not able to actively participate in the competitions will not be included in the study. It is expected the participation of at least 210 respondents (at least 70 professional athletes for each sport) that will be surveyed during prepa-

ration period before the beginning of the season and monitored during season for occurrence of sports injuries. Seriousness of the injury will be assessed depending on the length of non-participation in sports activities which will be obtained from the history of attending a sporting event through the course of the study. Psychological characteristics will be assessed with Sport Motivation Scale, General Anxiety Disorder Scale (GAD-7), Psychological Skill Inventory for Sport and Self-report Depression Scale for Research in the General Population (CES-D Scale).

**Expected scientific contribution:** This survey will obtain information on the psychological characteristics of professional soccer, handball and basketball players compared with the incidence of sports injuries specific to individual sports. Just knowing all the variables and their interactions that affect the occurrence of certain sports injuries may be efficient in planning targeted prevention. Therefore, the scientific contribution of this study is to produce the best possible methodology psychological preparation of athletes for the prevention of sports injuries.

**Acknowledgments:**

**MeSH/Keywords:** professional athletes, soccer, handball, basketball, psychological characteristics, sports injuries

Poster code: C-3-138

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Adamec Ivan	INCIDENCE, ACUTE MANAGEMENT AND LONG-TERM FOLLOW-UP OF PATIENTS WITH VESTIBULAR NEURITIS	R-B-30-80	47
Antunac Golubić Zrna	PROGNOSTIC AND PREDICTIVE SIGNIFICANCE OF 25OH D IN COLORECTAL CANCER PATIENTS	T-B-19-49	125
Bačić Antun	CHARACTERIZATION OF IMMUNOSUPPRESSIVE PROPERTIES OF MESENCHYMAL STEM CELLS DERIVED FROM HUMAN PALATINE TONSILS	T-B-21-71	131
Badovinac Sonja	PREDICTIVE SIGNIFICANCE OF NONSPECIFIC LABORATORY PARAMETERS TO THE RESPONSE TO FIRST LINE CHEMOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED AND METASTATIC NON-SMALL CELL LUNG CANCER	T-B-19-54	126
Bakota Bore	ANESTHETIC TECHNIQUES FOR OPEN INGUINAL HERNIA REPAIR IN ADULTS	R-B-10-67	30
Baković Marija	CARBOXYHAEMOGLOBIN HELPS TO IDENTIFY THE ENTRANCE GUNSHOT WOUND	T-B-27-100	156
Barbarić Jelena	CHARACTERISTICS OF INCIDENCE AND MORTALITY TRENDS OF MALIGNANT MELANOMA OF THE SKIN IN CROATIA AND SOUTH-EASTERN EUROPEAN COUNTRIES	T-C-1-98	166
Baričević Denis	THE ROLE OF CHEMOPROPHYLAXIS IN IMMUNOCOMPROMISED PATIENTS' WITH POSITIVE QUANTIFERON TEST BEFORE INTRODUCTION OF BIOLOGICAL TREATMENT	T-B-9-94	103
Baričević Hilarije	PRIORITIES FOR NATIONAL MEDICINES POLICY IN THE EUROPEAN UNION	T-C-2-124	168
Basara Toromanović Latinka	BIOLOGICAL, PSYCHOLOGICAL AND SOCIAL FACTORS AS DYSPNEA PREDICTORS AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASES	T-B-9-74	99
Bečejac Tomislav	PENTADECAPEPTIDE BPC 157 AS A THERAPY FOR CORROSIVE MUCOSAL LESIONS IN RATS	R-A-4-133	7
Benčina Goran	THE HEALTH BURDEN AND ECONOMIC COSTS OF MELANOMA IN CROATIA	T-C-2-143	169
Beqiraj Qendresa	ROLE OF RHO/RHO-KINASE SIGNALING PATHWAYS IN DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN THE EXPERIMENTAL RAT MODEL	T-B-22-156	137
Berkopić Cesar Lidija	BPC 157 REDUCED POSTOPERATIVE ADHESIONS FORMATION IN RATS	T-A-4-139	65

## List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Bičanić Ivana	REGIONAL DIFFERENCES IN DENDRITIC MORPHOLOGY AND SPINE DENSITY OF STRIATAL MEDIUM SPINY NEURONS IN FOXP2 MICE	R-A-9-109	16
Blažina Katarina	THE ROLE OF ULTRASONOGRAPHIC ANALYSIS OF MESENCEPHALIC NUCLEI IN PATIENTS WITH PARKINSON'S DISEASE WITH AND WITHOUT DEPRESSIVE SYMPTOMS	R-B-30-149	49
Blekić Mario	17Q12-21 AND ASTHMA - INTERACTIONS WITH EARLY LIFE ENVIRONMENTAL EXPOSURES	R-B-24-95	43
Bohač Maja	COMPARISON OF FEMTOSECOND LASERS AND MECHANICAL MICROKERATOMES FOR LASER IN SITU KERATOMILEUSIS - PRELIMINARY RESULTS	R-B-18-41	36
Bokun Tomislav	CHARACTERIZATION OF LIVER TUMORS USING QUANTITATIVE SONOELASTOGRAPHY - PRELIMINARY RESULTS	R-B-9-108	29
Bolanča Željana	THE VALUE OF TRICHOSCOPY IN THE DIAGNOSIS OF PRIMARY CICATRICIAL ALOPECIAS	T-B-2-146	77
Božina Tamara	PPARG VARIABILITY IS AN IMPORTANT FACTOR IN THE DEVELOPMENT OF METABOLIC SYNDROME	R-A-6-29	9
Bralić Lang Valerija	HOW GOOD ARE WE IN ACHIEVING GUIDELINE-RECOMMENDED GOALS FOR T2DM PATIENTS IN GP OFFICES IN CROATIA?	R-C-4-61	56
Brborović Hana	DOES NURSES' ABSENTEEISM AFFECT PATIENT SAFETY?	R-C-3-32	55
Bulat Vedrana	STUDY ON THE IMPACT OF PSORIASIS ON QUALITY OF LIFE: PHYSICAL, PSYCHOLOGICAL, SOCIAL AND FINANCIAL IMPLICATIONS	R-B-2-164	21
Bumber Boris	ROLE OF MATRIX METALLOPROTEINASES AND THEIR INHIBITORS IN THE DEVELOPMENT OF CERVICAL METASTASES IN PAPILLARY THYROID CARCINOMA	T-B-21-174	136
Crnković Maja	ATTACHMENT STYLE AND EMOTIONAL REGULATION IN ADOLESCENT PATIENTS WITH ANOREXIA NERVOSA	T-B-29-15	160
Crnogaća Krešimir	CEFAZOLIN PROPHYLAXIS-GOLDEN STANDARD OR STANDARD MISTAKE?	T-B-20-167	129
Cuperjani Frederik	PROGNOSTIC VALUE OF RIBOSOMAL PROTEIN S6-PS240 IN INVASIVE DUCTAL BREAST CANCER	T-B-10-116	112

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Curić Radivojević Renata	THE ROLE OF PARATHYROID HORMONE CONCENTRATION MEASUREMENT IN EARLY POSTOPERATIVE DIAGNOSIS OF HYPOCALCAEMIA AFTER THYROID SURGERY.	T-B-1-57	73
Čavka Vlatka	HUMAN PAPILLOMAVIRUS - POSSIBLE COFACTOR IN DEVELOPMENT OF NONMELANOMA SKIN CANCER	T-B-2-83	76
Čegec Ivana	ATTITUDES OF CROATIAN INTERNAL MEDICINE RESIDENTS REGARDING AVAILABLE ONLINE RESOURCES FOR CLINICAL DECISION MAKING SUPPORT	R-B-13-69	31
Čukljek Snježana	CORRELATION OF FORMAL EDUCATION AND NURSING STUDENTS' ATTITUDES TOWARD NURSING AS A PROFESSION	T-C-2-114	167
Ćurković Marko	PUBLIC PERCEPTION OF PHYSICIANS' INTERPERSONAL RELATIONSHIPS - ARE CROATIAN PHYSICIANS PROFESSIONAL IN THE EYES OF THE PUBLIC?	R-B-15-119	33
Daka Qendrese	CLASSIFICATION AND QUANTIFICATION OF THE RISK FACTORS AND TREATMENT STRATEGIES FOR OCULAR HYPERTENSION AND PRIMARY OPEN- ANGLE GLAUCOMA	R-B-18-152	37
Dasović Buljević Andrea	ANALYSIS OF TREATMENT OUTCOME IN CHILDREN WITH HYPOPLASTIC LEFT HEART SYNDROME	R-B-24-171	44
Dawidowsky Barbara	DO CONVERGENCE INSUFFICIENCY PLAYS AN IMPROTANT ROLE IN CHILDREN DIAGNOSED WITH ADHD SY?	T-B-18-154	123
Dobrenić Margareta	HYBRID SPECT/CT WITH RADIOLABELED LEUCOCYTES IN PATIENTS WITH PAINFUL ARTHROPLASTY	T-B-17-165	122
Doko Ines	GRIP FORCEFULNESS IN RHEUMATOID ARTHRITIS	T-B-3-34	78
Džoić Dominković Martina	ELASTOGRAPHIC VALUES OF BREAST TISSUE IN WOMEN	T-B-25-75	152
Đanić Hadžibegović Ana	ANALYSIS OF SALIVA PEPSIN IN PATIENTS WITH VOICE PROSTHESIS	R-B-21-58	39
Ehrenfreund Tin	THE INFLUENCE OF THE BADLY CONTROLLED BONE DRILLING ON THE HEAT BUILDUP IN THE DRILLING ZONE	T-B-10-161	117

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Elezaj Shkelzen	POLYMORPHISM OF FOLLICULE-STIMULATING HORMONE GENE RECEPTOR IN ALBANIAN MALE POPULATION.	T-B-28-141	158
Erdelez Lidija	USE OF BLOOD AS A QUALITY INDICATOR IN VASCULAR SURGERY	T-B-10-130	115
Erjavec Igor	EFFECT OF BLOOD SEROTONIN LEVELS ON FOUR MONTHS OLD RAT SKELETON	R-A-5-142	8
Galunić Bilić Lea	DEMORALIZATION AND LUNG CANCER	T-B-26-44	155
Gashi Goneta	THE INCIDENCE OF MICRONUCLEI IN PERIPHERAL BLOOD LYMPHOCYTES AND BUCCAL EXFOLIATED CELLS IN WOMEN WITH AND WITHOUT CERVICAL CANCER	T-A-3-162	61
Gashi Musli	THE IMPACT OF PRE-HOSPITAL EMERGENCY CARE ON OUTCOME IN PATIENTS WITH ACUTE CORONARY SYNDROME	T-B-6-99	86
Gomerčić Palčić Marija	THE ROLE OF CAVEOLIN-1 AND TRANSFORMING GROWTH FACTOR BETA IN NONALCOHOLIC FATTY LIVER DISEASE	T-B-9-73	98
Gregurić Tomislav	CLINICAL SIGNIFICANCE OF COMPUTED TOMOGRAPHY FINDINGS IN PATIENTS WITH CHRONIC RHINOSINUSITIS	T-B-25-38	150
Grgić Dora	CALPROTECTIN IN ASSESMENT OF ACTIVITY OF ULCERATIVE COLITIS AND CROHN'S DISEASE	T-B-9-102	104
Grizelj Danijela	NECK CIRCUMFERENCE ASSOCIATION WITH METABOLIC RISK FACTORS IN PATIENTS UNDERGOING NECK SURGERY	R-B-9-89	28
Gršić Krešimir	IMMUNOHISTOCHEMICAL EXPRESSION OF ESTROGEN RECEPTORS BETA IN HEAD AND NECK SQUAMOUS CELL CARCINOMA	T-B-21-82	132
Halužan Damir	THERMAL CHANGES DURING HEALING OF DISTAL RADIUS FRACTURES	T-B-10-10	108
Hodžić Damir	QUALITY OF LIFE AFTER „SLING” OPERATION	T-B-5-97	82
Hostić Vedran	A COMPARISON OF THE C-MAC D-BLADE, C-MAC AND DIRECT LARYNGOSCOPY	T-B-1-91	75
Igrec Jasminka	COMPARISON OF DIFFERENT DIAGNOSTIC PROTOCOLS IN THE DIAGNOSIS OF ASSOCIATED FRACTURES OF THE FACE AND SKULL BASE COMPUTED TOMOGRAPHY	R-B-25-30	45



### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Jandroković Sonja	THE DIAGNOSTIC VALUE OBTAINED BY OPTIC NERVE HEAD ANALYSIS OF OPTICAL COHERENCE TOMOGRAPHY IN RELATION TO THE STAGE OF GLAUCOMA	R-B-18-159	38
Jurčić Petra	THE FREQUENCY AND TREND OF FACTOR CONCENTRATES' USAGE IN CHILDREN DIAGNOSED WITH HAEMOPHILIA IN CROATIA FROM 2008 TO 2012.	T-B-24-43	142
Katavić Nataša	MESIAL TEMPORAL SCLEROSIS: MRI AND HISTOPATHOLOGY CORRELATION	T-B-25-115	154
Katić Tina	ASSOCIATION BETWEEN THE MEASURES OF ARTERIAL STIFFNESS AND SERUM LEVELS OF PROINFLAMMATORY CYTOKINE IN ARTERIAL HYPERTENSION	T-B-9-147	107
Klepac Pulanić Tajana	QUALITY OF LIFE IN FEMALE PATIENTS WITH GENITAL CHRONIC GRAFT VERSUS HOST DISEASE	R-B-5-176	24
Knezović Ana	CORRELATION BETWEEN ASTROGLIAL CHANGES, COGNITIVE AND CHOLINERGIC DEFICIT IN A RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE: LONG-TERM FOLLOW UP	R-A-4-14	4
Kolumbić Lakoš Adela	THE ROLE OF CYTOKINES IN PROSTATITIS SYNDROME PATIENTS	T-B-7-121	89
Konjhodžić Rijad	SELECTION OF FORENSICALLY SIGNIFICANT SNPS INSIDE BIH POPULATION	R-A-6-144	13
Košec Andro	PROTEOMIC TISSUE PROFILING - A NEW GATEWAY TO UNDERSTANDING EARLY STAGE MELANOMA BIOLOGY	T-A-6-155	67
Kovačić Dražen	THE ROLE OF SEMEN MICROBIOLOGICAL DIAGNOSTICS IN THE DIAGNOSIS OF CHRONIC PROSTATITIS SYNDROME	T-B-7-153	90
Kovačić Jelena	EXPLORING THE RISK FACTORS FOR THE DEVELOPMENT OF ALLERGIC RESPIRATORY DISEASES BY BAYESIAN NETWORKS BUILT ON MULTIPLE-SOURCE DATA	T-C-1-42	165
Krajinović Vladimir	SEPSIS SEVERITY ESTIMATION AND INFLUENCE ON OUTCOME OF PATIENTS WITH INFECTIVE ENDOCARDITIS	R-B-7-50	25
Krasniqi Valon	GENETIC POLYMORPHISM OF CYP2C19, CYP2C9 AND VKORC1 IN KOSOVO'S POPULATION	T-A-4-88	62
Kuhar Martin	ANDRIJA ŠTAMPAR'S REJECTION OF EUGENICS	R-A-8-170	15

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Kulaš Tomislav	MONITORING OF ANTIHYPERTENSIVE THERAPY EFFECTS IN PREGNANCY	T-B-5-66	80
Kust Davor	CYTOKERATIN-20 POSITIVE CELLS IN BLOOD OF COLORECTAL CANCER PATIENTS AS A PROGNOSTIC MARKER	T-B-19-63	124
Kutleša Marko	EFFICACY OF THERAPEUTIC HYPOTHERMIA IN PATIENTS WITH INFLAMMATORY DISEASES OF THE CENTRAL NERVOUS SYSTEM	R-B-7-33	26
Lalić Hrvoje	AICAR INDUCES DIFFERENTIATION OF ACUTE MYELOID LEUKEMIA CELLS	R-A-7-68	14
Leci Tahiri Laura	APOPTOSIS IN NATIVE VEIN WALL IN FAILURE OF HEMODIALYSIS ARTERIOVENOUS FISTULAS	T-B-10-127	114
Ledinsky Iva	IMMUNOHISTOCHEMICAL EXPRESSION OF PROTEIN NEDD9 IN HEAD AND NECK SQUAMOUS CELL CARCINOMA	T-B-21-132	134
Lehman Ivan	MYOTONIC DISCHARGES IN CHILDREN WITH RADICULOPATHY	T-B-24-129	146
Lila Albert	IMPACT OF OBESITY ON THE INFERTILITY OF KOSOVO WOMEN - ASSESSMENT OF OVARIAN RESERVE	T-B-5-145	84
Lojo Nermin	THE EFFECT OF PENTADECAPEPTIDE BPC 157 AND HIGH DOSE DICLOFENAC ON INDUCED SHORT BOWEL SYNDROME	R-A-4-92	5
Lucijanić Marko	WNT AND SONIC HEDGEHOG SIGNALING PATHWAYS IN PRIMARY AND SECONDARY MYELOFIBROSIS	T-A-6-168	68
Lukić Edita	INTRINSIC INSULIN RESISTANCE AMONG NONDIABETICS AND OCCURRENCE OF HYPERGLYCEMIA IN CRITICAL ILLNESS	T-B-9-87	95
Maček Ivana	ROLE OF TRAUMA IN CONDUCT DISORDER	T-B-29-122	161
Madžar Tomislav	PSYCHOLOGICAL PREDICTORS OF SPORT INJURIES AMONG PROFESSIONAL SOCCER, HANDBALL AND BASKETBALL PLAYERS	T-C-3-138	170
Makar Aušperger Ksenija	INFLUENCE OF COMBINATION OF CYP2C9, VKORC1 AND MDR1 GENE POLYMORPHISMS ON INDIVIDUALIZATION OF WARFARIN THERAPY	T-B-13-103	119
Marčec Mateja	FOREARM ULTRASOUND AS A PRIMARY DIAGNOSTIC METHOD OF CHOICE FOR BLUNT FOREARM TRAUMA IN CHILDREN	T-B-10-17	109

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Martinaj Merita	ASSOCIATION OF DISEASE ACTIVITY MEASURED BY RAPID3 WITH PHYSICAL FUNCTION OF THE HAND AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS	T-B-3-107	79
Mašić Marijana	FORENSIC ROLE OF MTDNA SNPS	T-B-27-104	157
Mašić Silvija	EXPRESSION OF PLAKOPHILIN 3 IN DIFFUSE MALIGNANT PLEURAL MESOTHELIOMA	T-A-3-36	59
Matek Danijel	COMPARISON OF DIRECT AND INDIRECT COST AND OUTCOME OF OPERATIVE TREATMENT OF SUBACROMIAL IMPINGEMENT SYNDROME, BY OPEN AND ARTHROSCOPIC TECHNIQUES	T-B-20-45	128
Mažibrada Hana	EFFECT OF PROLONGED WORKING TIME ON ACTIVATION OF HEMOSTATIC SYSTEM	T-B-9-90	101
Meštrović Tomislav	COMPARISON OF AZITHROMYCIN AND DOXYCYCLINE IN VITRO ACTIVITY AGAINST CHLAMYDIA TRACHOMATIS STRAINS ISOLATED FROM CERVICAL SWABS	R-B-16-84	34
Miletić Vladimir	EFFECT OF BOTULINUM TOXIN - TYPE A ON NON-MOTOR SYMPTOMS AND COGNITION IN PATIENTS WITH PRIMARY FOCAL DYSTONIA	R-B-30-140	48
Moslavac Sandra	EXPRESSION OF PIWIL2 AND HMGA2 IN PAPILLARY THYROID CARCINOMA	T-B-23-76	141
Murgić Lucija	ETHICS AND PROFESSIONALISM: MEDICAL ETHICS AS PHYSICIANS PROFESSIONAL COMPETENCY ILLUSTRATED THROUGH PATIENTS' AUTONOMY ISSUES	R-B-15-52	32
Mustapić Jelena	THE RELATIONSHIP OF PEER PRESSURE, BODY SHAME AND BODY DISSATISFACTION WITH ADOLESCENT EATING BEHAVIOURS	R-B-29-56	46
Mustapić Matej	THE PREDICTIVE VALUE OF INITIAL SPINAL MRI FINDINGS FOR POST-THERAPEUTIC CLINICAL OUTCOME OF VERTEBRAL OSTEOMYELITIS	T-B-25-18	149
Nad Škegro Sandra	THE IMPACT OF UGT1A9 POLYMORPHISM ON MYCOPHENOLIC ACID PHARMACOKINETIC PARAMETERS IN KIDNEY ALLOGRAFT RECIPIENTS	T-B-28-158	159
Nanković Sibila	CLINICAL AND NEUROPHYSIOLOGICAL CHANGES IN PATIENTS WITH PINEAL REGION EXPANSIONS	T-B-30-110	162
Navratil Marta	BIOMARKERS OF UNCONTROLLED CHILDHOOD ASTHMA	R-B-24-51	42

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Nedić Antonela	ASSOCIATION BETWEEN ACTIVITY INTENSITY AND BIOMARKERS OF OXIDATIVE STRESS IN FOOTBALL PLAYERS	T-A-5-59	66
Nemir Jakob	NEUROSURGICAL IMPORTANCE OF SPHENOID AND CLIVUS-TENTORIUM ANGLE IN ANATOMICAL VARIATIONS OF SUBTENTORIAL SPACE	T-B-10-125	110
Novačić Karlo	NGAL IN EARLY DIAGNOSIS OF CONTRAST INDUCED NEPHROPATHY (CIN)	T-B-25-40	151
Novosel Luka	ROLE OF DIGITAL TOMOSYNTHESIS IN DIAGNOSIS OF SACROILIITIS	T-B-25-137	153
Novosel Tomislav	THYROTROPIN RECEPTOR MRNA (TSHR MRNA) AS A NOVEL MARKER FOR THYROID CANCER	T-B-21-136	135
Ostojić Alen	EPIDEMIOLOGY OF INVASIVE ASPERGILLOSIS IN PATIENTS WITH MALIGNANT HEMATOLOGIC DISEASES	T-B-7-72	88
Papić Neven	WHOLE GENOME SEQUENCING ANALYSIS OF HUMAN LIVER SINUSOIDAL ENDOTHELIAL CELLS REVEALS EVIDENCE FOR AN ANTI-INFLAMMATORY ROLE DURING HCV INFECTION.	R-A-6-37	10
Pavić Ivana	DETERMINATION OF EGFR, BCL-2 AND KI67 IN PATIENTS WITH ORAL LICHEN PLANUS	R-B-23-31	41
Planinić Pavao	CLINICAL SIGNIFICANCE OF SENTINEL LYMPH NODE DETECTION IN FIGO STAGES IA2 - IIA1 OF CERVICAL CANCER	T-B-5-151	85
Planinić Radoš Gordana	THE INFLUENCE OF TOBACCO SMOKE UPON BIOCHEMICAL CHANGES IN CERVICAL MUCUS OF WOMEN IN REPRODUCTIVE AGE	T-B-5-101	83
Podrimaj Bytyqi Arjeta	MICRONUCLEUS INDEX IN EPITHELIAL EXFOLIATED CELLS OF UROTHELIUM AND BUCCAL MUCOSA, AND PERIPHERAL BLOOD LYMPHOCYTES OF PATIENTS WITH PAPILLARY UROTHELIAL CARCINOMA	T-A-3-160	60
Pristaš Irina	ANALYSIS OF CHANGES OF BACTERIAL ISOLATES FROM SEVERE INFECTIONS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS WITH EMPIRIC ANTIMICROBIAL THERAPY IN UNIVERSITY HOSPITAL FOR INFECTIOUS DISEASES	R-B-16-150	35
Prka Željko	PROGNOSTIC SIGNIFICANCE OF FAS, FASL AND C-FLIP EXPRESSION IN CLASSIC HODGKIN LYMPHOMA	T-B-9-93	102
Puljević Mislav	VALUE OF T-WAVE ALTERNANS IN DIAGNOSTICS OF ISCHEMIC HEART DISEASE	T-B-9-177	93

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Qerimi Ardita	COMPARISON OF CLASSICAL AND ADVANCED DIAGNOSTIC TOOLS IN BONE TUMORS	T-B-23-163	138
Radočaj Tomislav	DOSE-DEPENDENT DEPRESSION OF PREBÖTZINGER COMPLEX (PBC) REGION NEURONS BY LOCAL APPLICATION OF THE	R-A-9-47	17
Radulović Bojana	THE CONNECTION BETWEEN HYPOCHLOREMIA AND HYPONATREMIA IN PATIENTS WITH HEART FAILURE	T-B-9-46	96
Radulović Petra	NEDD9 AS A PANCREATIC ADENOCARCINOMA METASTASIS GENE	T-B-23-64	140
Ramić Snježana	PHOSPHORYLATED HER2 RECEPTOR AS AN INDICATOR OF BREAST CANCER RESISTANCE TO TRASTUZUMAB	R-A-6-111	12
Ramosaj Morina Atifete	CLINICAL, BIOCHEMICAL AND GENETICAL CHARACTERISTICS OF ALBANIAN PEDIATRIC CELIAC DISEASE PATIENTS FROM KOSOVO	T-B-24-126	147
Rašić Ivan	EXPRESSION OF BORIS AND MYC IN HYPOPHARYNGEAL SQUAMOUS CELL CARCINOMA - PRELIMINARY RESULTS	R-A-6-65	11
Rešić Arnes	VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN SERUM AND BASIC FIBROBLAST GROWTH FACTOR (BFGF) IN URINE IN CHILDREN WITH HEMANGIOMAS	T-B-24-81	145
Rukavina Iva	DETERMINATION OF EARLY ATHEROSCLEROTIC CHANGES IN CHILDREN WHO SUFFER FROM JUVENILE IDIOPATHIC ARTHRITIS	T-B-24-173	144
Sadiku Zehri Fatlinda	COMPARISON OF PLEURAL LESIONS USING VIBRATIONAL SPECTROSCOPY	T-B-23-86	139
Sakan Sanja	FIBROBLAST GROWTH FACTOR 23 AND ACUTE KIDNEY INJURY	R-B-8-118	27
Sokol Vesna	AN ADEQUACY OF LOW MOLECULAR WEIGHT HEPARIN TREATMENT IN PATIENTS WITH HEREDITARY TROMBOPHILIA AS A CAUSE OF RECURRENT PREGNANCY LOSS.	R-B-5-166	23
Solak Mirsala	DO BIOMARKERS LEPTIN AND ADIPONECTIN HAVE IMPORTANT ROLE IN COPD?	T-B-9-123	105
Solter Darko	PITUITARY-THYROID FEEDBACK CONTROL IN HYPOTHYROID AND ATHYREOTIC PATIENTS	T-B-21-113	133
Sović Slavica	QUALITY ASSESSMENT IN GENERAL PRACTICE	R-C-2-117	54

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Stemberger Lorna	CHEMOKINES IN CENTRAL NERVOUS SYSTEM DISEASES IN CHILDREN	T-B-7-35	87
Striber Neda	CHANGES OF THE NERVE FIBER LAYER THICKNESS EVALUATED BY OPTIC COHERENCE TOMOGRAPHY IN CHILDREN WITH CEREBRAL PALSY AND VISUAL IMPAIRMENT	T-A-9-172	69
Svetina Lucija	IMPACT OF EXTRACORPOREAL LIFE SUPPORT ON BLOOD CLOT VISCOELASTIC PROPERTIES AND PLATELET AGGREGATION	T-B-10-169	116
Šakić Ivana	CORRELATION BETWEEN EXPRESSION OF RESISTIN IN SERUM AND IN CAROTID PLAQUE AND HISTOLOGICAL FEATURES OF ATHEROSCLEROTIC PLAQUE	T-B-9-77	100
Šakić Livija	INFLUENCE OF DEXAMETHASONE ADMINISTRATION IN SPINAL ANESTHESIA IN FEMUR FRACTURE	T-B-1-85	74
Šepac Ana	DIFFERENTIATION OF CARDIOMYOCYTES FROM HUMAN INDUCED PLURIPOTENT STEM CELLS	R-A-3-148	3
Šitum Andrej	PENTADECAPEPTIDE BPC 157 AND WOUND HEALING AFTER HIND LIMB ISCHEMIA	T-A-4-120	64
Tesari Crnković Helena	THE IMPACT OF RISK FACTORS IN EARLY LIFE ON DEVELOPMENT OF ALLERGIC SENSITIZATION	T-B-24-135	148
Thaci Kujtim	IMMUNOGLOBULIN G GLYCOSYLATION IN PATIENTS WITH COLORECTAL CANCER	T-B-11-105	118
Tomić Ivan	PROGNOSTIC VALUE OF LACTATE CLEARANCE AND CENTRAL VENOUS BLOOD OXYGEN SATURATION	T-B-8-175	92
Tomljenović Dejan	RELATIONSHIP BETWEEN SPECIFIC AND NONSPECIFIC NASAL HYPERREACTIVITY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS	R-B-21-112	40
Trogrlić Mate	(99M)TC HYNIC-TOC SOMATOSTATIN RECEPTOR SCINTIGRAPHY	T-B-17-48	121
Udovičić Mario	EFFECT OF PENTADECAPEPTIDE BPC 157 ON MONOCROTALINE INDUCED COR PULMONALE IN RATS	T-A-4-134	63
Varda Brkić Dijana	DETECTION OF CAG PATHOGENICITY ISLAND VIRULENCE GENES AND DUPA GENES OF HELICOBACTER PYLORI ISOLATES AFTER FAILED ERADICATION THERAPY	T-B-16-39	120
Vargović Martina	INCIDENCE AND SIGNIFICANCE OF T. VAGINALIS IN PATIENTS WITH CHRONIC PROSTATITIS SYNDROME	T-B-7-157	91

### List of Candidates, Abstract Titles and Poster Codes

PhD candidate	Abstract Title	Poster code	Page number
Vlaić Josip	COMPARISON OF BIOMECHANICAL PROPERTIES OF THE PLANTARIS AND GRACILIS TENDONS FOR MEDIAL PATELLOFEMORAL LIGAMENT RECONSTRUCTION	T-B-20-131	130
Vrdoljak Ana	EFFECTS OF POLYPHENOLS FROM GRAPE SEEDS EXTRACT ON BLOOD PRESSURE AND ENDOTHELIAL FUNCTION ON PREHYPERTENSIVE	T-B-9-19	94
Vučemilo Luka	ARE PHYSICIAN-PATIENT COMMUNICATION PRACTICES SLOWLY CHANGING IN CROATIA? - A CROSS-SECTIONAL QUESTIONNAIRE STUDY	R-C-2-53	53
Vučić Katarina	METABOLIC SYNDROME, CHARACTERISTICS OF BREAST CANCER AND 25-HYDROXYVITAMIN D STATUS AT DIAGNOSIS	T-B-19-78	127
Zejnullahu Ylber	EFFECTS OF COMBINED TOPICAL HYALURONIC ACID AND SYSTEMIC DICLOFENAC SODIUM ON FORMATION OF ADHESIONS ON INJURED FLEXOR TENDONS IN CHICKENS	T-B-10-106	113
Zibar Karim	THE RELATIONSHIP OF PLASMA CONCENTRATIONS OF GLUCAGONE-LIKE PEPTIDE 1 AND FIBROBLAST GROWTH FACTOR-21 WITH GLUCOREGULATION, LIPIDEMIA AND MICROVASCULAR COMPLICATIONS IN DIABETES MELLITUS TYPE 1 PATIEN	T-B-9-55	97
Zlojtro Marija	IMPACT OF STRESS HYPERGLYCEMIA ON HOSPITAL OUTCOME OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE	T-B-9-128	106
Zmijanac Partl Jasenka	TROPHOBLAST DIFFERENTIATION IN NORMAL AND PATHOLOGICAL PREGNANCY	R-B-5-60	22
Zrno Mihaljević Martina	EFFECT OF ELEVATED PREOPERATIVE HEMOGLOBIN A1C ON OUTCOMES IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING AND COMPARISON WITH THE STANDARDIZED METHOD OF ASSESSMENT OF OPERATIVE RISK	T-B-10-70	111
Zudenigo Damir	CHARACTERISTICS OF GASTRIC MYOELECTRICAL ACTIVITY IN PREGNANCY	T-B-5-79	81
Žigman Tamara	THE CORRELATION OF ANTISTREPTOLYSIN O LEVEL WITH CHILDHOOD ATTENTION DEFICIT, HYPERACTIVITY AND IMPULSIVITY DISORDER	T-B-24-62	143
Živanović Posilović Gordana	PENTADECAPEPTIDE BPC 157 ANTIARRHYTHMIC EFFECT IN RATS TREATED WITH BUPIVACAINE TOXIC DOSES	R-A-4-96	6

Sveučilište u Zagrebu, Medicinski fakultet/University of Zagreb, School of Medicine  
**Doktorski studij Biomedicina i zdravstvo/PhD Programme Biomedicine and Health Sciences**  
**Dan doktorata 2013/PhD Day 2013**  
**Knjiga sažetaka/Abstract book**

---

*Publisher*

MEDICINSKA NAKLADA  
Cankarova 13, 10000 Zagreb, Croatia

*For the publisher*

ANĐA RAIČ, Director

*Editors*

ZDRAVKO LACKOVIĆ  
DRAGO BATINIĆ  
ANA BOROVEČKI  
ANTE TVRDEIĆ  
ROBERT LIKIĆ  
MARKO JAKOPOVIĆ  
INGEBORG REMICH  
JASMINA ŠTIMAC

*Design and typesetting*

MARKO HABUŠ

*Cover page*

ALMA ŠIMUNEC-JOVIĆ