MONTENEGRIN INTERNATIONAL MEDICAL SUMMIT

October, 3-6. 2019.

Podgorica, Montenegro

ABSTRACT BOOK

LIVE, LEARN AND RESEARCH

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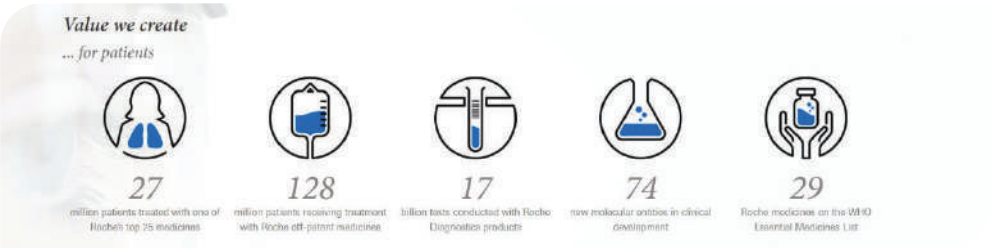

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INVITATION LETTER

Dear Colleagues,

It is my honor and pleasure to invite you to participate in the 1st Montenegrin International Medical Summit (MIMS 2019), which will be held from 3rd to 6th October 2019, in Podgorica, Montenegro.

The organizer of the 1st Montenegrin International Medical Summit is Faculty of Medicine, University of Montenegro. After more than twenty years of existence, the Faculty of Medicine of the University of Montenegro has established itself as an important scientific and research center in our country, as well as in the region. Therefore, it is with great pride that we now announce this pioneering venture, since this is the first congress of this type in Montenegro.

We are hoping that the conference will be an excellent opportunity for students and young doctors of medicine, dentistry and pharmacy, from Montenegro and the region, to exchange their knowledge, ideas and insights, as well as achievements and experiences, that can enhance our knowledge and broaden our horizons.

Students and young doctors who choose to be part of our congress will have the opportunity to get involved in various topics, many of whom will surely identify as a valuable foundation for future education and employment.

In addition to presentations and lectures by leading experts in our country, the choice of current topics and attractive presentation forms such as plenary lectures, oral and poster presentations and interesting workshops, the expected attendance should exceed 200 participants.

With your help and valuable contribution we are confident that the conference will assist in better and greater development of medical sciences. This year's motto of the congress is Live, learn and research.

We hope you will enjoy the meeting and we are looking forward to welcome you in Podgorica in October 2019.

Best regards on behalf of Organizing Committee!

Milovan Roganović, MD
President of OC MIMS 2019

WELCOME LETTER

Dear colleagues,

It is my honor and privilege to welcome you on behalf of the Faculty of Medicine, University of Montenegro, to the first Montenegrin International Medical Summit (MIMS 2019), which will be held from 3rd to 6th October 2019, in Podgorica, Montenegro.

The Faculty of Medicine, University of Montenegro has been educating healthcare professionals for over twenty years, who through their expertise, contribute to the progress of health care service, as well as the development of health sciences. Our Faculty represents a diverse and progressive community, characterized by dedication to teaching, healthcare profession and science and which is progressing with big steps on daily basis.

Our satisfaction is even bigger that, after more than twenty years of dedicated work, we are embarking upon another new adventure called the first Montenegrin International Medical Summit. I would be proud to point out that our teaching staff and associates achieve outstanding scientific results. The students, future healthcare professionals, from their first steps at the Faculty, are being challenged and inspired to move their own limits in thinking and learning.

For many years, we have been investing a lot of efforts and energy in developing international cooperation. Our students, teachers and associates proudly sign the name of our institution on scientific papers in international journals, oral and poster presentations, as well as plenary presentations at international conferences, but also on the leadership positions of regional and international projects. Cooperation with foreign universities, student exchanges and trainings are just some of the visible effects of international cooperation.

The world of science is trying and challenging; it requires a lot, but gives back much more! Therefore, investment in education will help you become successful healthcare professionals. That is why this congress is the right opportunity to start investing in your future, because even the longest roads begin with the first step!

The task of all of us at this congress will be to give our contribution, to choose from many interesting statements, those that have a characteristic of scientifically confirmed facts, because only with knowledge and truth, we can make the solid foundation of scientific knowledge. I sincerely hope that your time spent at this Congress will result in achieving the intentions and wishes you had in mind when you made the decision to join us.

At last, I would like to emphasize our interest in cooperation, communication and constructive suggestions. With the hope that you will enjoy the beauties of Podgorica and feel at home, I invite you to join us in October 2019!

Dean of Faculty of Medicine,
University of Montenegro
Miodrag Radunović, MD, PhD, Full Professor

PLENARY LECTURES

THE INVESTIGATION OF THE POVERTY AND OBESITY AMONG CHILDREN IN MONTENEGRO- CLINICAL, PATHOPHYSIOLOGICAL, BIOCHEMICAL, PREVENTIVE ASPECTS – KEY RESULTS

MILICA MARTINOVIĆ, PhD, Full Professor
University of Montenegro, Faculty of Medicine, Department of Patophysiology and Laboratory Medicine

Abstract

Obesity is defined as the abnormal or excessive fat accumulation caused by a positive energy balance, which has been associated with a negative impact on health. Childhood obesity is one of the most serious public health challenges of the 21st century. According to the data from World Health Organization, the prevalence of overweight and obesity among children and adolescents aged 5-19 has risen dramatically from just 4% in 1975 to just over 18% in 2016. Obesity is preventable.

The mechanism of obesity development is not fully understood. It is believed to be a disorder with multiple causes. Environmental factors, lifestyle preferences and cultural environment play pivotal roles in the rising prevalence of obesity worldwide. Obese children are more likely to become obese adults. This disease leads to multiple disorders in many systems of the human body and decreases the quality of life and the life expectancy. The pathophysiological mechanisms of obesity and its complications are partially recognized, including the important role of low-grade inflammation and oxidative stress.

We performed (Medical Faculty of University of Montenegro, 2013-2015), a study among Montenegrin elementary school children. The final sample included 2076 boys (50.7%) and 2021 girls (49.3%), aged from 7 to 13 years (mean ± SD = 10.2 ± 1.7 years). Overall percentage of Montenegrin children who were overweight or obese (IOTF) is 22.9% of which 5.3% were obese (7.0% boys vs. 3.5% girls). Among the investigated children in Podgorica there were 21.2% and 6% overweight and obese children, respectively. Obesity was more frequent among boys (7.6%) compared to girls (4.4%). The prevalence of hypertension was 10.4%, without differences between sexes. We showed that poverty was linked to elevated blood pressure in girls but not boys; this effect was statistically significant for diastolic pressure. Both overweight and obesity even among young population were related to higher cardiometabolic risks, and this effect was more prominent among boys compared to girls. We showed that pre-obesity and obesity in childhood were positively associated with oxidative stress and inflammation, and inversely associated with vitamin D status. Copper and zinc concentrations were not associated with excess fat in children. Self-medication of children by their parents may be expected for every fourth child in Montenegro. Maternal education, health profession and cigarette smoking are decisive factors for self-medication in children by their parents.

There are numerous steps we can take to help prevent overweight and obesity during childhood and adolescence. Good education of all included groups leads to good prevention. It is a very important goal for any country that is struggling with this problem. Anyone who is able to contribute, should act so, every child or citizen, if possible. This should be understood as the fight for our common better future.

Biography

Prof. Milica Martinović was born in Nikšić, Montenegro. Primary School and High School she finished in Nikšić. Educations: Medical Doctor (General Medicine) (1983), Medical School, Belgrade University, Serbia; Specialization in Pediatrics, (1988-1992), Medical School, Belgrade University, Serbia; Master degree (1997), Medical School, University in Niš, Serbia; PhD degree (2000), Medical School, University in Niš, Serbia.

Academic History: Teaching assistant (1999-2003); Assistant Professor (2003-2008); Associate Professor (2008-2013); from 2013 – present Full Professor and Head of Department of Pathophysiology and Laboratory Medicine.

Prof. Martinović published (in the journals from SCI list or from other indexed basis, in the international or national conferences, or as invited lecures) about 60 articles. She was an author of some chapters in the Textbook on Pathophysiology, member of the team in 7 national or international projects. Prof. Martinović made study visits at the Medical Faculty of Transilvania University in Brashov (Romania), Medical Faculty of Medical University of Warsaw (Poland), Medical Faculty of Charles University in Prague (Czech Republic).

HOW TO OVERCOME ANXIETY: WHAT ARE THE OPTIONS?

LIDIJA INJAC STEVOVIĆ, PhD, Associate Professor
University of Montenegro, Faculty of Medicine, Department of Psychiatry

Abstract

Anxiety could be described in terms of tension, uneasiness, worry and negative anticipation. It could be regarded as a personality trait or a current psychological state. Most studies confirm that anxiety is associated with depression and psychosomatic problems. In a recent Montenegrin research, 9.25% of students reported high levels of anxiety (BAI > 35) whilst 23.12% experienced moderate anxiety levels (BAI between 22 and 35). Anxiety could be reduced by using the following CBT techniques: progressive relaxation, working on negative beliefs and replacing them with realistic ones, assertiveness training, self-monitoring etc.). Exercising on a regular basis, getting a better night's sleep, time management, and socializing (participating in social activities) could help as well.

Biography

Assistant Professor Lidija Injac Stevovic, PhD in Medical Science, was born in 1961 in Mojkovac, Montenegro, where she finished elementary and secondary school. She enrolled at the Faculty of Medicine, University of Prishtina in 1982/3 and graduated in 1989. She started specialization in Psychiatry in 1993 at the Clinical Center of Montenegro, Department of Neuropsychiatry, and continued her studies at the Institute for Psychiatry of the Clinical Center of Serbia in Belgrade (1994-1997). She passed the specialist psychiatric examination at the Medical Faculty of the University of Belgrade in 1997. Dr Injac Stevovic defended her master's thesis entitled "Suicide, research of motives, causes and consequences" at the Faculty of Medicine, University of Belgrade, in 2006. She defended her doctoral dissertation, entitled "Factors of suicidal risk: gender differences" at the Faculty of Medicine, University of Montenegro, Podgorica, in 2011, being the first one to obtain PhD degree in Faculty of Medicine in Montenegro.

Since 1989, she has been working at the Clinical Center of Montenegro in Podgorica where she has been delivering medical services, and since 1990 she has been employed in the Health Care Center in Podgorica. Since 1991 she worked in the Health Center of the Ministry of Internal Affairs of Montenegro, and in 1992 she was appointed Head of the Health Center of the Ministry of Internal Affairs of Montenegro. In addition, she was a lecturer for various courses and symposiums for members of the Ministry of Internal Affairs of Montenegro. Since March 2012 she has been working at the Psychiatric Clinic of KCCG. She has been working at the Medical Faculty of the University of Montenegro in Podgorica since October 2005, as an associate in Psychiatry. In July 2006, she was selected as teaching assistant and she was elected Assistant Professor in 2012, being in charge of Psychiatry and Fundamentals of Behavioral Science at the Faculty of Medicine and Dental Medicine. Since 2011 she has been teaching at the Medical College in Berane.

From 2012 to 2017, she has been teaching at the Faculty of Philosophy in Niksic at the Department of Psychology and the Department of Pedagogy as well as at the Faculty of Political Sciences, Department of Social Work. She is a regular lecturer at the Specialist Studies in the field of Family Medicine at the Faculty of Medicine in Podgorica. Since 2014, she has been appointed as the Chief Mentor of the Psychiatric Coordinator as well as mentors for specialization in psychiatry and related disciplines.

She is the main researcher and manager in project IMPULSE, H2020, approved by the European Commission, which is the first project from the H2020 group in Montenegro. She attended several psychiatric educations, such as cognitive psychotherapy education at the Psychiatric Clinic and Department for Psychotherapy - Warneford Hospital-Department of Psychology, Oxford, England (1996), Berlin Summer School Course on “Psychiatry, a Science”, Berlin-Brandenburg Academy of Sciences and Humanities in Berlin (2000), and attended the Benjamin Franklin Psychiatric Clinic, Berlin. She participated in the European Forum, Symposium "Modern Strategies in the Treatment of Psychiatric Disorders", Berlin, Germany (2000). She completed her education in Primary prevention of addictive diseases (ECPD), Belgrade (2004). She participated at the Maudsley Forum, the Institute of Psychiatry at the Maudsley, King’s College, London (2005). She completed the Training GCP (Good Clinical Practice) in 2009. She participated at the International Invitation Conference Amsterdam, organized by the Netherlands Psychiatric Association, EACCME (2011). She participated in the first meeting of the IMPULSE project at the Queen Mary University of London (2018).

STATE OF THE ART OF RARE GENOMIC DISEASES: ADVANTAGES AND CHALLENGES

OLIVERA MILJANOVIĆ, PhD, Associate Professor
University of Montenegro, Faculty of Medicine, Department of Pedatrics
Clinical Center of Montenegro, Center for Medical Genetics and Immunology

Abstract

The development of science and technology, along with the advancement of living standards, have led to dramatic changes in the causes of human disease and death. With the successful treatment of infections and addressing the problem of hunger globally, a new Era in the phylogeny of Homo sapiens marks the development of new diseases, among which genomic disorders take one of the leading places. Almost all genomic diseases belong to the category of rare diseases, because they individual occurrence is very rare.

Rare diseases are considered as diseases with a prevalence of less than five in 10,000 in the general population. The special significance of rare diseases is reflected in the fact that they represent a huge heterogeneous group of about 7000 diseases, most of them are (80%) of genetic origin, difficult to diagnose, treatment is not available or available for a small number of diseases and is very expensive and with uncertain outcome.

Since rare diseases are predominantly of genomic origin, they are mostly manifested in childhood (about 75% of rare diseases) and are recognized as a particular challenge in pediatric medicine. A progressive, degenerative course on one hand, and very limited therapeutic options on the other, result in an unfavorable outcome affecting over 40% of children with rare diseases by the age of 15. Furthermore, the EURORDIS study showed that within EU countries, 40% of patient with rare diseases firstly received an erroneous diagnosis, and the average time to set a definitive diagnosis of rare diseases is 4.8 years. The European Union recognized rare diseases as one of its public health priorities, with a need for action on the preparation of regulations in the field of health policy and the need for adopting national strategies for the rare diseases In 2013, Montenegro adopted the National Strategy for Rare Diseases and it covers all relevant topics related to rare diseases.

Management of rare disease is focused on early identification, effective diagnosis and recognition of the risk for rare diseases in families. A key step in the prevention of rare genomic diseases is to conduct diagnostics prior to family planning and to prevent offspring birth with genomic rare disease. Following the growing need for reliable diagnostics, new diagnostic methods have been developed with the aim of providing as reliable and rapid diagnostics as possible and reducing invasiveness of prenatal diagnostics. The introduction of new Next Generation Sequencing technologies has enabled extensive genomic testing based on the integration of patient clinical phenotyping and clinically focused exome and genome analysis (Clinical Exome and Whole Exome / Genome Sequencing).

The purpose of this lecture is to present the management model of rare genomic diseases in Montenegro, developed by combining our own clinical professional resources with advanced technological capabilities througt intensive international cooperation with genetic diagnostic centers in Europe. The lecture also includes a review of Montenegrin patients with very rare genomic diseases and our contributions to discovering and describing some particular rare genomic diseases.

Biography

Professor Olivera Miljanovic, MD, PhD was born in Titograd (now Podgorica). She is a specialist in pediatrics and a subspecialist of clinical genetics. She graduated from the Faculty of Medicine, specialization in pediatrics and sub-specialization in clinical genetics at the Faculty of Medicine in Belgrade. She holds a master's degree and a doctor of medical sciences degree.

Olivera Miljanovic is an associate professor in the fields of pediatrics, medical and clinical genetics, bioethics and biomedicine and clinical practice at the Faculty of Medicine – University of Montenegro. She is the head of the Center for Scientific Research, the President of the Council for Scientific Research, the President of the Committee for Medical Ethics and Bioethics at the Faculty of Medicine, University of Montenegro. She was the Vice-dean for educational affairs in the years 2013 - 2018. Olivera Miljanovic began her academic career at Faculty of Medicine in 2001 with the appointment of an assistant teacher for practical education.

From the beginning of her professional career she has been working at the Clinical Center of Montenegro. She was the director of the Clinical Center of Montenegro from 2007 to 2011 and the director of the Institute for Diseases of the KC CG from 1999 to 2005. With a team of associates, she introduces modern procedures of medical genetics and forms the Center for Medical Genetics and Immunology of the KC CG. founding in 2000.

She was the head of one and principal investigator in three national scientific research projects. She has over 100 author and co-author papers, published introductory lectures and presentations in international and national journals and at congresses, 11 of which are in SCI list journals. She is the author of 8 chapters in monographs, professional books and manuals.

She has been a member of the CANU Committee for Medical Research since 1998, the UNESCO Chair of Bioethics International Lecturer Forum since 2014, the Council of Europe Committee on Bioethics and the Council of Europe Committee on the Prevention of Trafficking of Organs, Tissues and Cells since 2011, the Council of the Association of Preventive Pediatrics. She is the Editor-in-Chief of Medical Records and a member of the editorial board of Medical Data.

ROLE OF MEDICAL STUDENTS IN DEVELOPMENT OF TRANSPLANTATION PROGRAMME IN MONTENEGRO

MARINA RATKOVIĆ, PhD, Full Professor
University of Montenegro, Faculty of Medicine, Department of Internal Medicine
Clinical Center of Montenegro, Department of Nephrology

Abstract

In Montenegro there was no transplantation program until 2012. On the other hand, there were 89 patients with transplanted kidney. These transplantation were performed abroad; 15% in areas of black organ markets (India, Pakistan, Russia). Beside the ethical problems, these transplantation carried high risk of complications. Patients who underwent such transplantation developed a lot of complications. Our health system had to ensure the solution for patients with terminal organ failure. Preparation of all necessary conditions for the beginning of transplantation program in Montenegro started in 2006 with different activities including public, legal, medical, educational and international cooperation aspects.

Public campaigns organized by medical students of School of Medicine, University of Montenegro focusing on the importance of organ donation and transplantation had been carried out since 2006. First workshop organized by medical students School of Medicine, University of Montenegro named „Organ transplantation in our country-reality or fairaway future“ was in December 2006. Medical students from our faculty activily participated in IFMSA transplantionl project Organ donation and took active role in workshop in Malta 2010. The law about organ donation and transplantation was conducted in 2009. The best support was brought through collaboration with international societies: RHDC (Regional Health Development Center), SEEHN (South-Eastern Europe Health Network) and Clinical Center Zagreb, Croatia. Memorandum about collaboration between Montenegro and Croatia was signed between two ministries of health in April 2012. Medical stuff from Clinical Center of Montenegro underwent education in Croatia. The first kidney transplantation from living donors in Montenegro were preformed on 25th and 26th September 2012. We received congratulations from WHO (World Health Organization), Eurotransplant and ERA EDTA (European Renal Dialysis and Transplantation Association). Regulation for brain death diagnosis was brought in 2012. First deceased donor and first kidney transplantation from deceased donor was performed on 8th December 2013. Heart and liver from the same donor were allocated in Croatia and Slovenia, through the Eurotransplant system.

Ensuring the transplantation program allowed controlled transplantation and the safety of patients. The development of transplantation system improved many medical fields and continuous education of medical staff. Medical students of School of Medicine, University of Monetenegro made a crucial role in development of transplantation programme in our country. We are working on the development of transplantation of other organs and deceased donation as our major aims.

Biography

Prof. Ratković was born on 18.06.1953. god. in Cetinje, Republic of Montenegro. She finished elementary education and high school in Titograd with great success. She enrolled in the School of Medicine, University of Belgrade in 1971/72. god. where she graduated on December 30, 1976. god. She completed her specialist studies in internal medicine at the Faculty of Medicine, University of Belgrade. Subspecialty studies in nephrology, she completed in 1994. at the Clinic of Nephrology, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, defending specialization thesis: "The importance of residual renal function for the clinical condition of patients treated with dialysis". Prof. Ratković finished master's studies at the Faculty of Medicine, University of Belgrade, defending master's thesis: "Growth hormone and insulin-like growth factor in patients with chronic kidney failure" in 2000. Her doctoral dissertation was "Evaluation of the quality of treatment of patients with terminal renal insufficiency of hemodialysis"; she defended it in 2003 at the Faculty of Medicine, University of Belgrade and obtained the academic title of Doctor of Medical Sciences.

At the moment, prof. Ratković is full professor at Department of Internal Medicine, Faculty of Medicine, University of Montenegro. She is also medical director of Clinical Centre of Montenegro and Director of Nephrology Clinic.

She is a founder of transplantation system in Montenegro. Shee is a member of numerous national and international physician associations.

PREGNANCY AND MALIGNANCY

SNEŽANA CRNOGORAC, PhD, Full Professor
University of Montenegro, Faculty of Medicine, Department of Obstetrics & Gynecology
Clinical Center of Montenegro, Clinic for Obstetrics & Gynecology

Abstract

Cancer association with pregnancy (CAP) is defined as the cancer diagnosed from the first day of childbearing to one year post partum. Malignant disease in pregnancy is rare, the incidence is same as of non-pregnant women at same age (1:1000 pregnancies). About 3500 new cases of cancer are diagnosed annually in pregnant women in the US, 3000-5000 in Europe. Postponing of pregnancy and labour is the reason for increase of CAP incidence in the developed countries.

The most common malignant diseases that occur in pregnancy are the tumours whose incidence reaches its peak in the reproductive period: breast and cervical cancer followed by melanoma, leukaemia and lymphoma. They represent 85% of CAP but any other malignant disease such as lung cancer or sarcomas may occur in pregnancy.

The most important goals in curing are: treating the patient with the optimal oncology treatment, to preserve mother's health, without harming the fetus.

The procedures carried out during establishing of diagnosis and staging, ionizing radiation treatment, chemotherapy and surgical treatment undertaken sometimes may have adverse effect to fetus development.

When suspition of malignant disease in pregnancy exists, we should prove it. Recommendations are to apply standard methods which would be also used in non-pregnant women if it is possible without harming a fetus.

Once the diagnosis of cancer during pregnancy is confirmed, it is necessary to determine clinical stage in order to conduct appropriate treatment. In pregnancy, it is necessary to select the methods which will give satisfactory clinical answer without harming a fetus. If possible, ionizing radiation should be either avoided or, at least doses should be limited within recommended scale.

Ultrasound examination is a method of choice for breast, abdomen and pelvis. If necessary, chest x-ray and mammography can be done safely with abdominal shielding. MRI may be conducted

After confirming the diagnosis of malignant disease in pregnancy and determining the stage it is necessary to decide on further treatment. The gold standard of treatment in pregnancy should try to benefit mother's life; to treat curable malignant disease of pregnant women; to protect fetus and newborn from harmful effects of cancer treatment and to preserve fertility for future gestations.

Management should be undertaken by a dedicated multidisciplinary team consisting of a surgeon, a clinical oncologist, a specialist in radiation therapy, an obstetrician, neonatologist and a psychologist.

Surgical procedures are very important in the treatment of solid tumors and can be performed in all three trimesters in pregnancy. Chemotherapy can be administered after the first trimester of pregnancy to avoid harming the developing fetus. Embryo and fetus are very sensitive to ionizing radiation and it is necessary to know evidence and recommendations.

Maternal malignancy metastatic to the fetus is a rare event but some tumors have potential to metastasize to the placenta. When selecting treatment, desire of the patient, her attitude towards termination of pregnancy or damage of fetus, ethic and possible religious stand, must be considered.

Biography

Prof. Snežana Crnogorac is Chair of the Academic Department of Obstetrics & Gynecology, Faculty of Medicine, University of Montenegro; Specialist in Gynecology and Obstetrics at Obs&Gyn Clinic in Clinical Center of Montenegro and Associate Member of International Academy of Perinatal Medicine.

Professor Crnogorac graduated at Faculty of Medicine, University of Belgrade. Specialization in Gynecology and Obstetrics and Postgradate Studies she finished at Faculty of Medicine, University of Belgrade. PhD Thesis prof. Crnogorac defended at Faculty of Medicine, University of Kragujevac, Serbia.

Prof. Crnogorac was a visiting Professor at the Transilvania University of Brasov, Romania in 2011 and visiting Professor at the Charles University in Prague, Faculty of Pharmacy, Department of Biochemical Scienses in 2016. She is a member of the Executive Board of international societies: "Fetus as a patient" and South East European Society of Perinatal Medicine (SEESPM);

Prof. Crnogorac is an invited speaker at numerous national, regional, European and international Medicine schools/courses, congresses and trainings in Perinatal medicine among which World Congress of Perinatal Medicine in Developing Countries Cancun, 2014, 10th World Congress of Perinatal Medicine 2011, Uruguay, World Congress of Perinatal Medicine in Belgrade, 2017 and the 12th World Congress of Perinatal Medicine Madrid, 2015.

She is a member of numerous international associations in perinatal medicine and law working groups in the field of perinatal medicine and human reproduction as well as an author of many papers and publications in national and international scientific journals and books.

SUDDEN CARDIAC DEATH – WHO IS IN DANGER?

LJILJA GLEDOVIĆ MUSIĆ, PhD, Full Professor
University of Montenegro, Faculty of Medicine, Department of Internal Medicine
Clinical Center of Montenegro, Department of Cardiology

Abstract

Sudden cardiac death (SCD) is an unexpected death due to heart problems, which occurs within one hour from the start of heart related symptoms. In the past 20 years, cardiovascular mortality has decreased in high-income countries in response to the adoption of preventive measures to reduce the burden of coronary artery disease (CAD) and heart failure (HF). Despite these encouraging results, cardiovascular diseases are responsible for approximately 17 million deaths every year in the world, approximately 25% of which are SCD. The risk of SCD is higher in men than in women, and it increases with age due to the higher prevalence of CAD in older age. Cardiac diseases associated with SCD differ in young vs. older individuals. In the young there is a predominance of channelopathies and cardiomyopathies , myocarditis and substance abuse, while in older populations, chronic degenerative diseases predominate (CAD, valvular heart diseases and HF). Approximately 50% of cardiac arrests occur in individuals without a known heart disease, but most suffer from concealed ischaemic heart disease. As a consequence, the most effective approach to prevent SCD in the general population resides in quantification of the individual risk of developing ischaemic heart disease based on risk score charts, followed by the control of risk factors such as total serum cholesterol, glucose, blood pressure, smoking and body mass index. Approximately 40% of the observed reduction in SCD is the direct consequence of a reduction of CAD and other cardiac conditions. Rhythm disturbance is the most common cause of SCD. The important thing is screening patients with documented or suspected ventricular arrhythmias. Palpitations (or sensation of sudden rapid heartbeats), presyncope and syncope are the three most important symptoms that require a thorough clinical history taking and possibly further investigations to rule out a relation to ventricular arrhythmias (VA). Palpitations related to ventricular tachycardia (VT) are usually of a sudden onset/offset pattern and may be associated with presyncope and/or syncope. Episodes of sudden collapse with loss of consciousness without any premonition must raise the suspicion of bradiarrhythmias or VA. Syncope occurring during strenuous exercise, while sitting or in the supine position should always raise the suspicion of a cardiac cause, while other situational events may indicate vasovagal syncope or postural hypotension. Symptoms related to underlying structural heart diseases, such as chest discomfort, dyspnoea and fatigue may also be present and should be sought. Thorough inquiries about a family history of SCD and drugs, including dosages used, must be included in the evaluation of patients suspected of having a VA. A positive family history of SCD is a strong independent predictor of susceptibility to VA and SCD. Although physical examination is seldom revealing, it may sometimes give valuable clues. Non-invasive and invasive evaluation will obtained more information. A fundamental aspect of the successful management of VA and the prevention of SCD is effective management of underlying diseases and co-morbidities. The modern concept of the treatment of heart disease and arrhythmogenic substrate must be optimized.

Biography

Prof. Gledović Musić was born 1961 in Podgorica (Titograd), Montenegro, Yugoslavia. She finished Elementary and High school in Podgorica, and held the “Luca” certificate. She was enrolled at Medical University in Belgrade in 1981 and has graduated in 1986, with the average grade of 9.64. Specialization in Internal Medicine for the needs of Cardiology division in Clinical Center of Montenegro, she started in 1990 at Medical University in Belgrade and has completed it with excellence. She was enrolled in the Master of Science in Cardiology at Medical University Belgrade, and has completed it with excellence in 1998, with Master’s Thesis title “Atrial septal defect in adults over 40 years old”. She has started the Specialization in Cardiology in 1996 and completed it in March 1999, with excellence. The PhD degree she has finished in April 2003 at the Faculty of Medicine in Belgrade at Medical University in Belgrade. Her PhD thesis was "Echocardiography assessment of left ventricular function in patients with permanent right ventricular pacing ".

Prof. Gledović Musić has been permanently employed in Clinical Center of Montenegro since March 1986. As a general practitioner she was working in Emergency Unit until 1990. Currently she is working in the Department of Cardiology in Clinical Center of Montenegro. She has been the Medical Director of the Clinical Center of Montenegro since September 2011.

Since 2005, she is the full time Professor for the subject Internal medicine in Faculty of Medicine, in the University of Montenegro in Podgorica.

She was appointed by the World Health Organization as the National coordinator in Montenegro for the Program control and prevention of chronic non-communicable diseases. Also, she was appointed by the European Association of Cardiologists as National coordinator for the prevention of cardiovascular diseases in Montenegro.

Prof. Gledović Musić has published over 60 works in domestic and foreign journals, has been co-author in books on prevention, treatment and rehabilitation of cardiovascular patients and have over 50 lectures like invited speaker.

THE ROLE OF THE HISTONE DEACETYLASES III (HADIII) IN EPIGENETICS

LJUBICA PEJAKOV, PhD, Full Professor
University of Montenegro, Faculty of Medicine

Abstract

Waddington was the first who as far as 1939 defined epigenetics as "a heritable changes in gene function that cannot be explained by differences in DNA sequences". This is an increasing field of research because it provides a broader insight to many biological phenomena. Simply, epigenome is the connection between genome and environment. Nowadays epigenetics is considered as the study of temporal and permanent changes in gene expression not caused by changes in the DNA sequence. It has been known that epigenetics is related to the structure and configurations of chromatin in which DNA is organized in nucleosome within the nucleus. This organization enables DNA wrapping regulating gene expression and epigenetic activities, too. Besides DNA, chromatin complex is made of histone and non-histone proteins. Chromatin protects genetic material from external damage. There are two functional and structural states of chromatin – heterochromatin and euchromatin which cause different epigenomes within the same genome, resulting in the various phenotypes. Euchromatin is transcriptionally active chromatin which appears as uncondensed while heterochromatin is in compact forms, gene poor and transcriptionally inactive. Sophisticated balance between these two forms is necessary for adequate cell functions.

Interactions between the environment and the DNA through modifications of the chromatin are not only responsible for the expression of a normal phenotype. These may be involved in the development of various pathologies, too.

Chemical modifications of histone tails include acetylation, methylation, ubiquitination and phosphorylation. Acetylation has been closely associated with increases in transcriptional activation while deacetylation has been linked with transcriptional deactivation. These reactions occur post-translation and are reversible. Histone deacetylases (HDAC) are the enzymes that deacetylate lysine residue on histone tail and are involved in gene repression and promotion of heterochromatin formation, known as gene silencing. HDAC are classified in classical group (HDAC I, II, IV) and sirtuins or HDAC III. Sirtuins act by transferring an acety group from their substrate protein to the ADP-ribose moiety of Nicotin amide dinucleotide (NAD+). Although they are mainly involved in histone deacetylation, non- histone proteins could be deacetylated by sirtuins, as well. Sirtuins were first connected with the aging research, but they have emerged as critical regulators of many cellular pathways. Sirtuins are also known as Sir2 (Silent information regulator 2). The abnormal sirtuin activity has been implicated in various diseases, including diabetes, obesity, neurodegenerative disorders, inflammation and cancer. There are 7 known sirtuins members, 3 of them (1, 6, 7) being primarily nuclear.

Sirtuin 1 (SIRT-1) is considered as master regulator in cells and organisms. In acute systemic inflammation Sirtuin 1 has an important role in balancing immunometabolic processes through formation of facultative chromatin at genes' promoters that initiate sepsis (TNF-α and Il-1β) and at pro-inflammatory genes and other genes that control glycolysis. Other members of sirtuins participate in immune and metabolic reprogramming during acute inflammation.

Because DNA and chromatin alterations are reversible, the implementation of epigenetic therapies for the treatment of epigenetically based diseases seems to be promising.

This presentation aims to introduce sirtuins family members to the participants.

Biography

Prof dr Ljubica Pejakov completed high school and Faculty of Medicine at University of Novi Sad at which she earned Master degree in 1987. She has enrolled specialty training of anesthesia and reanimation at University Clinical Centre of Vojvodina in 1988, and has been trained at University Clinical Centre Ljubljana (Slovenia) and Belgrade. Prof Pejakov completed her residency program training in 1991. She continued working as a specialist of anesthesia and reanimation at the University Clinic for pediatric surgery, Novi Sad until 2000. During that time she spent six months at Ana Meyer hospital, Florence (Prof dr Paolo Busoni) in 1994 for education in regional anesthesia for children and was visiting doctor at the University Hospital for sick children in Toronto, 1994 (Prof J. Lerman). Dr Ljubica Pejakov was elected teaching assistant in 1992 at Faculty of Medicine (Surgery/Anesthesia), University of Novi Sad. She received her Ph.D. in medical sciences focused on acute pain markers in 1997 and was elected assistant professor at the same University in 1999. Since 2000. dr Pejakov has been working at Clinical Centre of Montenegro where she was appointed Head of the Clinic of anesthesia, reanimation and pain medicine until 2013. She was elected assistant professor at the Faculty of Medicine (Surgery/Anesthesia), University of Montenegro, Podgorica in 2001. Since 20014 she has been responsible for the First aid in the study program medicine and dentistry and since 2018 for the Bases of scientific research. Dr Pejakov enrolled sub-specialty training of clinical pharmacology in 2004 and completed it in 2007 (under supervision of Prof A. Sabo) at the Faculty of Medicine, University of Novi Sad. In 2006 she was elected associate professor at the Faculty of Medicine in Podgorica, and full professor at the same institution in 2011.Since 2013, Dr Ljubica Pejakov has been appointed co-ordinator for medical specialties training and education at the Faculty of Medicine in Podgorica, and since 2000 mentor-coordinator for residency training program for anesthesia and intensive care (Belgrade/Podgorica).

Dr Pejakov has been participant in many international projects (CEEPUS III (CIII-RO-0313-08-1516), CEEPUS (Central European University Network) II (CII-RO-0313), ASPPOC project (The Antibiotic Surveillance Project on Perioperative Chemoprophylaxis) No062-000000-3537, EPIC II (The Extended Prevalence of Infection in the ICU Study), 2007 (Investigator No 902); Global PPS (The Global Point Prevalence Survey on Antibiotic Consumption and Resistance, 2015, www.global-pps.com, Tempus project "Reform of Curriculum Content to Undergraduate Medical Education at University of Montenegro" (ID:CD-JEP-40106-2005(ME)-CARDS (No 40106-2005), 2006-9, ERASMUS + project (KA2 –Cooperation for innovation and the exchange of good practices –Capacity Building in the field of Higher Education 2017/18. Project HEPMP), Erasmus+, „Strengthening Capacities for Higher Education of Pain Medicine in Western Balkan countries (Higher Education Pain Medicine (No: 585927-EPP-1-2017-1-RS-EPPKA2-CBHE-JP (2017 – 3109 / 001 – 001), 2017/18.

Prof Pejakov gained Project 'Higher Education and Research for Innovation and Competitiveness"(HERIC) - National Excellence Scholarship Program 2016 (No: 01-2871) that enabled her 1-year postdoctoral research at the University College, London, UK. There she has participated on the project "Organ dysfunction following acute illness" (Project license holder Prof Mervyn Singer, Bloomsbury Institute of Intensive Care Medicine, UCL) in which she was focused on sepsis animal research. In London, she completed the course Biological Services Training under Royal Society of Biology at UCL (No UCL/17/001) and achieved personal license to carry out regulated procedures (A,B,C) on living animals (License No 114FC91F0).

Prof Ljubica Pejakov is active member of European Society of Anesthesiologists (Membership No145106), European Society of intensive care medicine (ESICM), Montenegrin Physicians` Society (Assembly President) and Chamber of Physicians. She has been member of editorial board of Medicinski zapisi since 2015, Anestezija i intenzivna terapija journal (since 2002 until 2006) and International Advisory Board, Journal of Anesthesia (JARSS) since 2018.

CHALLENGES IN HISTOPATHOLOGICAL ANALYSIS OF BREAST CANCER

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Clinical Center of Montenegro, Center of Pathology

Abstract

Breast cancer is a leading cause of morbidity and dying in the group of patients that suffer of malignancies in the female population. In Europe, 94.2/100,000 women get infected annually and 23.1/100,000 die. The incidence is in the rise in countries that organize screening programms. The most significant risk factors are genetic predisposition, estrogen exposure, ionizing radiation, low birth rates and proven atypical breast hyperplasia. Diet, obesity, alcohol consumption also contribute to the increase in incidence. The incidence varies with age. A quarter of the patients are under 50 years of age and less than 5% of these are under the age of 35. Cancer diagnosis and treatment decisions for patients who suffer from breast cancer are guided by clinical and radiological findings, as well as histopathological analysis of the tumour tissue. It is essential to obtain a core biopsy sample before planning any treatment, and when this is not possible, fine needle aspiration cytology (FNAC) is recommended. In some cases of breast tumours, such as a papillary tumours, it is not possible to make a diagnosis on a core biopsy or FNAC.

The histopathologic report of breast carcinoma, must include the histologic type of tumor (defined by WHO classification), tumor grade, immunohistochemical analysis of estrogen receptors, progesterone receptors, HER2 receptors and Ki67 index. According to the 2015 St Gallen Consensus, it is recommended to classify all breast cancers into the following molecular subtypes: Luminal A, Luminal B HER2 negative, Luminal B HER2 positive, HER2 overexpressing and triple negative breast cancer based on immunohistochemical (IHC) detection of estrogen receptor (ER), progesterone receptors (PgR), human epidermal growth factor receptor 2 (HER2) and Ki67 proliferative index in tumor cells.

Since CB is required prior to any treatment in patients with breast cancer in cases where preoperative systemic therapy is planned, only CB analysis provides information about the diagnosed tumor. Tissue fixation is better controlled in core biopsies and antigen preservation is better for immunohistochemical analysis. However, it could be argued that samples obtained by core biopsy are less reliable in the diagnostic process compared to surgical sample, due to smaller sample sizes, sampling errors, tumor heterogeneity, and/or edge artifacts in core biopsy.

Regarding the possibility of a heterogeneous antigen distribution within the tumor, it is important to retest on surgical sample all tumours in which the estrogen, progesterone and HER2 receptor are negative on core biopsy.

In everyday practice it is important to know the benefits and possible difficulties in histopathological analysis of breast cancer on core biopsy and surgical samples.

Biography

Prof. Vučković was born in Kotor, Montenegro, in 1973. Prof. Vučković graduated from Medical Faculty Belgrade, at the University of Belgrade, Serbia in 1999. She defended her master thesis "Immunohistochemical analysis of parafollicular – C cells in colloide goiter of thyroid gland" in 2004. PhD thesis entitled "Angiogenesis, VEGF, EGFR and MMP9 expressions in bronchial squamous cell carcinoma and its prognostic value" she defended in 2008.

She completed medical specialisation in Pathology in 2005, and then obtained medical subspecialisation in Medical cytology in 2011. She is promoted to Associate Professor of Histology and Embriology, at Medical faculty, University of Montenegro. She is Head of Cytology Department in Center of Pathology, Clinical center of Montenegro.

Associate Professor Ljiljana Vučković is author of numerous papers published in both national and international journals and conferences.

GINGIVAL FLUID AND SALIVA IN THE DIAGNOSIS OF LOCAL AND SYSTEMIC DISEASES

SAŠA ČAKIĆ, PhD, Full Professor
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Abstract

In all fields of medicine, researchers are looking for practically usable biological diagnostic indicators of the disease. An ideal diagnostic indicator should, among other conditions, indicate the presence of the disease before significant damage to the target tissue or organs occurs. Gingival fluid (GT) is, under physiological conditions, serum transudate, but also contains constituents of the origin of cells and tissues of periodontium, as well as microorganisms of the supragingival and subgingival plaque. The composition and quantity of GT depend on a number of factors, which makes it difficult to standardize its analysis. Changes in the concentration, prostaglandin, cytokine, enzymes, as well as their inhibitors in GT, are detectable during the periodontium inflammatory processes. Detectable changes in the composition of GT are also found in patients with atherosclerosis, in HIV, HBV and HCV positive individuals. Saliva (S) is a fluid that, in addition to saliva itself, is composed of the constituents of GT, microorganisms, the products of inflammatory processes in the oral cavity and. le. Or distant localities, p'roteolytic emzymes, and metabolic signaling molecules that accompany distant processes. Therefore, in S we find specific changes during inflammatory processes of periodontal tissues, but also during diabetes mellitus type 1 and 2, acute myocardial infarction, coronary artery disease, chronic obstructive pulmonary disease, ovarian, lung and pancreatic cancer. Also, some changes in the composition of S are found in premature birth, psychotic depression, dementia, as well as in the user of some psychoactive substances.

Biography

Sasa Cakic was born in 1958 in Belgrade. He graduated from the Faculty of Dentistry at the University of Belgrade in 1984. He received his master's degree (1992), passed a specialist exam in periodontology and oral medicine (1994) and defended his doctoral dissertation entitled "Immunological characteristics of salivary, gingival fluid and sera with periodontal disease" 1998 . years. He started working at the Faculty of Dental Medicine, University of Belgrade in 1989, and was appointed full professor in 2008. During 2000, he was a visiting assistant professor at the School of Medicine, University of Leuven, Belgium. At the Faculty of Dental Medicine, University of Belgrade, he is engaged in theoretical and practical teaching in the fields of Periodontology and Oral Medicine, as well as in the related elective subjects. He is currently the Head of Oral Medicine at the Faculty of Dental Medicine, University of Belgrade. By decision of the competent institutions, he is a mentor for the specialist field of Periodontology and oral medicine, as well as a member of the expert team for the control of health institutions in Serbia for the mentioned areas. So far, he has been the mentor of 4 master's degrees and 6 doctorates. He is a long-time associate on projects of the Ministry of Science and Technology of the Republic of Serbia. He is the author of 145 papers, of which 21 papers have been published in top journals of international importance with appropriate impact factor, as well as 4 textbooks for regular teaching in Serbian and English. Since 2009, he has been teaching theoretical courses in Periodontology I and Periodontology II at the Faculty of Medicine, University of Podgorica, and has been teaching Oral Medicine from 2009 to 2017.

MODERN CONCEPT IN PARODONTAL SURGERY

MILJAN PULETIĆ, PhD

Abstract

It was reported in the late 1970s that platelets have a good regenerative effects. Platelets include growth factors that increase vascularization and collagen production by cell mitosis.

Recently, most of the studies have indicated that platelet-rich fibrin (PRF) is a great healing potential for bony and soft tissue that derived from patients own blood. Most beneficial effects of PRF are easily derived directly from patient's venous blood without any ingredients, and it has a great potential for hard and soft tissue regeneration. PRF has no inflammatory effects and can be used with all kind of graft materials. When used as a membrane, it helps protecting the surgical area to stimulate the healing of soft and bone tissues.

Indications for using PRF membrane in dentistry: preservation of the alveoli after tooth extraction, repair of gingival recessions, sinus lift (acceleration of bone healing (osteogenesis), filling of perforation, as biomaterial), bone augmentation - the membrane itself as biomaterial or in combination with artificial bone replacement, wound healing (for example SMAT or TVT site donor), periodontology, immediate implant placement.

Today, PRF is being applied worldwide every day and its effectiveness has been proven. The large number of indications, as well as the results that are being achieved, allow for daily new research into the field of application of PRF.

The connective tissue transplant (TVT) is augmentation material. The region of the hard palate is the only region in the mouth that is a possible donor site for connective tissue transplantation, primarily due to the fact that the lamina epithelialis and lamina propria of the hard palate have the same histological characteristics as the lamina epithelialis and lamina propria of the gingiva.

The indications for the use of connective tissue grafts are Miller class I, II and III gingival recessions where the vertical dimension of the recession does not exceed 3mm.

Advantages of using TVT are successful root covering, enlargement of the keratinized gingiva zone, change of tissue biotype, and disadvantages are anatomic limitation of donor region, two surgical wounds, discomfort for the patient.

Biomimetic (biomimicry) signify the concept of active regeneration of periodontal tissues based on imitation of natural processes during the formation and development of periodontal tissues. Amelogenin is used for periodontal surgery for biomimetic purposes.

It has been found that amelogenin can increase platelet-derived growth factor (PDGF) concentrations, which inhibit epithelial proliferation, contributing to the regeneration of deeper periodontal tissues. Amelogenin stimulates proliferation and growth of fibroblasts originating from periodontium. It stimulates the formation of new cement and has an indirect effect on the formation of new bone tissue.

Indications for using Amelogenin are infrabony defects, recession defects and furcation defects.

Advantages are no secondary surgical procedure, little discomfort for the patient, improved tissue healing, regeneration 1mm. Disadvantages are keratinized gingival enlargement - still significantly less than TVT.

Modern concepts of therapy include a combination of all these options, in order to treat patients with complex problems in the field of periodontology and oral surgery.

Biography

Dr Puletic was born in Bijelo Polje, Montenegro in 1983. Dr Puletić graduated from the Faculty of Dentistry, University of Belgrade, Serbia in 2008. He defended his doctoral dissertation titled: "Relationship of individual members of the herpesviride family and paradontopathogenic microorganisms with complications of paradontopathy" in 2015. He enrolled in specialist studies at the Department of Periodontology and Oral Medicine at the School of Dental Medicine, University of Belgrade. Professor Puletić is the author of a large number of papers as well as a participant in national and international professional training.

AESTHETIC FACIAL ANALYSIS

ELVIR ZVRKO, PhD, Assistant Professor
University of Montenegro, Faculty of Medicine, Department of Otorhinolaryngology and Maxillofacial surgery
Clinical Centre of Montenegro, Department of Otorhinolaryngology and Maxillofacial surgery

Abstract

Throughout history mankind has tried to define beauty. Beauty and facial attractiveness are easy to identify but difficult to quantify. But, it is important to adopt an objective and systematic method of preoperative evaluation of patients seeking aesthetic surgery. Although facial proportions, angles, and contours vary with age, sex, and race, it is worthwhile to consider aesthetic "ideals" when analyzing the face preoperatively. The initial assessment of the face evaluates symmetry and midline points should lie on the axis line. The face is divided into horizontal thirds and vertically fifths. The eye usually measures one-fifth the width of the face. The lower third is further divided into its own thirds, defining the upper lip, lower lip, and chin. The rotation of the nose is described by the nasolabial angle: the angle formed between a line from the anterior columella and the subnasale and a line from the subnasale to the mucocutaneous border of the upper lip. The ideal nasolabial angle for women is 100 to 120 degrees and men between 90 and 105 degrees. The width of the ear is approximately one half its length and the long axis should be inclined approximately 20 degrees posteriorly. Objective analysis of facial balance and proportion is an essential part of preoperative planning before facial plastic surgery. It is important for surgeons to practice stepwise analysis of facial symmetry and proportion.

Biography

Elvir Zvrko is an assistant professor at the University of Montenegro, Faculty of Medicine. He graduated medicine from the Medical Faculty Belgrade, at the University of Belgrade, Serbia, completed medical specialisation in otorhinolaryngology in 2006 at the same University, and then obtained medical subspecialisation in facial plastic surgery at the University of Zagreb in 2016. He is head of the Department of Otorhinolaryngology and Maxillofacial surgery at the Clinical center of Montenegro. He is vicepresident of Council for Scientific Research Activity of Montenegro. Zvrko is president of ENT Society of Montenegro. He was president of the Center of Young Scientists of Montenegrin Academy of Sciences and Arts. He also has published numerous scientific papers.

Biography

Elvir Zvrko is an assistant professor at the University of Montenegro, Faculty of Medicine. He graduated medicine from the Medical Faculty Belgrade, at the University of Belgrade, Serbia, completed medical specialisation in otorhinolaryngology in 2006 at the same University, and then obtained medical subspecialisation in facial plastic surgery at the University of Zagreb in 2016. He is head of the Department of Otorhinolaryngology and Maxillofacial surgery at the Clinical center of Montenegro. He is vicepresident of Council for Scientific Research Activity of Montenegro. Zvrko is president of ENT Society of Montenegro. He was president of the Center of Young Scientists of Montenegrin Academy of Sciences and Arts. He also has published numerous scientific papers.

COMPLEX ROOT CANAL ANATOMY -DIAGNOSIS AND THERAPY

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School of Dental Medicine, University of Belgrade, Serbia

Abstract

Cone-beam computed tomography (CBCT) or Digital volumetric tomography (DVT) is the greatest "break-through" in dental imaging technology of 21st century, primarily because for the first time a practitioner can use harmless radiographic system as a powerful tool to visualize any area of interest in all three planes, obtaining 3D images.

The lecture presents CBCT series of images and detailed analysis of various morphological groups of teeth, with particular accent on the mandibular premolars and maxillary molars, in both extracted teeth and clinical cases with unusual and complex root and root canal anatomy, relation and special orientation of the roots to surrounding anatomical structures, and interrelationship among canals inside the multi-canal roots. The significance of the canal orifice geometry, number, location and dimension of the apical foramen/foramina and their impact on the working length determination, development and treatment plan of various periapical and periradicular pathosis is pointed out. Incidence/frequency of the anatomical modalities in maxillary molars and mandibular premolars in Serbian population, that has been studied throughout two last decades, with special interest on teeth with fused roots, is showed in details, with its impact on the difficulties and possible complications during operative procedures and root canal instrumentation, focusing on important stages of endodontic therapy, treatment outcome and follow ups of different types of endodontic pathology. Throughout the lecture the stress is put on the wide abilities of CBCT and its software to acquire and reveal "hidden" details of interest for clinical endodontics, like overlooked and un-instrumented canals.

Biography

Graduated in 1993, with Award of the City of Belgrade for the research article; specialization in Restorative Odontology and Endodontics in 2002, MSc in 2003, and PhD in 2015, all at School of Dental Medicine, University of Belgrade.

Co-author in the Serbian translation of the "Textbook Endodontology" (Bergenholtz G, Horsted-Bindslev P, Reit C) – "Endodontologija"; published 11 scientific articles in journals from SCI / ESCI list, and further 18 articles in international and national refereed journals; lectured at 31 international and national conferences, symposiums and congresses of which at five as the key-note speaker (Craiova 2014, Malta 2014, Helsinki 2015, Vienna 2016 and Craiova 2019); moderates and co-ordinates hands-on endodontic courses, and is recognized lecturer for continuing education and professional development, mostly in the field of endodontology and endodontic practice.

Dr Katarina Beljic-Ivanovic is specialized in the use and application of CBCT technique and technology in endodontics, both in research (PhD Thesis: "The Effect of Different Machine Driven Instrumentation Techniques on the Original Root Canala Anatomy of the First Maxillary Molars Studied With the Aid of CBCT") and endodontic treatment of clinical cases with complex root canal anatomy and complicated pathological status.

IMPLANT-SUPPORTED PROSTHETIC REHABILITATION OF MAXILLOFACIAL DEFECTS

ALMINA MURIĆ, PhD, Assistant Professor
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Abstract

Maxillofacial defects usually occur secondary to tumor management, trauma or congenital malformations. These defects, both due to functional dysfunction and aesthetic, affect the psychological well-being of patients, making their rehabilitation very complex and often requiring a multidisciplinary approach.

Rehabilitation of maxillofacial defects with prosthetic restorations is being used as an alternative to surgical methods. It is a very demanding task requiring a specific design of the retentive technique to be used in an individual patient.

Obturators with natural teeth support are successfully applied in the clinic. However, the loss of the support teeth adversely affects the retention and support of the prosthesis resulting in inadequate prosthetic replacement. The development of osseointegrated intraoral dental implants and their use, especially in patients with maxillectomy, has been very useful. In this way, more stable and retentive prostheses were obtained and the quality of life of the patient was improved.

In cases of a maxillectomy where prosthetic rehabilitation with standard intraoral implants is insufficient or due to lack of adequate bone standard implants can not be inserted, rehabilitation can be supported with zygomatic implants. These implants were originally designed by Branemark for the treatment of atrophic and edentulous maxilla, and then these implants were used in patients with maxillary defects to increase retention and support of the prosthesis. Thus, more stable and functional prostheses were obtained.

In addition to intraoral implants for the retention of maxillofacial dentures, extraoral implants also play a major role. Their use has emerged as a need for an alternative to conventional retention methods. In this way, in addition to better retention, the use of MFP is facilitated (placement, removal, and cleaning of the prosthesis).

Biography

Prof. Murić graduated from University of Montenegro, Faculty of Medicine and obtained her DMD diploma. Her PhD thesis she defended in 2017 at Istanbul University, School of Dentistry, Department of Dental Prosthetics

From 2013 to 2017 she was Teaching and Research Assistant at Department of Maxillofacial Prosthetics, Istanbul University School of Dentistry and in 2018 she became a lecturer at Department of Dental Prosthetics, Istanbul Aydin University School of Dentistry

Currently, she is an Assistant Professor at Department of Dental Prosthetics, Istanbul Aydin University School of Dentistry.

MICROBIOME - ORGAN OF THE 21ST CENTURY?

ZORICA POTPARA, PhD, Associate Professor
University of Montenegro, Faculty of Medicine, Pharmacy Study Program

Abstract

The human microbiome is made up of all microorganisms living in / on us: on the surface of the skin (skin microbiome), in the mouth (oral microbiome), in the gut (intestinal microbiome), in the vagina (vaginal microbiome) and in the ear (ear microbiome). The microbiome is established at the earliest stage of life - the fetus is sterile in the womb, and exposure to microorganisms begins with birth, when the newborn contacts the microorganisms present in the environment.

The microbiome has been the focus of research for the last ten years, because it recognizes the importance that bacteria in the gut have for the overall health of humans. Contemporary research has identified the link between the intestinal flora and diabetes, autoimmune diseases, immunity, and psychiatric conditions, such as depression. Each human being has a unique and peculiar microbiome, as a fingerprint, except that the fingerprint is immutable and the microbiome changes throughout life. The composition of the microbiome depends on habits, food, environment and is suitable for change. Scientific research shows that it can change for better or worse, and disturbing the balance of bacteria in the body leads to dysbiosis characterized by health problems such as inflammatory bowel disease, allergies, diabetes and obesity.

The hypothesis that the microbiome that inhabits the human body produces positive results was difficult to prove, until the launch of the Human Microbiome Project (HMP), which was a research initiative of the American National Institutes of Health (NIH). HMP research has shown that although the composition of the microbial community may vary from person to person, the metabolic abilities of those communities may be correlated with health and disease. With a better understanding of what a "normal" human microbiome looks like, research has focused on changes in the microbiome that are linked to or cause disease.

Our microbiome is more diverse as we are healthier and our immune system is stronger. Scientists around the world have made identical discoveries - food, life habits, our thoughts and social life affect the microbiome-the microbiome affects the body and the development of disease, aging. Further research is neededand for better understanding of the functioning of the microbiome as well as its role in disease pathology should be continued.

Biography

Zorica Potpara graduated from the Faculty of Pharmacy, University of Belgrade in 1985. She became a specialist of Pharmaceutical Technology in 1991. and earned a PhD degree in 2011. at the Medical Faculty in Kragujevac.

She is the Ass. Prof and head of the study program Pharmacy at the Medical Faculty in Podgorica.

She is also a member of the Pharmaceutical Association of Montenegro, President of the Commission for Continuing Education and the President of the Commission for Professional Issues in the Pharmaceutical Association of Montenegro.

She is a member of the Commission for the quality control of the Faculty of Medicine; member of the rewarding published papers; member of the equalization of qualification of the Faculty of Medicine.

INFLUENCE OF ADSORPTION CARRIERS ON THE DISSOLUTION RATE OF DRUG SUBSTANCES

TANJA VOJINOVIĆ, PhD
University of Montenegro, Faculty of Medicine, Pharmacy Study Program

Abstract

Introduction: Over 40% of new drug entities are BCS II class drugs (poorly soluble, highly permeabile). One approach to improving the solubility and dissolution rate of these drugs is to make formulations with the addition of adsorption carriers. Adsorption carriers of synthetic origin include the following substances: magnesium aluminometasilicate (Neusilin®), silicon dioxide (Sylisya®). Some of the features that recommend the use of Neusilin® are: large specific surface, high porosity, high water adsorption capacity. Silicon dioxide is safe and secure for human use. The key features that promote the use of adsorption carriers are first and foremost good biological tolerance, the absence of toxic-harmful effects, the very process of obtaining them, which is not complex, so that in economic terms their use is justified (cost-effective).

Carbamazepine and carvedilol are poorly soluble drugs. Solid dispersions of carbamazepine and carvedilol have been successfully formulated with these adsorption carriers. Solubility of carbamazepine and carvedilol formulated with carriers in solid dispersions are better than pure drug substances.

When designing formulations with adsorption carriers, careful attention should be paid to the selection of adsorption carriers, their characteristics, and their proportion, in

order to successfully formulate the desired formulations. Formulations which are made with synthetic adsorption carriers have been shown to have a higher have a higher dissolution rate than the pure drug substance.

Biography

Tanja Vojinovic is a Doctor of Pharmaceutical Sciences. She is employed by the Faculty of Medicine as a teaching assistant with a Ph.D. She is a member of the Pharmaceutical Chamber of Montenegro.She is a member of the Commission for Examination of the Expert Exam for Pharmacists, Ministry of Health of Montenegro. Representative of Montenegro in Simulation and pharmaceutical technologies for advanced patient-tailored inhaled drugs (SimInhale) - COST Action MP1404. Member of the Scientific Committee of the 3rd Congress of Pharmacists of Montenegro with international participation.

Chairman of the Commission for Publishing Activities of the Bulletin of the Pharmaceutical Chamber of Montenegro. Member of the research group in the innovative international project "Balneological effects of peloids, mineral waters, medicinal and aromatic herbs on inflammatory response in rheumatoid and cardiovascular diseases".

She participated in international and professional meetings with oral or poster presentation of scientific research work. Her research interest is focused on the development and optimization of formulations of solid pharmaceutical forms using optimization scales, testing and application of natural raw materials (active and excipients substances) in preparations for application to the skin, in vitro biopharmaceutical characterization.

BIOCHEMICAL PARAMETERS AND ADVERSE DRUG REACTIONS

SNEŽANA PANTOVIĆ, PhD, Assistant Professor
University of Montenegro, Faculty of Medicine, Department of Medical Biochemistry

Abstract

Adverse drug reactions (ADRs) are defined by the World Health Organization as any noxious, unintended, and undesired effect of a drug that occurs at doses used for prevention, diagnosis, and treatment. Traditionally, ADRs are classified into several types, of which two are the most important: type A- which are result of the exaggerated pharmacological action of the drug and type B- that are unexpected, dose independent, or independent of the underlying pharmacological effect of the drug administered. Recognition of ADRs is very important because the spectrum of clinical manifestation of ADRs is diverse: from commonly harmless conditions to life-threatening conditions. Prior to the occurrence of certain clinical signs and symptoms of ADRs, it is often the case that disorders of certain biochemical or laboratory parameters occur. A typical example of the importance of regular control of biochemical parameters is the use of statins in the treatment of hypercholesterolemia. A common side effect of these medications is impaired liver function, and it is therefore induced to periodically check all liver function. In addition, long-term administration of systemic corticosteroids can cause numerous side effects, of which hypertension, hyperglycemia and electrolyte imbalances are the most important for biochemical diagnostics. In the administration of nephrotoxic and hepatotoxic drugs in chronic conditions, regular examination of the functional status of the liver and kidney is necessary. For biochemical diagnostics, it is very important to monitor medications that have adverse effects of hyperglycemia. Because side effects can be presented by changing certain laboratory parameters, the pharmacist's role in familiarizing the patient with the possible ADRs manifested by changing laboratory parameters is of paramount importance. The joint work of pharmacists and physicians must focus on the prevention, diagnosis and treatment of side effects. The aim of this presentation is to acquaint the colleagues of the pharmaceutical profession with those changes in laboratory findings caused by drugs, and especially with those changes represented by ADRs.

Biography

Snežana Pantović, MD, PhD, Assistant Professor is responsible teacher of Medical Biochemistry for students of medicine, dentistry and pharmacy at the Faculty of Medicine, University of Montenegro (UoM). At the same time, she is a mentor of diploma thesis of students mentioned above, as well as member of commissions for the defense of graduation papers.

She was born on October 21, 1970. in Marbach - Germany. Primary and secondary school she finished in Banja Luka. She graduated at the Faculty of Medicine in Banja Luka in 1997. For a number of years, she worked at the Blood Transfusion Center, Clinical Centre of Montenegro, as a specialist of transfusion medicine.

She obtained her master of science degree at the Faculty of Medicine (UoM), in September 2007, under the mentorship of prof. Srđan Đurović, PhD, and at the same faculty in February 2015, under the mentorship of prof. Ivanka Marković she obtained PhD diploma. Researches during master and doctoral studies involved the monitoring and analysis of important markers of inflammatory response and parameters of oxidative stress in the development of restenosis after percutaneous coronary intervention in order to better interpret the pathogenesis of restenosis and faster and more effective prevention of it. As a PhD student, she conducted part of her research in the laboratory of the Medical Faculty of the University of Belgrade. As a researcher on the "Studyng Protein Evolution Model Based on Cellular Automata" (2013), she spent two months at the JingDeZhen Ceramic Institute in the People's Republic of China.

She is currently managing the scientific research project "Balneological effects of peloid, mineral water, herbs and aromatic plants in the inflammatory response in rheumatoid and cardiovascular diseases" (BEPMARK) funded by the Ministry of Science of Montenegro and she is a member of the team in a bilateral project with PR China named "Identification of antimicrobial peptides and their functional types using cellular automata".

She is the author and co-author of a number of scientific papers published in domestic and international journals, publications, co-author of the HIV / AIDS Guidelines for Safe Blood; she was an invited lecturer and participant in several international congresses and seminars; she was a member of the Scientific Committee of the Second Congress of Pharmacists with international participation (2015). She is currently a member of the Scientific Research Council of the Faculty of Medicine (UoM). She speaks English fluently, and passively German.

CLINICAL TRIALS CHALLENGES – GOOD CLINICAL PRACTICE GUIDELINES

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Abstract

Good Clinical Practice (GCP) is a set of internationally recognised ethical and scientific quality requirements that must be followed when designing, conducting, recording and reporting clinical trials that involve people. Guidance on good clinical practice has been produced by the International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use (ICH). Clinical trials of medicines in the European Union (EU) are currently regulated by Directive 2001/20/EC. Laws on medicines of the countries in the region (non-EU countries) are compliant with this Directive to the fullest extent. In addition to the numerous advantages it has brought, which is primarily reflected in the greater safety of subjects, better communication between sponsors and investigators, as well as greater reliability of data and results of clinical trials, after a certain time, the weaknesses of the directive have been identified, such are different concepts of clinical trials approval, divergent opinions on the same studies and various interpretations of its provisions. These disadvantages of the directive resulted in different protocols in international trials, cost increase, postponing of clinical trials onset and competitiveness reduction, which ultimately led to a decline in the number of clinical trials with a negative impact on innovative drugs development. Forasmuch, the European Commission in 2014 adopted Regulation EU 536/2014, which will replace Directive 2001/20/EC. The primary purpose of introducing this regulation is to simplify the procedure of request for the approval of clinical trials in all Member States through a single EU portal, a unique assessment of documentation and increased transparency of the authorization prosess, implementation and monitoring of clinical trials. The Regulation will be fully binding and directly applicable for all EU Member States six months after confirmation of the functionalities of the EU portal and database, which is expected in 2020. After that, the EU countries are expected to become a more competitive market for clinical trials conduction, which can reduce the participation of our region in the market of clinical trials.

Biography

Snežana Mugoša was born on 14 February 1979 in Nikšić, Montenegro. She graduated from Faculty of Medicine at the University of Montenegro, Podgorica in 2004 with a grade point average 9.69. In 2004 she entered masters programme – Clinical pharmacology and therapy, at the Faculty of Medicine of the University in Belgrade and in 2009 she defended master's thesis „Intensive monitoring of adverse drug reactions in hospitalized patients at cardiology department: pilot project" at the Faculty of Medicine, Podgorica. In 2015 she defended PhD dissertation „Analysis of risk factors for developing adverse drug reactions in hospitalised cardiac patients" also at the Faculty of Medicine, Podgorica. In 2011 she passed the Internal Medicine Certification Exam at the Faculty of Medicine of the University of Belgrade with an excellent grade. In the period 2006-2012 she was employed at the Center of Cardiology, within the Clinical Center of Montenegro, and since 2012 has been working as the Head of the Department for clinical trials of medicines for human and veterinary use and assessment of preclinical and clinical documentation for marketing authorization in the Agency for Medicines and Medical Devices of Montenegro.

Since 2004 she has been engaged at the Faculty of Medicine, Podgorica on the group of pharmacological subjects, initially as a teaching assisstant, and then, since 2015, as a lecturer in Pharmacology II, Pharmacotherapy I and II and Pharmacokinetics. Her students always give her the highest rating for the quality of teaching.

Her main research areas are pharmacotherapy, clinical pharmacology, pharmacogenetics, clinical trials and she has published numerous scientific papers in these areas. She cooperates with several foreign laboratories, within scientific projects managed by her mentor on postgraduate studies, Professor Zoran Todorović, from the Faculty of Medicine of the University of Belgrade.

She is an inspector of Good Clinical Practice, certified by the European Medicines Agency, and a member of the Good Clinical Practice Inspectors Working Group in the European Medicines Agency.

POSTER PRESENTATIONS

CHANGES IN SPLENIC VOLUME AFTER THE TREADMILL EXERCISE IN AEROBIC AND ANAEROBIC CONDITIONS IN RECREATIONAL RUNNERS AND ELITE LONG-DISTANCE RUNNERS

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Introduction: Spleen is the largest lymphoid organ in the human body. Beside other functions, spleen acts also as a blood reservoir. During the exercise,spleen has ability to contract, and so augment the systemic circulation and helps body to maintain longer on high intensity exercise.

Aim: To evaluate the percentage of the decrease in splenic volume after the treadmill exercise at specific workloads: aerobic threshold intensity, anaerobic threshold intensity, submaximal intensity and maximal intensity.

Material and Methods: This prospective study with repeated measurements included 16 healthy subjects (aged 18-25), divided in two groups. First group consisted of 8 elite long-distance runners and second group of 8 recreational runners.Ergospirometry test was performed for each athlete, and afterwards four specific workloads were set: aerobic threshold intensity, anaerobic threshold intensity, submaximal load (above the anaerobic threshold), maximal load (exercise to exhaustion). Next day, ultrasound measurements of spleen volume were performed before and after each workload. Workloads were controlled by the speed of treadmill, for each subject individually regarding the ergospirometry test. Break between the workouts was 30 minutes.

Results: Elite long-distance runners showed greater spleen contraction than recreational runners after four workloads. Spleen contraction was the biggest after the 3rd workload in elite long-distance runners. Smallest contraction was in group of recreational runners after the 1st workload. Statistically significant difference was not found between the groups, regarding the splenic volume after exercise at four specific workloads ($p>0.05$).

Conclusion: Elite long-distance runners had greater decrease in splenic volume than recreational runners, after exercise at four specific workloads, without significant difference. Greatest decrease happened in elite long-distance runners, after exercise at submaximal intensity - 49% decrease in splenic volume.

Key words: spleen, contraction, treadmill,runners

ANEMIA STATUS IN PATIENTS UNDERGOING HEMODIALYSIS IN THE CLINICAL CENTER OF MONTENEGRO

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Aim: The purpose of our study was to assess anemia status and to investigate common factors that lead to anemia and affect its management in hemodialysis patients.

Settings and design: The study was conducted at the department of nephrology in the Clinical Center of Montenegro. Demographic data; data on adequacy and time spent on hemodialysis, data on anemia parameters, iron and PTH levels was collected. The data was collected for 6 months retrospectively from November 2018 to April 2019 from patient files. All patients undergoing hemodialysis at the facility in mentioned time frame were included.

Results: Data was collected from 74 patients; average age of patients was 57.84 year, 55.5% patients ware male. Most common comorbidity was hypertension (74.3%). Eighteen patients (24.3%) had mean Hgb values between 110 and 120 g/L the target range recommended by KDOQI guideline. Twenty (27.1%) had mean Hgb values between 100 to 110 g/L; these values are associated with lowest mortality rates. Unessesery Hgb values exceeding 120g/L ware recorded in 13.5%. The mean S-Fe concentration measured was 11.24 µmol/L. Mean Kt/V value was 1.3. Information on PTH concentrations was available for 69 (93.24%) patients. Mean PTH value was 61.4 pmol/L. Adequacy of hemodialysis (Kt/V), serum Iron concentration, PTH level all showed a positive correlation to Hgb concentration. Positive correlation between PTH values and Hgb values was an unexpected result but it is not uncommon as it was already observed in other studies. Patients who spend longer on hemodialysis also had higher Hgb values. This could be explained with higher Kt/V values in these patients but it needs to be investigated further.

Conclusion: There is an opportunity to improve anemia management in investigated hemodialysis patients trough further evaluation of causes of anemia and better monitoring and management of iron status, PTH levels and hemodialysis adequacy.

Key words: Anemia; Chronic kidney disease; Dialysis; Erythropoietin; Iron status; Parathyroid hormone

SYNDROMA MAYER – ROKITANSKY – KÜSTER – HAUSER IN ETIOLOGY OF CHRONIC RENAL INSUFFICIENCY

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Introduction: (MRCH) syndrome is a rare congenital anomaly characterized by complete or partial congenital aplasia of the uterus and vagina in women who develops normal sexual characteristics related to the female and normal karyotype (46, XX). But during the embryonic development and differentiation of the urogenital system, the absence of (Müller) channels occurs.

Case report: Patient I.Dj., 38 years old, presents for the first time with elevated serum nitrogen levels at the age of 25, because of that a complete nephrological examination was performed. At the age of 15, she was gynecologically examined for primary amenorrhea. Laparoscopically found to lack the uterus with rudimented fallopian tubes about 1 cm long with the existence of the ovary when diagnosed with Syndrome MRKH. On detailed nephrological examination has diagnosed chronic renal insufficiency.Over time, CRI progressed to the terminal stage when hemodialysis treatment was initiated. Six months after starting treatment, a left acoustic nerve and sy Ramsay - Haud lesion was diagnosed. Discreet varicosities around the gallbladder and pathological flow around both port vein arcus were then diagnosed. Half a year later, hospitalized for ascites, laparoscopically evacuated 8l of fluid, the histopathological result of a liver biopsy is normal. A complete laboratory analysis was performed that showed no specific changes from the reference limits. The problems persisted, an abdominal CT scan showed micronodular hypodense changes in the liver and spleen. The patient did not respond well to antibiotic therapy, so subtotal laparatomy and splenectomy were performed, followed by regression of abdominal problems while respiratory problems persisted, and pulmonary fibrosis was suspected after all analyzes.

Conclusion: The relationship between renal and pulmonary aplasia and hypoplasia has not been fully explained, although there are several factors that may be associated with malformations of these systems. Sy Mayer - Rokitansky - Küster - Hauser (MRKH) is very often associated with anomalies of the urological tract and other organ systems. For these reasons, renal function should be carefully and regularly monitored in all patients diagnosed with MRKH sy.

Key words: Mayer – Rokitansky – Küster – Hauser (MRKH) syndrom, CRI, hemodialysis, pulomaly fibrosis

METHIONINE-CHOLINE DEPRIVATION MODULATES LIVER AND BRAIN ACETYLCHOLINESTERASE ACTIVITY IN MICE

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Introduction: Choline and methionine are precursors of acetylcholine, whose hydrolysis is catalyzed by acetylcholinesterase (AChE). Considering the possibility of their common deficiency, we investigated the influence of methionine-choline deprivation on AChE activity in liver and various brain regions (hypothalamus, hippocampus, cerebral cortex and striatum) in mice fed with methionine-choline deficient (MCD) diet.

Material and Methods: Male C57BL/6 mice (n = 28) were randomly and equally divided into following groups: control group fed with standard diet for 6 weeks (C) and groups fed with MCD diet for 2 weeks (MCD2), 4 weeks (MCD4) and for 6 weeks (MCD6). After the diet, mice were sacrificied and AChE activity in liver and brain was determined spectrophotometrically.

Results: Hepatic AChE activity was higher in MCD2, MCD4 and MCD6 compared to control ($p < 0.01$), with most prominent increase in MCD6. AChE activity in hypothalamus was higher in MCD4 and MCD6 vs. control ($p < 0.05$ and $p < 0.01$, respectively), as well as in MCD6 compared to MCD4 ($p < 0.01$). In hippocampus, increase in AChE activity was shown in MCD6 compared to control ($p < 0.01$). In cortex and striatum, increase in AChE activity was noted in MCD6 compared to control ($p < 0.05$).

Conclusion: Our findings indicate the increase of hepatic and brain AChE activity in mice caused by methionine-choline deprivation.

Key words: choline, methionine, acetylcholinesterase, liver

IS THE TREATMENT OUTCOME DIFFERENT IN ELDERLY PATIENTS WITH IMMUNE THROMBOCYTOPENIA?

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Introduction: Immune thrombocytopenia (ITP) is a bleeding disorder caused by accelerated autoimmune destruction of platelets and defects in thrombopoiesis and megakaryopoiesis. It can be observed in both adults and children, with both sexes being affected. Primary ITP in adults has a prevalence and an incidence of about 9.5/100000 and 3.3/100000 per year, respectively. Mean age at diagnosis has been reported to be 40-60.

Therapy of ITP mainly depends on steroids. Frequent relapses or refractory disease can be treated by splenectomy, other immunosuppressive agents including, rituximab and thrombopoietin analogues with various response rates.

The aim of this study was to compare response rates and course of the disease in young versus old patients with ITP.

Material and Methods: A total of 109 patients followed at Cerrahpaşa Medical Faculty Haematology Department between 2013-and 2018 have been retrospectively included in the study. Data on age at diagnosis, treatment, response to treatment, complications were retrieved from patient files. Patients were divided into 2 groups (young vs. elderly) based on their age being <60 and ≥ 60 years of age.

Results: There were 77 and 32 patients aged <60 and ≥ 60 years, respectively. Results are summarised in Table 1. Groups were similar with regard to the platelet counts at diagnosis and number of treatment series. Significant differences ($p< 0.05$) between the 2 groups were noted in the number of patients with splenectomy and refractory ITP, as well as relapse rates after 1st-line treatment.

Conclusion: The management of ITP in patients ≥ 60 years of age might require a different approach considering the relatively high number of patients with relapse/refractory disease to standard treatment of ITP. Another challenge in the elderly group seems to be the avoidance of splenectomy due to increased risk of morbidity and mortality. Personalised treatment for elderly patients with ITP might help improve the outcome.

Key words: Elderly, Immune thrombocytopenia, ITP, Treatment

RISKS FACTORS FOR STRESS URINARY INCONTINENCE

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Introduction: Urinary incontinence has substantial and important impacts on quality of life. Our objective is to determine risk factors for female stress urinary incontinence.

Material and Methods: Study included 515 female patients divided in two groups. Group I with stress urinary incontinence and Group II as control group without stress urinary incontinence. All of the patients were interviewed by (ICIQ-FLUTS) questionaries and done gynecological examination, urine culture and abdominal ultrasound.

Results: The statistical analysis revealed that menopause, constipation, BMI, alcohol consumption, smoking, hypertension, diabetes, family history and parity are associated with UI as risk factors.

Conclusion: The incidence of stress urinary incontinence is related with multiple factors, especially with obesity, obstetric factor, constipation.

Key words: Stress urinary incontinence, Risk factor, Female, Quality of life

SOMATOSENSORY EVOKED POTENTIALS IN JUVENILE MYOCLONIC EPILEPSY

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Introduction: Juvenile myoclonic epilepsy (JME, Janz syndrome) belongs to a group of idiopathic generalized epilepsies, and is the most common entity amongst them. The main characteristic of the disease is myoclonus without unconsciousness. The disease have early onset. Somatosensory evoked potentials are a brain response to repeated stimulation, in this case, of n. medianus. The importance of SSEP is in contributing to the diagnosis of JME and the evaluation of the therapeutic effect.

Material and Methods: The research involved two groups of patients: the examined and control group. The study group consisted of 93 patients in total, of which 62 women and 31 male patients. The control group consisted of 47 patients (Clinic for Neurology and Psychiatry for Children and Youth). SSEP in patients with JME can be physiological and "giant" SSEP. The analyzed parameters are shape, amplitude, absolute latency values and lateralization.

Results: It was found that there was a statistically significant difference between the investigated and the control group on the value of the primary cortical response (P20-N25), the association of morning myoclonus and the "giant" SSEP, with the prevalence of the female sex. The connection between duration of therapy and lateralization was not statistically significant.

Conclusion: The association of myoclonus with the "giant" SSEP, which is confirmed, and the possible impact of therapy on the SSEP should be further investigated. The differences in the SSEP parameters in cases and controls exist in terms of differences in the primary cortical response.

Key words: juvenile myoclonic epilepsy, SSEP, antiepileptic therapy

GENDER DIFFERENCIES IN RISK FACTORS, CLINICAL AND NEURO-VUSUALIZATION MANIFESTATIONS OF CEREBRAL SMALL VESSEL DISEASE

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Introduction: Term cerebral small vessel disease (CSVD) refers to group of clinical, neuroradiological and neuropathological findings, developing as a consequence of atherosclerosis affecting small perforating arteries and arteriolas. Beside motor manifestations, typical clinical manifestation comprises vascular cognitive impairment (VCI) and vascular depression and this condition is associated with common vascular risk factors (RF).

Aim: To analyse sex difference in RF, clinical presentation and neuroimaging correlates of CSVD.

Material and Methods: In this cross-sectional study we enrolled 137 patients with CSVD hospitalized at the Neurology Clinic, Cinical Center of Serbia, at the Department for Cerebrovascular Diseases and resistant headaches in period January 1st 2015 – January 1st 2019. Vascular RF, clinical presentation, MRI and transcranial parenchymal sonography findings were analyzed and compared between sexes.

Results: In our cohort, male patients more frequently had diabetes, hyperlipidemia, and smoking as RF when compared to women. VCI (p=0,031) and depression (p=0,005) were more frequent in women than men. Vascular lesion severity on MRI scanes did not differ between sexes. In women, VCI was more frequently associated with increased diameter od third ventricle (r=0,395, p=0,00038). In both men and women, depression correlated with brainstem raphe hypoechogenity.

Conclusion: CSVD pathogenesis is a multifactorial process still not fully elucidated. Our results indicate statistically significant correlation between vascular RF, MRI and TPS findings and clinical manifestations of the disease, with some gender specificities.

Key words: cerebral small vessel desease; risk factors; transcranial parenchymal sonography; magnetic resonance imaging; sex

RISK FACTORS FOR THE MELANOMA IN MONTENEGRO

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Introduction: Melanoma is a malignant tumor of melanocytes and non-virulent cells. We have witnessed a record number of newly diagnosed skin cancers in the world and in our country, with the incidence of melanoma increasing faster than almost all other cancers. The aim of this paper is to draw the attention of citizens to risk factors in order to prevent the occurrence of skin melanoma.

Material and Methods: The survey was conducted in April 2019 by filling the questionnaire in several Montenegrin municipalities. The results were processed using decriptive statistics.

Results: The total number of respondents was 200(65% female and 35% male) with the average age of 55 years. Most participants have III (36%) and IV (34%) skin phototype, while the rest had phototype I (14%) and II (16%) cases. Almost 23% of respondents had severe sunburn in childhood. We found that 32% of respondents have more than fifty nevuses on their skin. Two-thirds of the respondents have a dysplastic nevus. Only 11% of respondents have a positive family history of malignant skin cancers and melanoma. Almost 85% of respondents do not have any hereditary skin disease. Only 18% of respondents used solarium. Nearly 15% of respondents exposed their one-year-old children to the sun. Only 25% of respondents do not use a skin protective factor. Only 18% of the respondents control their skin with doctors, while 44% do not control and 38% self-check.

Conclusion: Our results suggest that there are a number of risk factors that can affect the occurrence of melanoma. Our goal in the future will be to reduce the number of risk factors and to raise public awareness of the importance of early recognition of skin cancer

Key words: melanoma, skin cancer

CHILDHOOD OBESITY-WHAT DO PARENTS THINK ABOUT RISKS?

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Introduction/Objective: Childhood obesity has reached epidemic levels in developed as well as in developing countries. Overweight and obesity in childhood are known to have significant impact on both physical and psychological health. Overweight and obese children are likely to stay obese into adulthood and more likely to develop non-communicable diseases like diabetes and cardiovascular diseases as young adults. The present study examined parental perceptions of childhood obesity related health risks and association with child weight status.

Material and Methods: The sample included parents of 1,133 schoolchildren (49.9% boys) aged 7–12 years, from 10 elementary schools in Podgorica. The research instrument was a closed type of the original questionnaire. Nutritional status was assessed according to the criteria recommended by the American Centers for Disease Control and Prevention, World Health Organization and International Obesity Task Force.

Results: Study showed there exists statistically significant difference in a number of parents that differently perceive danger for health from child's overweight/obesity (χ^2=258,051; p<0,001). Majority of them, 594 (52.4%) considered the childhood obesity as "high dangerous", 340 (30%) as "medium dangerous" and 162 (14.3%) thought of obesity in children as "low dangerous". No answers given were 37 (3,3%) parents.

Conclusion: Almost 20% of parents are unaware of health risk from childhood obesity, which is significant percentage. Also, just 64% of parents who recognised the danger from childhood obesity gave the prefix "high". There exists space to work on education of parents' population in order to achieve better prevention of overweight and obesity among the children and young.

Key words: parental perception; children; obesity; health risk

PATHOHISTOLOGICAL CLASSIFICATION AND INVASIVENESS OF MELANOMA IN MONTENEGRO

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Introduction: Melanoma is known to be an aggressive type of cancer, whose incidence is increasing globally. Early diagnosis is the best way to significantly improve the prognosis. Pathohistological characteristics at the time of diagnosis such as Breslow's thickness, histological subtype, and TNM classification can be used to predict the 5 year survival rate. The objective of this study was to determine the frequency of histological subtypes of melanomas, their invasiveness, using Breslow's classification, and primary tumor classification (pTx) using the TNM system in Montenegro.

Material and Methods: The data was collected retrospectively at the Center of Pathology of the Clinical Center of Montenegro in the period from January 1st to December 31st, 2018. During that period 39 patients were diagnosed with melanoma, 31 of which were primary tumors of the skin. Information about the Breslow's thickness, ulceration, histological subtypes, and dimensions of 27 primary tumors was taken from the diagnosis register, and 4 patients were excluded due to incomplete information. Using the 8th volume of TNM classification, the primary tumor stage was determined (pTx). The information on metastasis in regional lymph nodes and other organs (pNx and pMx) was not available.

Results: The study showed that 74% of melanomas diagnosed in Montenegro were the most invasive, nodular subtype. In addition, 70.4% of melanomas were Breslow IV and 70.4% were classified as the stage p4b. Therefore, at the time of diagnosis a majority of melanomas in Montenegro are already in advanced stages, with an estimated 5 year survival rate of 53% or less, depending on the presence of metastases in regional lymph nodes and other organs.

Conclusion: This study emphasizes the need for screening and better public education of the signs and symptoms of melanoma.

Key words: Malignant melanoma, TNM classification, Breslow's thickness, pathohistology

RENAL CANCER AS SECONDARY MALIGNANCY AFTER PREVIOUSLY TREATED PROSTATE CANCER

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Introduction/Objectives: Data on the risk of developing a second cancer after a diagnosis of prostate cancer are limited. We used our database to investigate the incidence of RCC in men with previously treated prostate cancer and the incidence of prostate cancer in men with RCC.

Material and Methods: We evaluated the database from 2004 to 2018 of the oncological registry, pathohistological reports, operative urological registry as well as patient postoperative follow up to calculate the incidence of RCC in men with prostate cancer and the incidence of prostate cancer in men with RCC. The standardized incidence ratio (SIR, observed/expected) was calculated for each of the scenarios of interest, as well as for RCC and prostate cancer in men with other common malignancies.

Results: There was a higher incidence of RCC in men with prostate cancer (SIR 1.48, $P < 0.03$). RCC incidence was also higher in men with each of the other malignancies. Prostate cancer incidence was higher in men with RCC (SIR 1.32, $P < 0.001$) than in other malignancies.

Conclusion: Urologist and/or other specialist should be alerted to possibility of secondary malignancy when evaluating patients for the initially presenting symptoms and/or detected tumor, as well as during the follow-up evaluations of primary tumors.

Key words: Prostate cancer, Renal cancer, Secondary malignancy

NANOPARTICLES COMPRISED WITH HIGHLY SKIN PERMEABLE GROWTH FACTORS IN ENHANCED REGENERATIVE DIABETIC WOUND THERAPY

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Abstract: Approximately 25% of the total health care expenditure, among the diabetic population, is related to foot complications, and recently, advanced therapies have not responded to standard care. Failure to treat wounds in diabetics leads to infections of various natures, which lead to amputations, especially frequent in the elderly population.

Knowledge of the molecular, cellular, and tissue structure of the skin, as well as physiological and homeostatic processes, allows the improvement of topically applied formulations. Because diabetic foot ulcer and its complications become a serious health issue, new methods, including the incorporation of growth factors in nanodelivery systems, are developed. These systems, prepared in the form of nanosuspensions, nanoemulsions, or other nanoparticles, contain substances that synergistically accelerate the epithelization and tissue granulation in a diabetic wound.

Jee et al. have developed topical delivery system with a highly permeable growth factor which contains thecombination of the epidermal growth factor, insulin growth factor, the basic fibroblast growth factor,boundedwith protaminein order to make complexes of different structures. The effect of high permeability growth factors was enhanced by quercetin and oxygen, which were converted into nanoemulsions with 1-bromoperfluoroctaneincreasingthe thermal release of quercetin and oxygen.

Paladini et al. concluded that silver nanoparticles have important potential in thestrategy of makingnewanti-bio films on the wound surface.Barriers to successful treatment arebacterial colonies, which are resistant to conventional antimicrobial agents.Because of its favored antimicrobial properties and broad antimicrobial spectrum, silver nanoparticles represent the potential for controlling infections in the healing of diabetic wound healing.

Key words: Diabetic wound, foot ulcer, nanoparticles, growth factors

MALOCCLUSIONS AND SIGMATISM

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Introduction: In the field of dentistry, speech disorders expressed in various degrees of intensity and form are frequently encountered. This is a critical reason why research that investigates the correlation between orthodontic anomalies and the articulation of speech must be carried out.

Aim: To determine the correlation between the degree and type of disrupted speech and the orthodontic anomaly; and to gauge the level of familiarity that Dental Students at UKIM in Skopje have with speech therapy terminology, as well as their ability to recognize sigmatism.

Material and Methods: In the clinical study, 35 male and female respondents, aged four to 25 years, were inspected to determine the dentition, type of malocclusion,presence of sigmatism and to recognize any bad dental habits. Concurrently, for the other portion of the investigation, 38 students from the Faculty of Dentistry were surveyed using a questionnaire that tested knowledge on dyslalia, sigmatism, fricatives/affricates and the organic causes of sigmatism.

Results: Patients with malocclusion and without malocclusion were examined. The results showed that there is a presence of sigmatism in patients with specific malocclusions. In patients with normocclusion, sigmatism was not present in every case, which supports multifactoriality in the changes in speech articulation. Of the students interviewed, a large proportion was knowledgeable on the concept of sigmatism, but relatively unfamiliar with the other terms.

Conclusion: This research represents a preliminary contribution in determining the conditions for cohesive interdisciplinary cooperation between dentists, orthodontists, speech therapists and other stakeholders investigating speech disorders, developing preventative measures, and correcting orthodontic irregularities.

Key words: malocclusion, sigmatism, speech, speech therapy

PERIODONTITIS AS MANIFESTATION OF SYSTEMIC DISEASE

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Introduction: Periodontitis and diabetes are chronic diseases with high incidence in the population (diabetes 1% and periodontitis 14%). Periodontitis is defined as inflammation of the whole periodontium, it affects all periodontal structures. In time, if periodontitis isn't treated right, the tooth lost its connection within the alveolar bone and eventually, the only therapy option is extraction.

Case report: Female student, 21 years old, suffers from diabetes mellitus type I since she was twelve. She uses insulin therapy. In a time of final exams, due to high-stress levels, she got increased glucose levels in the blood. Four weeks after, she comes to the dental office because of the bleeding during the toothbrushing and pain sensations during the chewing. She filled the WHO standardized question mark and talked to dental medicine doctor to complete her general and dental anamnesis. Afterward, she underwent full oral cavity examination and radiological evaluation. She was diagnosed with periodontitis as a manifestation of diabetes mellitus. The patient was informed about the treatment protocol and agreed to do supragingival and subgingival root planing and scaling. Mechanical removal of debridement was done by ultrasonic and hand instruments. Also, she was informed about the importance of appropriate oral hygiene. Recall and reevaluation are arranged in 3 months.

Conclusion: In the present case report, we describe the association of diabetes mellitus and periodontal disease in 21 years old student. It is known that diabetes mellitus and other systemic diseases can cause periodontal disease because they can interfere with host resistance to infection. As it was mentioned before, there is a continuous increase in the prevalence of periodontal diseases and diabetes mellitus, so it is of high importance to educate and inform patients about association and mechanisms of control them both.

Key words: periodontitis, diabetes mellitus, periodontal health, gums, periodontal therapy

SOCKET PRESERVATION USING INJECTABLE BIPHASIC CALCIUM PHOSPHATE PASTE AND PORCINE COLLAGEN MEMBRANE: A CASE REPORT

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Introduction: To promote better bone healing it is recommended to do socket preservation following tooth extraction. Biomaterials for bone augmentation can be classified as bone substitute materials (allografts, xenografts, and alloplastic bone substitutes) and resorbable and non-resorbable membranes. Biphasic calcium phosphate is a mixture of hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP), of varying HA/β-TCP ratios, most commonly 60:40 and 70:30. The aim of this case report is present socket preservation technique using biphasic calcium phosphate in injectable form, in combination with porcine collagen membrane.

Case report: A healthy 35-years-old male was referred to an oral surgeon in Community Healthcare Center in Osijek, for extraction of the tooth 24 and 25, due to subgingival crown fracture along with unsuccessful endodontic treatment. An x-ray showed severe bone destruction in the periapical region of tooth 24 and 25. The site of extraction was exposed via elevation of a mucoperiosteal flap. Atraumatic tooth extraction was performed and was followed by curettage of the infected tissue in the socket. The socket was filled with biphasic calcium phosphate in injectable form and whole defect was covered by resorbable membrane made of porcine collagen. Primary closure was achieved by using 5/0 single sutures. The healing period was uneventful. Seven days after the surgical procedure, control Cone Beam Computed Tomography (CBCT) showed no dislocation of bone substitute and good volume stability of the bone graft.

Conclusion: This case highlights the use of biphasic calcium phosphate in injectable form and porcine collagen membrane in socket preservation. The viscosity of biphasic calcium phosphate allowed excellent filling of the bone defect and easy handling during surgical procedure. Follow-up is needed to determine volume stability six months after healing and prior implant placement.

Key words: biphasic calcium phosphate, resorbable membrane, socket preservation, augmentation, implant dentistry

KNOWLEDGE AND ATTITUDES OF THE PATIENTS TOWARD DENTAL IMPLANTS AS THERAPEUTIC SOLUTION FOLLOWING TOOTH EXTRACTION

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Introduction: The aim of the study is to examine the knowledge and attitudes of patients on dental implants as a therapeutic option after tooth extraction and to examine the sources of dental implant information as well as to determine which the most common barriers against decision making for such type of therapy are.

Materials and Methods: The survey included 130 patients of the Health Center in Osijek. The research was conducted in April and May 2019. An anonymous questionnaire was used to conduct the research.

Results: The survey involved 130 participants. Most participants lack at least one tooth. Participants showed good knowledge of dental implants with the exception of dental implant lifetime where participants mostly suggested that the dental implant lasts for a lifetime. The majority of participants know the possibility of implanting dental implants. The cost of the procedure for most participants is the main barrier when deciding on using dental implants. Statistically significant differences were observed in the knowledge of patients in relation to age and degree of education and the attitudes of patients in relation to gender, age and degree of education.

Conclusion: Most participants lack at least one tooth, but most of them consider the replacement of the removed teeth very important. The majority of participants know that the dental implant is embedded in the bone, but they do not know how long the lifetime of the dental implant is. Most of the participants know that dental implants need the same hygiene as the natural teeth and that they are implanted by oral surgeons. The cost of the procedure is the main barrier against deciding on dental implant implantation. To conclude, patient education about dental implants as a therapeutic solution should have a higher importance in dental offices, as well as in different media.

Keywords: dental implants, teeth, patients, knowledge, attitude

OPTIMIZATION OF ETHYL- LACTATE PRODUCTION PROCESS

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ABSTRACT

Ethyl-lactate, as a green solvent, is used more and more in pharmaceutical industry. Comapring to previous solvents, that are used in production of pharmaceutical substances, ethyl-lactate has more advantages. It presents lower chemical risk, it does not accumulate and it does not polute an environment, it's biodegradable, has relatively high boiling point. The aim of our experiments is to optimize the process of getting ethyl-lactate using esterification of lactic acid with ethanol. We studied influence of : different molar ratio of acid and alcohol, different amount of catalizator and different temperature on reaction of esterification. Esterification reactions were done with sulfate acid as catalizator, in balloon with reversible condenzator, on atmospheric pressure and constant temperature, for a period of 210 minutes. For determination of perecentage of conversion of lactic acid to ester during esterification, we used titration method with standard solution of NaOH. With the rise of molar ratio acid/alcohol from 1:5 to 1:10 in the beginning there is small difference of speed and yield of esterification. With rise of duration of reaction that difference becomes bigger. At the end of experiment, yield of ester increases from 52.8% at molar ratio 1:5 to 60.7% at molar ratio 1:10. Studying influence of amount of catalizator (H_2SO_4) on esterification was done at three different molar ratios acid/catalizator. After 210 minutes yields were 60.7% ; 65.0% ; 67.8% for molar ratios 1:0.125 ; 1:0.2 ; 1:0.25. Studying temperature influence on esterification latic acid with ethanol was done at four different temperatures: 35°C, 45°C, 55°C, 65°C. With rise of temperature there is a rise of speed of reaction and yield of ester. In our experiments, maximal yield of ester was gotten at ratio acid/alcohol/catalizator 1:10:0.125 at T=65°C where is 71.9% of lactic acid is converted to ethyl-lactate.

Keywords: Ethyl-lactate, esterification, lactic acid, ethanol

THE IMPORTANCE OF SOLUBILITY

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ABSTRACT

Solubility is defined as the maximum amount of a substance that can be dissolved in a given volume of a given solvent, at a constant temperature. This is one of the basic factors affecting the rate of dissolution of the drug substance from the dosage form and the bioavailability of the drug. This is one of the basic parameters to consider when formulating a new medicinal product, both with regard to the choice of the dosage form itself and with respect to the selection of the excipients themselves and the process for the preparation of the preparation. Solubility means the maximum amount of a drug substance that can be dissolved in a given volume of a solvent at a constant temperature. The rate of dissolution of a solid phase is defined as the change in mass in unit time. The rate of dissolution can be affected by increasing the surface area of the solid phase in contact with the medium, which can be achieved by grinding it, as well as by the increased intensity of agitation in the system. A large number of medicinal substances are poor soluble in water. There are several methods for increasing the solubility of poore soluble drug substances. One is making solid dispersions.The production of solid dispersions is a significant technique for increasing the solubility of difficultly soluble medicinal substances. Solid dispersions are dispersions of one or more drug substances in an inert, solid matrix, obtained by melting or using a solvent. The formation of the amorphous form of the drug in the matrix, the reduction of particle size and agglomeration, improved wetting and solubilization by carrier molecules are the main mechanisms that contribute to improving the solubility and dissolution rate of the drug by the formulation of solid dispersions.

Keywords: solubility, solid dispersions

ECZEMA

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ABSTRACT

Eczema is a group of pruriginous dermatoses. The three main mechanisms of dissemination are: contact with an external allergen, ingestion or injection of allergens, and eczema, which is conditioned by hyperirritability. In the acute phase, they are characterized by erythema, edema, wetting, while lichenification, desquamation, and hyperkeratosis are characterized in the chronic phase. The terms eczema and dermatitis are considered synonymous today, although some authors still use the term dermatitis to cover all types of skin diseases, so all eczema is actually dermatitis, but not all dermatitis is eczema. The group of endogenous eczema includes: atopic dermatitis, seborrheic dermatitis, fist eczema, gravitational eczema. Whereas exogenous eczema includes irritating dermatitis, contact allergic dermatitis, infectious dermatitis. Each form of eczema requires specific treatment. This is a common therapy, starting with the urgency of change: Acute eczema requires dressings, baths of potassium permaganate, aluminum acetate solution, silver nitrate, after which a thin layer of corticosteroid cream or solution should be applied and coated without tightening. Corticosteroid creams or calamine solution should be applied to larger areas. Subacute eczema is treated with steroid lotion or cream with neomycin incorporated. Chronic eczema responds best to steroid fats, but is also enhanced by salicylic fat and zinc paste. Hydrocortisone at a concentration of 0.5 to 1% is applied to the face, as well as other potent nonfluorinated corticosteroids. In very intense eczema, acute and subacute, systemic corticosteroids may be administered. With regard to herbal cosmetics, the following herbs are used in eczema: aloe gel (in sun lotions, lip balm), german chamomile (in shower infusions, as a bath additive), evening oil (in atopic eczema), hamamelis, calendula and tea tree. The most important dermatoses from this group are: Dermatitis e contactu allergica, Dermatitis e concactu irritativa, Dermatitis atopica, Eczema dyshidroticum, Eczema nummulare, Dermatitis coccica.

Keywords: eczema, treatment

DECRIMINALIZATION VERSUS LEGALIZATION OF MARIJUANA

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Introduction: Under international laws, cultivation, supply and possession of cannabis should be allowed only for "medical and scientific purposes". In general, possession of the drug for personal use should be a crime, to deter use, and most countries make this punishable by imprisonment. In recent years, however, several jurisdictions have reduced their penalties for cannabis users, and some have permitted supply of the drug, allowing us to observe different control models and their consequences. Policy discussions are complicated by conflicting claims-decriminalization or legalization, medical or recreational use. Decriminalization is an exemption from criminal penalties for personal use of marijuana, although the production and sale of this substance remains illegal. Legalization, on the other hand, is the repeal of laws banning the possession and personal use of marijuana. More importantly, legalization allows the government to regulate and tax the use and sale of marijuana.

Case study: In some European countries, national law does not prevent cannabis, or cannabis based products, being used as a medicine to treat defined indications. Authorised medicines may include THC in capsules, cannabis extract as a mouth spray, and dried cannabis flowers for vaporizing or making "tea". On the other hand, recreational marijuana is subject to quite complex laws and regulations. Male cannabis plants, cannabis seeds, roots and dried stems typically have either a very low THC content or no THC at all and are not subject to prosecution in most EU countries. Several countries in the European Union started to experiment with models that incorporate a legal marijuana supply. This includes the coffee shops in the Netherlands, cannabis social clubs in Spain, as well as decriminalisation measures in the Czech Republic. While these models have been at least partially considered to be a success, they still lack a proper legal framework which has often laed to confused and controversial situations.

Conclusion: Medical marijuana is legal in most of EU countries. Recreational marijuana is illegal in every country within the EU. But, strict policies are decreasing, many countries are thinking about decriminalisation, some even about legalisation.

Keywords: Marijuana, Decriminalization, Legalization, Europe Union

HEALTH TECHNOLOGY ASSESSMENT: APPROACH IN THE TREATMENT OF DIABETES MELLITUS

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Introduction: Health technology assessment (HTA) is a comparison of new or existing health technology with the technology used in practice or considered the best one, based on clinical efficiency, safety, economic analysis and ethical, legal and social principles. It is used to improve the treatment of various diseases, particularly diabetes mellitus, due to its high prevalence in the world.

Material and Methods: Systematic research of scholarly and scientific literature, databases (PubMed, Medline, EBSCO, Science Direct), electronic journals and books, via general-purpose and specialized search engines (Google, Google Scholar), using keywords.

Results: When using HTA in improving the treatment of diabetes mellitus, three aspects are important: clinical benefits, economic benefits and patients' preferences. In studies conducted so far, two main problems were investigated: benefits of continuous glucose monitoring compared to self-monitoring of glucose and incorporation of long-acting insulins (glargine and detemir) in the therapy of patients who stopped responding to oral antidiabetics. Firstly, continuous glucose monitoring was shown to be preferred by patients, especially children, because it is simpler and more effective (9,6 - 10%), compared to self-monitoring of glucose. This is a more expensive way of glucose monitoring, which can be a burden for the health care system. Secondly, when oral antidiabetics are not effective anymore, current guidelines suggest using either intermediate-acting insulins, like Neutral Protamine Hagedorn (NPH), or long-acting insulins (glargine and detemir). It was shown that long-acting insulins cause less nocturnal hypoglycaemic episodes than intermediate-acting insulins, but they are more expensive, and detemir requires higher doses than glargine.

Conclusion: HTA gives a lot of information to clinicians and public health experts to improve the guidelines for the treatment of diabetes mellitus, but it raises many ethical dilemmas, such as denying access to continuous glucose monitors or long-acting insulins to patients, because of their higher prices, and consequently providing patients with less effective alternatives.

Keywords: health technology assessment; diabetes mellitus.

DRUG RESISTANCE AS A CAUSE OF TREATMENT FAILURE

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Introduction: Drug resistance poses one of the biggest problems of the 21st century worldwide, with both economic and social consequences. It is currently a growing threat to global public health due to its progress, which is faster than finding and implementing new strategies for overcoming this issue as well as developing new drugs. The objective of this paper is to evaluate the causes, risk factors, molecular and biochemical mechanisms of drug resistance development and its influence on the treatment progress and its eventual failure.

Material and Methods: Systematic research of scholarly and scientific literature, databases (PubMed, Medline, EBSCO, Science Direct), electronic journals and books, via general-purpose and specialized search engines (Google, Google Scholar), using keywords.

Results: The development of resistance to commonly used classes of drugs may result in an increase in the treatment failure and a decrease in the therapeutic options, due to the loss of their effectiveness. In Europe, 25.000 people annually die due to resistance-caused treatment failure. Some of the factors that facilitate the spread of drug resistance and thus treatment failure are mutations and gene transfer in bacterial populations, inadequate diagnostics, overprescription of various drugs, inappropriate drug use, drug use in the hospital conditions, poor infection-control demands in the health care system and poor hygiene and sanitation.

Conclusion: To prevent drug resistance, joint action and education of physicians, pharmacists, politicians and patients should be ensured. Recognition of the mutation place, hence alterations and modifications, can be used as a strategy for reducing drug resistance complications as well as creating new drugs that will affect only targeted sites inside the cell or combining drugs with different mechanisms of action during the treatment. The use of sensitive and rapid diagnostic tests can contribute to the early identification and detection of drug-resistant species and a well-timed treatment, thereby minimizing its failure rate.

Keywords: drug resistance; treatment failure.

ANTIBIOTIC PRESCRIBING IN MONTENEGRO FROM 2013 TO 2017

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Introduction: The inappropriate and irrational use of antibiotics leads to development and spread of antimicrobial resistance. The aim is to analyze trends in antibiotic prescribing in primary health care in Montenegro from 2013 to 2017.

Methods: Data on antibiotic prescriptions were collected from public primary health institutions through the Health Information System. Prescription rate per 1000 inhabitants and the number of packages per 1000 inhabitants per day were calculated.

Results. Prescription rate for antibiotics decreased from 939 prescriptions / 1000 inhabitants in 2013 to 762 prescriptions / 1000 inhabitants in 2017 . Also, the number of packages per 1000 inhabitants per day fell from 3.25 packages /1000 inhabitants/day in 2013 to 2.54/1000 inhabitants /day in 2017. The most commonly prescribed antibacterial drugs were amoxicillin, followed by cephalexin and amoxicillin/clavulanic acid. The prescribing of third-generation cephalosporins (cefixime) showed reduction of 20% in 2017 compared to 2013.

Conclusions: It could be concluded that there is significant decrease in antibiotic prescribing in public primary health institutions. Nonetheless, total outpatient consumption of antibiotics in Montenegro is still high. Further work should be done to raise awareness among medical professionals and general population in order to reduce irrational use of antibiotics and consequently bacterial resistance.

Keywords: antibiotics, prescriptions, primary health care

ANTIBIOTIC PRESCRIBING FOR UPPER RESPIRATORY CONDITIONS IN MONTENEGRO

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Introduction: Upper respiratory infections are one of the most common causes of consultations in primary health care. In vast majority of cases, the upper respiratory infections are of viral origin. However, antibiotics are still prescribed for the treatment of these infections, or patients resort to self-medication, which contributes to the development of bacterial resistance. The aim is to analyze trends in antibiotic prescribing for the treatment of theupper respiratory conditions from 2013 to 2017.

Methods: Data on antibiotic prescriptions were provided through the Health Information System from public primary health institutions. Antibiotic prescriptions were linked to ICD-10 codes (International Classification of Diseases, 10th Revision).

Results: Of 474375 antibiotic prescriptions in 2017 in Montenegro, 208682 prescriptions were for the upper respiratory conditions (44%). The proportion of antibiotics prescribing for upper respiratory conditions in 2017 fell compared 2013, 48% respectively. Tonsillopharyngitis (J02 / J03) is the leading cause for antibiotic prescribing over 5-year period, over 60% of all prescriptions for upper respiratory conditions. The most commonly prescribed antibiotic for tonsillopharyngitis was amoxicillin (more than one third of antibiotic prescriptions for tonsillopharyngitis). Beta-lactamse/sensitive penicillins (J01 CE), as the antibiotics of choice for confirmed streptococcal tonsillopharyngitis, was found in about 10% of antibiotic prescriptions for tonsillopharyngitis.

Conclusions: The level of antibiotic prescribing for upper respiratory infections in primary health care is still high and futher reduction in antibiotic precribing is needed. Antibiotics were prescribed still unnecessary and too broad.

Keywords: antibiotic prescribing, primary health care, upper respiratory infections

ANXIETY - DAILY EMOTION OR PROBLEM

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ABSTRACT

Anxiety is a complex and heterogeneous psychiatric disorder manifested by feelings of fear, psychomotor tension and internal restlessness without obvious cause. As research shows that the number of people struggling with anxiety is increasing, it is important to point out diverse therapeutic approaches in the treatment of this disorder.

The aim of this research is to raise awareness among people of adequate psychological help and the use of natural preparations in order to overcome this problem.

Data from the available literature were used to construct this research.

The results show that the plants most commonly used as anxiolytics are: kava, valerian, passion flower, hops, chamomile and lavender. Kava extract and its constituents show anticonvulsant, local anesthetic and muscle relaxant properties. More recent studies indicate that anxiolytic action of kava is due to the binding of kava pyrones to GABA A receptors. Also, the anxiolytic action of valerian is achieved by potentiation of the GABA-ergic system, agonist effect on adenosine A1 receptors as well as 5HT1A receptors.

Despite the fact that passion flower and hops are increasingly used today, their mechanisms of action have not been elucidated yet. However, the sedative effect of passion flower is attributed to vitexin, maltol and harman, while in the case of hops it is due to 2-methyl-3-butene-2-ol. Lavender essential oil rich in linalool and linalyl acetate has a sedative effect and prolongs the duration of sleep, while in the case of chamomile, apigenin excerts anxiolytic action.

Due to the fact that patients are very often unaware of this problem in itsearly stages, it is necessary to advise them and recommend herbal remedies. These herbal remedies do not show their effects immediately but gradually, they are well tolerated and do not involve risk of habituation, addiction and overdose.

Keywords: anxiety, herbal remedies, medicinal plants

DETERMINATION OF VITAMIN CONCENTRATIONS IN DIETARY SUPPLEMENTS

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ABSTRACT

Vitamin supplements in recent years are becoming more widespread and are being consumed even if we do not need them. There are many products on the market that offer great availability and the various forms and dosages in which these supplements can be taken. Although taking high doses of vitamins (well above the recommended daily dose) is popular, it should be kept in mind that randomly taking high doses of some vitamins, minerals and phytochemicals can be detrimental to health. The aim of this study is to determine the concentration of vitamins in vitamin supplements.

The test was performed on nine samples of different vitamin supplements. LC-MS-liquid chromatography with mass and DAD detector was used as the method.

Based on the test results, it can be concluded that the concentration of vitamins is within the limits stated on the packaging. Vitamin E concentrations in 3 samples ranged from 20-100mg / tablet, in 3 samples Vitamin C concentrations varied from 152-1200mg / tablets, while for Vitamin B group and vitamin D concentrations varied up to 100mg / tablet depending on from the sample and individual vitamins.

In Montenegro, a rulebook currently in force recommends a concentration that should be taken daily through the diet but does not prescribe the maximum allowable concentration of vitamins in dietary supplements, the same is true with the FAO / WHO rulebook, so in some cases we have products that even several times have higher concentrations of vitamins than recommended. The therapeutic effect of multidose supplements can only be safely carried out under clinical conditions or with the supervision of a physician, and it is therefore necessary to adjust the dose of vitamins in supplements to protect the health of the individual and prevent possible intoxication due to excessive consumption of the supplements.

Keywords: Vitamins, Supplementation

DETERMINATION OF CORTICOSTEROID CONTENT IN ANTI-AGE CREAMS

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ABSTRACT

Anti-age products are cosmetic skincare products used to treat aging, slowing down, reducing or masking the appearance of signs of skin aging. Such preparations usually contain, in addition to moisturizing ingredients, special ingredients that are believed to have the effect of slowing skin aging. Such ingredients are: retinoids (as retinyl palmitate), epidermal growth factor, alpha and beta hydroxy acids, antioxidants, coenzyme Q10 ... Despite the high demand, many anti-age products have not been shown to produce lasting or major positive effects, so manufacturers are increasingly masking the effects by adding forbidden ingredients such as corticosteroids. This is not the case for dermocosmetic preparations where these rules do not apply because they are intended for use in various types of diseases. The aim of this study is to determine the concentration of corticosteroids in anti-age preparations and thus prove their safety.

The test was performed on four samples of different anti-age preparations. LC-MS-liquid chromatography with mass and DAD detector was used as the method.

Test results showed that in these samples the concentrations of corticosteroids expressed as Betamethasone, Prednisolone, Dexamethasone and Flumetazone were less than 10 µg / kg, which is the detection limit of the apparatus itself.

Based on the studies conducted, we confirm that the concentration of the four corticosteroids tested is not exceeded in the anti-age preparations tested, on the basis of which we conclude that they are safe for use. Such testing should be carried out regularly in order to ensure the safe application and protection of consumer health.

Keywords: anti-age, corticosteroids

DETERMINATION OF ACRYLAMIDE CONTENT IN FOOD

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ABSTRACT

Acrylamide is found in various types of food products used in daily diet. Among starch-rich products, the largest source of acrylamide is potato products: chips and French fries, as well as various types of pastries and breads. Because it is a small molecule, it is quickly and easily absorbed in the gut and then distributed through the body via blood. Cytochrome P450 it biotransforms into glycinamide, which then acts genotoxically. The aim of this study is to determine the concentration of acrylamide in starch-rich foods.

Tests were performed on 5 different food samples using GC chromatography with mass spectroscopy. Based on the test results, it can be concluded that the concentration of acrylamide in the samples is within the recommended intake. In the sample of chips the concentration is by far the highest and is 1834 μg / kg, then in the sample of French fries 1216 μg / kg, in two bread samples the concentration varies from 56-97 μg / kg and in biscuits 98 μg / kg.

In recent years, the monitoring of acrylamide concentrations in various food products has received special attention from the WHO, as it is a molecule that acts genotoxically and disrupts the order of amino acids in the DNA molecule, which can cause malignant changes in the lungs, brain, testes, thyroid gland, etc. . It is necessary to determine the maximum permissible concentration of acrylamide in foods in order to reduce intake through daily diet. This will also reduce the number of new patients with various malignancies and improve the health of the individual.

Keywords: Acrylamide, Genotoxicity

CLASSIFICATION OF PERSONAL CARE PRODUCTS CATEGORIES BASED ON FUNCTION AND WEIGHT FRACTION OF CONTAINED CHEMICALS

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Introduction: Exposure to chemicals contained in personal care products which are in daily use is the subject of a numerous recent researches. The aim of this research is to classify the categories of personal care products according to the function and weight fraction of the chemicals they contain.

Materials and Methods: A publicly-available dataset of chemicals, that are included in the composition of the personal care products with their functions and weight fractions, has been used. The dataset was downloaded from the U.S. Environmental Protection Agency (EPA) site. Using the method of k-means clustering, chemicals have been divided into 5 clusters according to their functions and weights in the products. In the second phase, the product categories have been classified using the Decision Tree (DT) method based on these 5 clusters.

Results: The results show that the baby care products and the products for face, eyes and lips care have a low fraction of chemicals with different functions. Categories of products that have a high fraction of chemicals with all observed functions are hair sprays, deodorants, dry shampoos, perfumes, nail agents, hair care products and hair dyes. Categories that have a high weight fraction of chemicals with solvent function are nail polish removers, skin toners, acne products, depilatory agents, hair whiteners, hair color activators, mascara, make-up removers, nail polishers and removers. Low-level preservative products are baby-waxes and wipes, after shave products, body powders, body scrubs, eye creams, pencils and eye shadows, face creams, hand lotions and body lotions, soaps for hands, lip gloss etc.

Conclusion: Data about the products chemical composition are often unavailable or incomplete due to limited public information, business policy of manufacturers or the mismatch in the categorization of chemicals and products. The results of this research can help users to choose personal care products in case of the lack of such information.

Keywords: personal care products, chemical function, chemical weight fraction, classification

PHYSICAL STABILITY OF 5-FU LOADED SILICA NANOPARTICLES IN SIMULATED GIT CONDITIONS

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ABSTRACT

The main concept of the Targeted Drug Delivery System is to transport the pharmacologically active ingredient or in some cases the prodrug to the site of action. This enhances the therapeutic efficacy, reduces the side effects of the drug, and also improves the in vivo and in vitro stability of incorporated API. In this study, we have evaluated the physical stability of silica nanoparticles loaded with 5-Fluorouracil in different media simulating GIT conditions.

Twenty two different formulations of silicate nanoparticles (N1-N22) were prepared with the sol-gel method. Tetraethoxysilane and a combination of tetraethoxysilane and 3-aminopropyltriethoxysilane were used as precursors for the synthesis of the formulations. The process involves hydrolysis of metal alkoxides in alcohol and their condensation in the presence of mineral acid or base as catalysts. The physical stability of the formulations was examined by measuring the size (hydrodynamic diameter) and zeta potential of the nanoparticles by dynamic light scattering (Malvern Zetasizer Nano ZS90) after incubation in different media (Phosphate buffer pH 7.4, Acetate buffer pH 4.5, and 0.1M HCl pH 1) for several time points in the period of 7h.

The size of the nanoparticles in the formulations ranges from 46.7 to 3332.6 nm, while the zeta potential ranges from -12.2 to 53.1 mV in all three media and depends on the conditions of preparation, initial physical stability, and changes in pH and ionic strength of media. In the formulations N1 and N11, the physical properties remain unchanged over time and in different media, while the rest of the formulations undergo changes that are likely due to the aggregation of the nanoparticles. Therefore, we can conclude that some formulations presented satisfactory stability in all three media without altering their physical characteristics for the tested time period, this showing potential for clinical application that should be further investigated.

Keywords: targeted drug delivery system, silica nanoparticles, 5-Fluorouracil, physical stability

PAMPA TEST AS A METHOD FOR PERMEABILITY TESTING

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ABSTRACT

Permeability is a key factor affecting the resorption process of the drug substance, in addition to the solubility and dissolution rate of the drug substance. Based on permeability, they classify substances within the BSC system. A drug substance is considered highly permeable if the rate of absorption in humans is greater than 90%.

Permeability can be determined by mathematical calculation based on the chemical structure of molecules, in vitro testing using artificial membrane models, in vitro testing on different cell cultures (Caco-2 cells, MDCK cells), in vitro testing on human or animal intestinal tissue, in vivo studies of intestinal perfusion in humans, or in vivo or in situ studies of intestinal perfusion in animal models, as well as studies in which absolute bioavailability and mass balance studies are determined (Mass Balance Studies).

The PAMPA test (Permeability Tests on Parallel Artificial Membranes) is a technique that can test permeability through an artificial membrane to assess the permeability or absorption of many compounds at the same time in vivo. The PAMPA test uses an artificial membrane to separate the donor compartment from the acceptor one. A test compound dissolved in a suitable solvent is introduced into the donor compartment and only the solvent is introduced into the acceptor compartment. By connecting the donor and acceptor compartments, a PAMPA system ("sandwich") is formed in which diffusion of the test substance through the artificial membrane takes place between compartments, in the direction of the concentration gradient - from the donor to the acceptor compartments.

The advantages of the PAMPA model over some other models are greater test efficiency and greater cost-effectiveness. The PAMPA test has been widely used in the pharmaceutical industry to determine the permeability of various compounds at an early stage in the drug development process.

Keywords: permeability, PAMPA test

STATINS – A POTENTIALLY NEW PLAYER IN THE THERAPY OF CARCINOGENESIS

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ABSTRACT

Statins are among the most prescribed drugs in the world. Statins are medicines used primarily as hypolipidemics because they have been designated as 3-hydroxy-methylglutaryl-CoA (HMG-CoA) reductase inhibitors. In addition to this primary effect of statins, more recently, the study of statins and their role in the process of carcinogenesis has become increasingly important. These other effects may be explained by the fact that statins, in addition to cholesterol synthesis, also inhibit the synthesis of a number of other metabolites, especially isoprenoid units, that serve as substrates in the post-transcriptional modifications of many proteins.

The aim of this research is precisely to draw the attention of our health care profession to another under-researched area that could potentially contribute to some of the new reach of cancer patients in the future. In this research, an analysis of the importance of statins in the process of carcinogenesis was performed, by reviewing the available literature data. Emphasis is placed on the importance of statins in colon and breast cancers.

The results of numerous studies have shown that statins have an antitumor effect on tumor cells of different organs. This effect is mainly due to the suppression of proliferation and induction of apoptosis and is shown by lipophilic statins. In colon cancer, results have shown that statins can influence the outcome by reducing the invasiveness or metastatic properties of colorectal cancer. The literature data also indicate a positive statin outcome in breast cancer patients in terms of reducing relapse rates, reducing mortality, and having a positive role as a neoadjuvant agent. Differences in antitumor potential are explained as a consequence of different physicochemical characteristics of statins, primarily differences in lipophilicity. It is concluded that different types of statins act differently on different types of tumor cells.

Keywords: statins, carcinogenesis, antitumor effect

SYNTHESIS OF SCHIFF BASES AND THEIR ANTIMICROBIAL ACTIVITIES

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ABSTRACT

Schiff bases are organic compounds synthesized by combining aldehydes/ketones and amines. The purpose of this scientific work was to synthesize organic compounds with two Schiff base groups and to evaluate their antimicrobial and antifungal activities.

The starting compound employed was thiocarbohydrazide which comprises of two amino groups, thus in a reaction with aldehydes or ketones it can produce a product with Schiff bases on both sides. The thiocarbohydrazide was refluxed with a mixture of water and ethanol, until completely dissolved, followed by the addition of aldehyde or ketone. The acid catalyzed reaction was done under reflux for 3 hours. Afterwards the product was placed in the ice bath and taken out after 24 hours, followed by filtration and evaporation. The compound was purified by recrystallization and subsequently analyzed by NMR (13C, 1H) for confirmation of structure analyses. Pure and solid product was then tested on bacteria and fungi.

Following this protocol, 10 Schiff bases were synthesized using thiocarbohydrazide and different aldehydes and ketones. Schiff bases are known for their strong antimicrobial and antifungal activities, increasing the number of reactive Schiff bases would enhance the antimicrobial and antifungal effects of the compound.

To conclude, this study involved the synthesis of Schiff base compounds with strong potential as antimicrobial and antifungal reagents. It is hoped that, these compounds based on Schiff bases would further be optimized from the further perspective of future antibiotics and antifungal drugs.

Keywords: Schiff bases, synthesis, antibiotics, antifungal drugs

HERBS IN PREGNANCY: IS NATURAL ALWAYS SAFE?

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ABSTRACT

Pregnancy, medically described as a physiological condition, is normally followed by changes in the morphology and function of many organs and organ systems. Adaptation to such changes is varied and specific, and often accompanied by problems that require therapy. Researches show that many women use herbs during pregnancy, based primarily on traditional experiences. However, taking in account that natural isn't always safe, this research obtains collected data on herbs that are contraindicated in pregnancy.

The aim of this research is to raise awareness among pregnant women, future mothers and medical public of the dangers of using certain herbs in pregnancy.

Data from the available literature were used to construct this research.

The results show that the most common reasons limiting the use of herbs in pregnancy are their potentially emmenagoge and / or uterotonic (abortive) effects, and carcinogenic, mutagenic, teratogenic and hepatotoxic effects. The most common constituents responsible for these side effects are anthraquinone heterosides, essential oils and alkaloids.

Most herbs containing alkaloids show toxic effects. For example comfrey contains pyrrolizidine alkaloids which shows hepatotoxic effect. Usage of bearberry, parsley and juniper is contraindicated in the treatment of urinary tract infections, while on the other hand it is safe to use horsetail, corn silk and cranberry. The treatment of constipation avoids the use of aloe, frangula bark, flax and castor oil, while the use of bulk forming laxatives is safe. Usage of essential oils, especially orally, is not recommended because of constituents such as thujone, apiol and pulegone which show toxic effects.

Beside mentioned results, it is important to point out that a large number of herbs do not have safety data for use in pregnancy, and that more attention needs to be paid to investigating the safety profiles of these herbs.

Keywords: herbs, pregnancy, safety of use

SYNTHESIS OF THE SCHIFF BASES OF CARBONYLES WITH THIOCARBOHYDRAZIDE AND OPTIMIZATION OF THEIR 3D STRUCTURE AND GEOMETRY

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Introduction: Schiff bases represent organic compounds which are consisted of a carbon double bonded to a nitrogen. Among other things, they have noticeable antioxidant activity. The main purpose of this scientific study is synthesis of new organic precursors and optimisation of their geometry. One direction of our research is examination of the interactions of such optimized Schiff bases with selected receptors in the cell membrane.

Materials and Methods: Schiff bases were synthesized in a reaction between aldehydes/ketones with thiocarbohydrazide (dHS). Thiocarbohydrazide consists two amino groups,so therefore it can form Schiff base from both sides, when it reacts with aldehydes and ketones. The reaction is carried out by heating of the aldehyde / ketone mixture with dHS, in a mixture of ethanol and water for 3 hours and then crystallizing the resulting product for 12 hours. After recrystallization from pure ethanol, the desired Schiff base was obtained in excellent yields (>90%). The corresponding coordination compounds were formed in reaction with the transition metal salts (cooper and nickel). To optimize the molecule geometry, we used standard chemical packages: Chem Draw and Chem Scatch, that offer us those opportunities.

Results: In our experiments, we performed the reaction between the three carbonyl compounds: acetone, benzaldehyde and citral with dHS. According to the described procedure, we obtained the corresponding Schiff bases. Complex of copper and nickel salts were prepared in reaction with benzaldehyde imine. After optimization of the geometry of all three synthesized bases as well as the two synthesized complexes, we obtained a computer prediction of the most stable possible conformations of all molecules, ie their most stable 3D geometries

Conclusion: There are a number of publications where Schiff bases and their complexes with the transition metals are tested as antitumor, antimicrobial, and antifugal agents. Our study is an attempt to synthesize a number of such compounds, and carried geometry optimization is the first step in modeling the obtained compounds within the receptor, in order to study possible interactions.

Keywords: Shiff bases, thiocarbohydrazide, optimisation, carbonyls, receptors