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Medical Publications

Macedonian International Medical Publications Indexed in PubMed in 2013

Macedonian Journal of Medical Sciences*

Faculty of Medicine, Ss. Cyril and Methodius University of Skopje, Skopje, Republic of Macedonia

Abstract

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Key words: Medical Publications; Medical research; Republic of Macedonia.

***Correspondence:** Macedonian Journal of Medical Sciences. Faculty of Medicine, Ss. Cyril and Methodius University of Skopje, Republic of Macedonia. 50 Divizija No 16, 1109 Skopje, Republic of Macedonia. E-Mail: mjms@ukim.edu.mk

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We present abstracts of published papers in international journals deposited in PubMed. Search details were: ((Macedonia[Affiliation] NOT Greece[Affiliation]) NOT "Prilozi"[Journal]) AND ("2013/01/01"[PDAT] : "2013/12/31"[PDAT]), dated March 01, 2014. A total number of 138 papers were selected in PubMed during 2013 year, 23 of which were not from Republic of Macedonia and were excluded.

A total number of 105 papers are included in 2013 year in Pubmed from Republic of Macedonia. Four papers are deposited in the PubMed without abstracts.

Editorial Board does not take any responsibility either for the content, nor the quality of the abstracts.

Alcheva G(1), Gerovski F(2), Beletsky L(3). Implementation of patients' rights legislation in the Republic of Macedonia: gaps and disparities. *Health Hum Rights*. 2013 Dec 12;15(2):20-31.

(1)Human Rights in Patient Care Program at the Association for Emancipation, Solidarity and Equality of Women in Skopje, Republic of Macedonia. (2)Program Human Rights in Patient Care at the Centre for Regional Policy Research and Cooperation "Studiorum" in Skopje, Republic of Macedonia. (3)Law and Health Sciences at the Northeastern University School of Law and Bouvé College of Health Sciences, Boston, USA and Adjunct Professor at the Division of Global Public Health, UCSD School of Medicine, San Diego, USA.

BACKGROUND: Since its formation after the breakup of Yugoslavia, Macedonia has made major strides in formulating a framework for protecting patient rights through extensive legal reform. The impact of this reform had not been assessed before the work of this project. **METHODS/OBJECTIVES:** Within the context of a larger project on improving human rights in patient care, this paper provides an overview of patients' rights legislation in Macedonia and uses research, case reports, and other empirical information to highlight the gaps in the implementation of patients' rights legislation on the ground. **RESULTS:** The Law on the Protection of Patients' Rights (2008) and attendant legislation governing health care provision and other aspects of the social

contract in Macedonia provide extensive protections for the rights of patients in such domains as the right to access health care, the right to information, and the right to remedy. This legislation also outlines several new procedural channels to enable patients to vindicate their rights within institutional and governmental structures on the local and national levels. Data from a number of studies and case file reviews suggest, however, that the implementation of many key provisions is lacking, both in terms of quality and presence of services or mechanisms contemplated by Macedonian law. Gaps in implementation disproportionately affect vulnerable and marginalized groups, including women, rural residents, and Roma. **DISCUSSION:** Although the letter of Macedonian law generally complies with international best practices in patients' rights, these rights are not fully implemented and the mechanisms implied are not fully functional. Additional investment must be made in monitoring systems, education, and incentive mechanisms to ensure effective implementation, including the formation of a mandated commission for the protection of patients' rights. PMID: 24421164

Ambarkova V(1), Galić I(2), Vodanović M(3), Biočina-Lukenda D(4), Brkić H(5).Dental age estimation using Demirjian and Willems methods: cross sectional study on children from the Former Yugoslav Republic of Macedonia. *Forensic Sci Int*. 2014

Jan;234:187.e1-7.

(1)Department of Pediatric and Preventive Dentistry, Faculty of Dentistry, The Saints Cyril and Methodius University of Skopje, Vodnjanska 17, 91000 Skopje, Former Yugoslav Republic of Macedonia. Electronic address: ambveki@yahoo.com. (2)University Department of Health Studies, University of Split, Ruđera Boškovića 31, 21000 Split, Croatia; Department of Dental Medicine, School of Medicine, University of Split, Ruđera Boškovića 31, 21000 Split, Croatia. Electronic address: igalic@mefst.hr. (3)Department for Dental Anthropology, School of Dental Medicine, University of Zagreb, Gundulićeva 5, 10000 Zagreb, Croatia. Electronic address: vodorovic@sfzg.hr. (4)Department of Dental Medicine, School of Medicine, University of Split, Ruđera Boškovića 31, 21000 Split, Croatia. Electronic address: dlukenda@mefst.hr. (5)Department for Dental Anthropology, School of Dental Medicine, University of Zagreb, Gundulićeva 5, 10000 Zagreb, Croatia; University Hospital Centre Zagreb, Gundulićeva 5, 10000, Croatia. Electronic address: brkic@sfzg.hr.

To evaluate applicability of Demirjian and Willems methods for calculating dental age of children in the Former Yugoslav Republic of Macedonia we analyzed panoramic radiographs of 966 children (485 female and 481 male, aged 6-13 years) treated at the University and Community Dental Clinics in Skopje using four Demirjian methods and a Willems method for determining dental ages. Intra-rater and inter-rater agreement of mineralization stages were 0.86 and 0.82, respectively. All methods significantly overestimated dental age when compared to the chronological age ($p < 0.001$). In males, the lowest overestimation was shown using Willems method (0.52 ± 0.87 years), followed by Demirjian methods from 1976 using PM1, PM2, M1, M2 teeth (0.69 ± 0.92 years) and using I2, PM1, PM2, M2 teeth (0.80 ± 0.98 years). The greatest overestimation were shown using Demirjian methods using 7 teeth from 1976 (0.92 ± 0.99 years) and method from 1973 (1.06 ± 1.07 years). In females, the lowest overestimation was shown using Willems method (0.33 ± 0.83 years) than the Demirjian method using PM1, PM2, M1, M2 teeth (1.00 ± 1.01 years), following methods from 1976 using 7 teeth (1.03 ± 1.01 years) and I2, PM1, PM2, M2 teeth (1.12 ± 0.96 years). The greatest overestimation was for method from 1973 using 7 teeth (1.17 ± 0.98 years). Willems method was the most accurate while Demirjian's methods for dental age calculation are not suitable on children from the Former Yugoslav Republic of Macedonia. PMID: 24262808

Andonov S(1), Ødegård J, Svendsen M, Ådnøy T, Vegara M, Klemetsdal G. Comparison of random regression and repeatability models to predict breeding values from test-day records of Norwegian goats. J Dairy Sci. 2013 Mar;96(3):1834-43.

(1)Faculty of Agricultural Sciences and Food, University Ss Cyril and Methodius, PO Box 297, 1000 Skopje, Macedonia. sandonov@zf.ukim.edu.mk

One aim of the research was to challenge a previously selected repeatability model with 2 other repeatability models. The main aim, however, was to evaluate random regression models based on the repeatability model with lowest mean-squared error of prediction, using Legendre polynomials up to third order for both animal additive genetic and permanent environmental effects. The random regression and repeatability models were compared for model fit (using likelihood-ratio testing, Akaike information criterion, and the Bayesian information criterion) and the models' mean-squared errors of prediction, and by cross-validation. Cross-validation was carried out by correlating excluded observations in one data set with the animals' breeding values as predicted from the pedigree only in the remaining data, and vice versa (splitting proportion: 0.492). The data was from primiparous goats in 2 closely tied buck circles (17 flocks) in Norway, with 11,438 records for daily milk yield and 5,686 to 5,896 records for content traits (fat, protein, and lactose percentages). A simple pattern was revealed; for daily milk yield with about 5 records per animal in first lactation, a second-order random regression model should be chosen, whereas for content traits that had only about 3 observations per goat, a first-order polynomial was preferred. The likelihood-ratio test, Akaike information criterion, and mean-squared error of prediction favored

more complex models, although the results from the latter and the Bayesian information criterion were in the direction of those obtained with cross-validation. As the correlation from cross-validation was largest with random regression, genetic merit was predicted more accurate with random regression models than with the repeatability model. PMID: 23357012

Antovska P(1), Petruševski G, Makreski P. Solid-state compatibility screening of excipients suitable for development of indapamide sustained release solid-dosage formulation. Pharm Dev Technol. 2013 Mar-Apr;18(2):481-9.

(1)Research and Development, ALKALOID AD, Aleksandar Makedonski 12, 1000 Skopje, Republic of Macedonia. pantovska@alkaloid.com.mk

Differential scanning calorimetry and Fourier transform infrared spectroscopy were applied as screening analytical methods to assess the solid-state compatibility of indapamide (4-chloro-N-(2-methyl-2,3-dihydroindol-1-yl)-3-sulfamoyl-benzamide) with several polymers aimed for development of 24 h sustained release solid-dosage formulation. After the initial research phase which was directed towards selection of suitable polymer matrices, based on their solid-state compatibility with the studied pharmaceutical active ingredient, the second phase of evaluation was intended for compatibility selection of other excipients required to complete a sustained release formulation. The preformulation studies have shown that polyvinylpyrrolidone/polyvinyl acetate might be considered incompatible with indapamide, and the implementation of this polymer carrier should be avoided in the case of the entitled development. The experimental data additionally have revealed that sorbitol is incompatible with indapamide. The obtained results afforded deeper insight in to the solid-state stability of the studied binary systems and pointed out directions for further development of indapamide sustained release solid-dosage formulation. PMID: 22998073

Antovska VS. Pleated colposuspension: Our modification of Burch colposuspension. Indian J Urol. 2013 Jul;29(3):166-72.

Department of Urogynaecology and Pelvic Floor Disorders, University Clinic for Gynaecology and Obstetrics, Medical Faculty, Saint Cyril and Methodius University, Skopje, Republic of Macedonia, Europe.

INTRODUCTION: Burch colposuspension is a standard treatment for stress urinary incontinence. However, it is associated with recurrence and urinary retention. We describe a modification of this technique to overcome these problems and evaluate the results in comparison with the standard procedure. MATERIALS AND METHODS: A total of 145 patients with isolated stress urinary incontinence (SUI), underwent either our modified pleated colposuspension (PC); $n = 97$ or standard Burch colposuspension (BC) ($n = 48$). Description of PC: Three No. 0 non-absorbable sutures were placed in the side-to-side manner at the mid-urethral level with 0.5-1.0 cm distance between them using double bites and were passed through the Cooper's ligament. The patients were followed-up every 6 months for SUI and genital prolapse evaluation. Successful surgery was defined as (1) No self-reported SUI symptoms, (2) Negative Marshall's coughing test (MT), (3) No retreatment for SUI, (4) Absence of urodynamic SUI. In addition, failure was defined as the occurrence of urinary retention, use of catheter on 6-week visit, maximum flow rate >15 ml/s, flow time <60 s, or residual urine <100 ml. Data was compared using Student's paired test and Mantel-Haenzel's $\chi^2(2)$ test. $P > 0.05$ was considered significant. RESULTS: The mean follow-up after surgery for PC was 102.4 months and for BC was 103.6 months. At last follow-up, data suggesting failure (Stress score ≥ 7 , urge score ≥ 7 , Pad test with weight < 15 g/day and positive MT during lithotomic/upright position) were more frequent in BC group ($P > 0.05$; $P > 0.01$; $P > 0.05$; $P > 0.05$, respectively). The incidence of recurrent SUI was 5.2% after PC and almost triple (14.6%) after BC. Residual urine <100 ml and weak stream were more frequent in the BC group ($P > 0.05$; $P > 0.01$, respectively). Detrusor over-activity on urodynamic studies, Flow time <60 s, urethral pressure profilometry positive for obstruction had a higher incidence in BC group (P

>0.01; $P > 0.001$; $P > 0.01$, respectively). **CONCLUSION:** Our modified pleated colposuspension showed improved outcomes when compared with standard Burch colposuspension. **PMCID:** PMC3783692. **PMID:** 24082433

Arsov S(1), Trajceska L, van Oeveren W, Smit AJ, Dzekova P, Stegmayer B, Sikole A, Rakhorst G, Graaff R. Increase in skin autofluorescence and release of heart-type fatty acid binding protein in plasma predicts mortality of hemodialysis patients. *Artif Organs.* 2013 Jul;37(7):E114-22.

(1)Department of Nephrology, Clinical Centre, Skopje, Macedonia.

Advanced glycation end-products (AGEs) are uremic toxins that accumulate progressively in hemodialysis (HD) patients. The aim of this study was to assess the 1-year increase in skin autofluorescence (Δ AF), a measure of AGEs accumulation and plasma markers, as predictors of mortality in HD patients. One hundred sixty-nine HD patients were enrolled in this study. Skin autofluorescence was measured twice, 1 year apart using an AGE Reader (DiagnOptics Technologies BV, Groningen, The Netherlands). Besides routine blood chemistry, additional plasma markers including superoxide dismutase, myeloperoxidase, intercellular adhesion molecule 1 (ICAM-1), C-reactive protein (hs-CRP), heart-type fatty acid binding protein (H-FABP), and von Willebrand factor were measured at baseline. The mortality of HD patients was followed for 36 months. Skin autofluorescence values of the HD patients at the two time points were significantly higher ($P < 0.001$) than those of healthy subjects of the same age. Mean 1-year Δ AF of HD patients was 0.16 ± 0.06 , which was around seven- to ninefold higher than 1-year Δ AF in healthy subjects. Multivariate Cox regression showed that age, hypertension, 1-year Δ AF, hs-CRP, ICAM-1, and H-FABP were independent predictors of overall mortality. Hypertension, 1-year Δ AF, hs-CRP, and H-FABP were also independent predictors of cardiovascular mortality. One-year Δ AF and plasma H-FABP, used separately and in combination, are strong predictors of overall and cardiovascular mortality in HD patients. **PMID:** 23635017

Atanasovska-Stojanovska A(1), Popovska M, Trajkov D, Spiroski M. IL1 cluster gene polymorphisms in Macedonian patients with chronic periodontitis. *Bratisl Lek Listy.* 2013;114(7):380-5.

(1)Department of Oral Pathology and Periodontology, University Ss Cyril and Methodius, Skopje, Republic of Macedonia.

Several studies have investigated the genetic polymorphisms for cytokines as potential genetic markers for periodontitis. The aim of this study was to determine the prevalence of IL1 cluster genes polymorphisms and their association with chronic periodontitis in the Macedonian population. The group of 114 unrelated Macedonian subjects with chronic periodontitis and 301 periodontitis-free Macedonian subjects were studied. DNA was isolated from peripheral blood leukocytes by phenol-chloroform extraction method. Cytokine genotyping was performed by PCR-SSP. The population genetics analysis package (PyPop) was used for analysis of the cytokine data for this report. Crude odds ratio (OR) was calculated as estimates of the relative risk with 95 % confidence interval (CI). Genotype frequency of IL1B -511/C:T was significantly higher in patients with periodontitis than in controls (OR=2.11, 95 % CI=1.35-3.32, $p=0.001$). IL1 cluster gene haplotype frequencies of TTTCT and TCTTT were associated with higher risk for periodontitis (OR=5.06, 95 % CI=1.68-15.26, $p<0.0014$ and OR=8.35, 95 % CI=1.67-41.69, $p<0.002$, respectively). No significant association of IL1 composite genotype (IL1 -889A:IL1B +3962) with periodontitis in Macedonians was found. The latter association was found to be significant in genotype IL1B -511/C:T, haplotype TTTCT, and haplotype TCTTT, but without significant association in IL1 composite genotype (Tab. 5, Ref. 43). **PMID:** 23822621

Avramovski P(1), Janakievska P, Sotirovski K, Zafirova-Ivanovska B, Sikole A. Aortic pulse wave velocity is a strong predictor of all - cause and cardiovascular mortality in chronic dialysis patients. *Ren Fail.* 2014 Mar;36(2):176-86.

(1)Department of Internal Medicine, Clinical Hospital, Bitola, Republic of Macedonia.

Background/Aims: The aim of this study was to investigate all-cause and cardiovascular mortality in chronic hemodialysis patients (CHP) and to identify the determinants of mortality predictors. **Methods:** In this study with 3 years of follow-up period, we studied a cohort of 80 CHPs. Mean age at entry was 59.3 ± 11.8 years (duration of dialysis 5.47 ± 5.16 years). At entry, together with standard clinical and biochemical analyses, pulse wave velocity (PWV) was determined from time diversity propagation of the common carotid artery and common femoral artery flow signals by Doppler ultrasound. **Results:** The mean PWV (m/s) was presented at entry: in survived (12.5 ± 2.01) and deceased (13.13 ± 1.70) patients. The PWV cutoff point (by ROC curves) was 11.8. The regression coefficients (b) and Exp (b) hazard ratio coefficients of covariates in Cox-regression survival analysis in all-cause and CV outcomes was: PWV (b = 0.2617, Exp[b] = 1.2992, $p=0.0027$; b = 0.3569, Exp[b] = 1.4289, $p=0.0005$), CRP (b = 0.0776, Exp[b] = 1.0807, $p=0.0001$; b = 0.0832, Exp[b] = 1.0868, $p=0.0001$) and albumin (b = -0.1302, Exp[b] = 0.8779, $p=0.0089$; b = -0.1881, 0.8285, $p=0.0030$), respectively. Relative risk for exposed groups according to all-cause and CV events was 4.2976 (95% CI = 1.6051-11.5071) and 14.3590 (95% CI = 1.6051-11.5071), $p=0.0037$, respectively. **Conclusions:** We conclude that PWV, CRP and serum albumin are strong independent predictors of overall and CV mortality in patients undergoing dialysis. **PMID:** 24131155

Avramovski P(1), Janakievska P, Sotirovski K, Sikole A. Accelerated progression of arterial stiffness in dialysis patients compared with the general population. *Korean J Intern Med.* 2013 Jul;28(4):464-74.

(1)Department of Internal Medicine and Hemodialysis, JZU Clinical Hospital Dr Trifun Panovski, Bitola, Republic of Macedonia. avramovski@gmail.com

BACKGROUND/AIMS: The aim of this study was to compare the progression of aortic stiffness in chronic hemodialysis patients (CHP) with that of general population patients (GPP) over a 36-month period and to evaluate the determinants of this progression. **METHODS:** The study group included 80 patients undergoing hemodialysis (aged 59.3 ± 11.8 years; duration of dialysis 5.47 ± 5.16 years). The control group consisted of 60 patients (aged 57.5 ± 10.9 years) with a glomerular filtration rate of > 60 mL/min/1.73 m²). Pulse wave velocity (PWV) was determined from time diversity propagation of the common carotid artery and femoral artery by Doppler ultrasound. Clinical and biochemical parameters were determined in serum using standard laboratory procedures. **RESULTS:** The mean PWV values at baseline and 36 months were 11.18 ± 2.29 and 11.82 ± 2.34 m/sec in the CHP group, and 9.02 ± 1.89 and 9.29 ± 1.93 m/sec in the GPP group, respectively. The average PWV progressions were 63.95 ± 18.373 cm/sec in CHP and 27.28 ± 28.519 cm/sec in GPP. By multiple regression analysis, hemoglobin (standardized coefficient β [β st] = -0.405, $p=0.004$; β st = -0.364, $p=0.011$), albumin (β st = -0.349, $p=0.042$; β st = -0.303, $p=0.034$), CRP (β st = 0.458, $p=0.002$; β st = 0.187, $p=0.008$), and total cholesterol (β st = 0.236, $p=0.038$; β st = 0.171, $p=0.078$) were independently associated with PWV in the CHP and GPP groups, respectively. **CONCLUSIONS:** Accelerated arterial stiffness was more pronounced in the CHP group than in the GPP group. The independent determinants of this progression in both groups include traditional risk factors and blood levels of hemoglobin, albumin and CRP. Cholesterol and uremia-related factors are determinants only in CHP. **PMCID:** PMC3712155. **PMID:** 23864805

Bačeva K(1), Stafilov T, Šajn R, Tănăselia C. Air dispersion of heavy metals in the vicinity of the As-Sb-Tl abounded mine and responsiveness of moss as a biomonitoring media in small-scale investigations. *Environ Sci Pollut Res Int.* 2013 Dec;20(12):8763-79.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, POB 162, 1000, Skopje, Republic of Macedonia.

A systematic study was carried out to investigate air deposition and to explore the natural distribution and enrichment (contamination) with trace elements in the small area (cca. 13 km²) of an antimony-arsenic-thallium mineralization outcrop at an abandoned mine "Allchar." The mine is located on the northwestern part of Kožuf Mount, Republic of Macedonia. The locality of Allchar is unique in its mineral composition; besides a very intriguing mineral, lorandite, there are 45 other minerals, some of which are rare. The distribution of 53 elements (with special attention to As, Sb, and Tl) were detected in 69 moss samples from eight various species collected from this area. Moss samples were analyzed following microwave digestion by inductively coupled plasma-mass spectrometry and inductively coupled plasma-atomic emission spectrometry. It was found that the atmospheric deposition for As in the moss samples on or around the Allchar mine is >6.5 times higher and for Tl is 19 times higher compared to values for the samples from the rest of the Allchar area. By the application of multivariate cluster and R-mode factor analyses (FA), five geochemical associations were determined. Cluster and R-mode FA were used to identify and characterize element associations, and five associations of elements were determined by the method of multivariate statistics. F1 (Co, Cr, Fe, Sc, Li, V, Ga, Y, Ni, Mn, Al, La-Lu, Cu, Ge, Be, Bi, and Hf); F2 (As, Tl, Sb, and Mg); F3 (Rb, Cs, and Mo); F4 (Sr, Ba, Hf, Zr, La-Lu, and Bi), and F5 (Cd, Zn, Ag, and Cu). PMID: 23729028

Berbebi P(1), Tougard C, Dubois S, Shao Z, Koutseri I, Petkovski S, Crivelli AJ. Genetic diversity and conservation of the Prespa trout in the Balkans. Int J Mol Sci. 2013 Nov 28;14(12):23454-70.

(1)Institut des Sciences de l'Evolution, UMR 5554 CNRS/UM2/IRD, Université Montpellier 2, cc065, Place Eugène Bataillon, Montpellier cedex 05 34095, France. patrick.berbebi@univ-montp2.fr.

The Balkans are known to have a high level of biodiversity and endemism. No less than 15 taxa have been recorded in salmonids of the *Salmo* genus. Among them, the Prespa trout is found in only four river systems flowing into Lake Macro Prespa, three in the Former Yugoslav Republic of Macedonia and one in Greece. This is the first comprehensive survey of all streams located within the Macro Prespa Basin, encompassing the whole taxon range. A large genetic sample of 536 Prespa trout was collected mainly between 2005 and 2007. The sampling included 59 individuals from the Golema river system, 93 from the Kranska, 260 from the Brajcinska, 119 from the Agios Germanos, and five individuals from the lake itself. These specimens were analyzed with six microsatellite markers and by sequencing the mitochondrial control region. Nuclear data were examined through multidimensional analysis and assignment tests. Five clusters were detected by assignment: Golema, Kranska, Brajcinska upstream, Rzanska Brajcinska tributary and Brajcinska downstream. Most of these river systems thus hosted differentiated Prespa trout populations (with past gene flows likely dating before the construction of dams), except Agios Germanos, which was found to be composed of 5% to 32% of each cluster. Among the five trout individuals from the lake, four originated from Kranska River and one was admixed. Supported parsimonious hypotheses are proposed to explain these specificities. Conservation of this endemic taxon should take these results into account. No translocation should be performed between different tributaries of the lake and preservation of the Brajcinska populations should address the upstream-downstream differentiation described. PMID: PMC3876056. PMID: 24287917

Bino S(1), Cavaljuga S, Kunchev A, Lausevic D, Kaic B, Pistol A, Kon P, Karadjovski Z, Georghita S, Cicevalieva S. Southeastern European Health Network (SEEHN) Communicable Diseases Surveillance: a decade of bridging trust and collaboration. Emerg Health Threats J. 2013;6.

(1)Regional Development Center of Communicable Diseases Surveillance and Control, Institute of Public Health, Tirana, Albania. silvia.bino@gmail.com

The communicable disease threats and changes that began emerging in south-east Europe in the early 1990s - after a decade

of war and while political and health systems region-wide were undergoing dramatic changes - demanded a novel approach to infectious disease surveillance. Specifically, they called for an approach that was focused on cross-border collaboration and aligned with European Union standards and requirements. Thus, the Southeastern European Health network (SEEHN) was established in 2001 as a cooperative effort among the governments of Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Moldova, Montenegro, Romania, Serbia, and the former Yugoslav Republic of Macedonia. In 2002, SEEHN initiated a communicable diseases project aimed at strengthening both national and regional surveillance systems with a focus on cross-border collaboration. Over time, SEEHN has nurtured growth of a regional fabric of SEE experts in communicable diseases surveillance and response who are able to discuss emerging issues and best practices at any time and without being constrained by the rigidity of traditional or existing systems. Main achievements to date include joint preparation of influenza pandemic preparedness plans at both national and regional levels and the introduction of molecular techniques into influenza surveillance laboratories region-wide. Here, we describe the history of the SEEHN communicable disease project; major activities and accomplishments; and future sustainability of the regional infectious disease surveillance network that has emerged and grown over the past decade. PMID: PMC3557907. PMID: 23362410

Boev B(1), Stafilov T, Bačeva K, Šorša A, Boev I. Influence of a nickel smelter plant on the mineralogical composition of attic dust in the Tikveš Valley, Republic of Macedonia. Environ Sci Pollut Res Int. 2013 Jun;20(6):3781-8.

(1)Goce Delčev University, Štip, Republic of Macedonia.

Mineral phases and their content were determined in attic dust samples collected from 27 houses in the Tikveš Valley, Republic of Macedonia. By using quantitative X-ray diffraction, the principal mineral phases were determined to be the serpentinite group (chrysotile, lizardite) and amphibole group of minerals (ribecite, tremolite, actinolite) present in the attic dust samples from this region which are not common constituents of urban dust. Strong correlations existed between these mineral phases in the dust and those in ores processed at a ferronickel smelter plant situated in this region. Spatial distributions of specific mineral phases were made and were consistent with wind directions and predicted deposition (60-70 %) of dust emitted from the metallurgical plant. PMID: 23179222

Bosevski M(1), Peovska I. Clinical usefulness of assessment of ankle-brachial index and carotid stenosis in type 2 diabetic population--three-year cohort follow-up of mortality. Angiology. 2013 Jan;64(1):64-8.

(1)University Cardiology Clinic, Vasil Gorgov, Skopje, Republic of Macedonia. marijanbosevski@yahoo.com

We evaluated the clinical usefulness of assessing the ankle-brachial index (ABI) and carotid stenosis (CS) in a type 2 diabetic population. Patients with type 2 diabetes and coronary artery disease (n = 265) were enrolled in a prospective 3-year cohort study. The cardiovascular mortality rate was 8.7% (23 of 265) during the 36-month study and the all-cause mortality rate was 9.5% (25 of 265). Multivariate logistic regression analysis revealed that age (odds ratio [OR] 2.09), hypertension (OR 7.99), obesity (OR 4.86), internal CS (OR 262.17), and Gensini score (OR 1.15) were independent predictors of cardiovascular mortality. Mean ABI value (OR 0.15) was the only predictor of all-cause mortality in this population. The ABI and carotid artery ultrasound have independent prognostic value in a type 2 diabetic population. PMID: 22323833

Bosevski M(1), Bosevska G, Stojanovska L. Influence of fibrinogen and C-RP on progression of peripheral arterial disease in type 2 diabetes: a preliminary report. Cardiovasc Diabetol. 2013 Feb 1;12:29.

(1)Medical Faculty, University Cardiology Clinic, Skopje,

Macedonia.

BACKGROUND: Limited studies have suggested that inflammatory biomarkers play a role in the initiation and progression of atherosclerosis in diabetic patients. This study assesses the effect of inflammatory biomarkers: fibrinogen and C-reactive protein (C-RP) on the progression of peripheral arterial disease (PAD) in type 2 diabetic (T2D) patients. **METHODS:** Sixty two patients with T2D and PAD (mean age 60.28 ± 27 years and diabetes duration of 8.58 ± 6.17 years) were enrolled in a cohort prospective study of 36 months. Ankle-brachial index (ABI) was measured in all patients at baseline and after 36 months. Multiple linear regression analysis was used to determine the predictivity of variables for fibrinogen, C-RP, plasma lipid fractions, fasting plasma glucose, Body Mass Index (BMI), duration of diabetes status and the age on changes in ABI value. **RESULTS:** Linear regression analysis defined F as a predictor for endpoint value of ABI ($\beta = 0.469$, $p = 0.007$). Value of C-RP determinates change of minimal value of ABI ($\beta = 0.449$, $p = 0.037$) and change of mean ABI per year ($\beta = 0.442$, $p = 0.025$). **CONCLUSION:** Our data indicate that plasma determination of fibrinogen and C-RP might have a clinical implication in defining the process of progression of PAD in T2D population. PMID: PMC3598335. PMID: 23375154

Bosilkovski M(1), Kirova-Urosevic V, Cekovska Z, Labacevski N, Cvetanovska M, Rangelov G, Cana F, Bogoeva-Tasevska S. Osteoarticular involvement in childhood brucellosis: experience with 133 cases in an endemic region. *Pediatr Infect Dis J.* 2013 Aug;32(8):815-9.

(1)University Clinic for Infectious Diseases and Febrile Conditions, Skopje, Republic of Macedonia. milebos@yahoo.com

AIM: To describe the main clinical and laboratory characteristics, frequency and distribution of osteoarticular involvement, therapeutic options and outcome in children with osteoarticular brucellosis. **METHODS:** This descriptive study includes 133 pediatric patients with osteoarticular brucellosis who were treated at the University Clinic for Infectious Diseases and Febrile Conditions in Skopje, Republic of Macedonia, during the period between 1989 and 2011. Brucellosis was presumptively diagnosed on the basis of clinical signs and confirmed by the detection of specific antibodies at significant titers. **RESULTS:** The median age of patients was 9 years (range, 2-14 years) and 63.9% were males. Family history of brucellosis was present in 54.1%. The dominant clinical symptoms were arthralgia and fever in 77.4% and 73.7%, respectively, and the dominant sign was hepatomegaly in 73.7% of patients. The main laboratory abnormalities were elevated C-reactive protein (81.0%) and circulating immunocomplexes (80.7%). In 71.4% of patients, the osteoarticular involvement was monoarticular. Hip arthritis was present in 49.6%, followed by the knee in 30.1%. Various therapeutic regimens with a duration of 6 weeks were used. In 87 patients during a follow-up of at least 6 months, relapse occurred in 13.8%. **CONCLUSIONS:** Osteoarticular involvement is frequent in children with brucellosis. It is most often manifested with monoarthritis of the large weight-bearing joints. Brucellosis should be included in the differential diagnosis of childhood arthritis in endemic countries, especially in the presence of family history, contact with infected animals or ingestion of unpasteurized food products, fever and hepatomegaly. PMID: 23446445

Brezovska-Kavrakova J(1), Krstevska M, Bosilkova G, Alabakovska S, Panov S, Orovchanec N. Hyperhomocysteinemia and of Methylene tetrahydrofolate Reductase (C677T) Genetic Polymorphism in Patients with Deep Vein Thrombosis. *Mater Sociomed.* 2013;25(3):170-4.

(1)Institute of Medical and Experimental Biochemistry, Medical Faculty, Skopje, Republic of Macedonia.

AIM: To determine the concentration of total plasma homocysteine (tHcy) as well as different genotypes of methylenetetrahydrofolate reductase MTHFR (C677T) in healthy subjects and patients with deep vein thrombosis (DVT). **MATERIAL AND METHODS:** The investigation comprised a total of 160 subjects divided in two main groups: 80 healthy subjects (control group) and 80 patients with

deep vein thrombosis. Concentration of tHcy was determined by spectrophotometric cyclic enzymatic method and mutation of MTHFR (C677T) gene was examined by polymerase chain reaction according to Schneider. **RESULTS:** The results obtained for plasma tHcy in the control group were 11.62 ± 3.43 $\mu\text{mol/L}$, while tHcy level was significantly higher in patients with deep vein thrombosis as compared to the control group, 15.19 ± 3.63 $\mu\text{mol/L}$ ($p < 0.001$). The analysis of the results has shown that MTHFR (C677T) genetic polymorphism was responsible for mild to moderate hyperhomocysteinemia in the majority of subjects. **CONCLUSION:** The level of tHcy in the examined patients was significantly higher in comparison with the control group. Multiple regression analysis has shown that tHcy level in CT and TT genotypes of MTHFR (C677T) was statistically higher in comparison with CC genotype of MTHFR (C677T) in both, the control group and the DVT patients. PMID: PMC3804432. PMID: 24167429

Chibishev A(1), Sikole A, Pereska Z, Chibisheva V, Simonovska N, Orovchanec N. Severe renal function impairment in adult patients acutely poisoned with concentrated acetic acid. *Arh Hig Rada Toksikol.* 2013;64(1):153-8.

(1)University Clinic of Toxicology, Skopje, Republic of Macedonia. toksikourgentna@gmail.com

Acetic acid is a widely used organic acid with corrosive properties that depend on its concentration. If acetic acid is ingested in concentrations above 30 % it may severely damage the upper gastrointestinal tract and cause intravascular haemolysis, which can result in severe kidney and liver disorders and disseminated intravascular coagulation. In this retrospective study, we analysed acetic acid ingestion data collected at the University Clinic for Toxicology of Skopje, Macedonia from 1 January 2002 to 31 December 2011. The analysis included systemic complications, kidney damage, and the outcomes in particular. Over the ten years, 84 patients were reported at the Clinic to have ingested highly concentrated acetic acid. Twenty-eight developed kidney disorders, while the remaining 56 had no complications. Fatal outcome was reported for 11 patients, seven of whom had systemic complications and four severe gastrointestinal complications. PMID: 23585201

Cvetkovikj I(1), Stefkov G, Acevska J, Stanoeva JP, Karapandzova M, Stefova M, Dimitrovska A, Kulevanova S. Polyphenolic characterization and chromatographic methods for fast assessment of culinary *Salvia* species from South East Europe. *J Chromatogr A.* 2013 Mar 22;1282:38-45.

(1)Institute of Pharmacognosy, Faculty of Pharmacy, Ss. Cyril and Methodius University, Skopje, Macedonia. ivanacvetkovikj@gmail.com

Although the knowledge and use of several *Salvia* species (*Salvia officinalis*, *Salvia fruticosa*, and *Salvia pomifera*) can be dated back to Greek Era and have a long history of culinary and effective medicinal use, still there is a remarkable interest concerning their chemistry and especially the polyphenolic composition. Despite the demand in the food and pharmaceutical industry for methods for fast quality assessment of the herbs and spices, even now there are no official requirements for the minimum content of polyphenols in sage covered by current regulations neither the European Pharmacopoeia monographs nor the ISO 11165 standard. In this work a rapid analytical method for extraction, characterization and quantification of the major polyphenolic constituents in Sage was developed. Various extractions (infusion - IE; ultrasound-assisted extraction - USE and microwave-assisted extraction - MWE) were performed and evaluated for their effectiveness. Along with the optimization of the mass-detector and chromatographic parameters, the applicability of three different reverse C18 stationary phases (extra-density bonded, core-shell technology and monolith column) for polyphenolics characterization was evaluated. A comprehensive overview of the very variable polyphenolic composition of 118 different plant samples of 68 populations of wild growing culinary *Salvia* species (*S. officinalis*: 101; *S. fruticosa*: 15; *S. pomifera*: 2) collected from South East Europe (SEE) was performed using HPLC-DAD-ESI-MS(n) and more than 50 different compounds were identified and quantified. With this work the knowledge about

polyphenols of culinary Sage was expanded thus the possibility for gaining an insight into the chemodiversity of culinary *Salvia* species in South East Europe was unlocked. PMID: 23415138

Damevska K(1), Gocev G, Nikolovska S. A Case of Burn-Induced Bullous Pemphigoid. J Burn Care Res. 2013 May 31.

(1)Clinic of Dermatology, Medical Faculty, Ss. Cyrilus and Methodius University of Skopje, Skopje, Republic of Macedonia.

No abstract available. PMID: 24165668

Damevska K(1), Neloska L, Gocev G, Mihova M. Metabolic syndrome in untreated patients with psoriasis: case-control study. J Dtsch Dermatol Ges. 2013 Dec;11(12):1169-75.

(1)University Clinic of Dermatology, Medical faculty, Ss Cyril and Methodius University, Skopje, Republic of Macedonia.

BACKGROUND AND OBJECTIVES: Previous studies have shown a higher prevalence of metabolic syndrome in patients with psoriasis compared to controls. However, little attention has been paid to the effect of systemic anti-psoriatic drugs on the metabolic syndrome. The aim of this study was to investigate the association between psoriasis and the metabolic syndrome, by comparing untreated patients with psoriasis and population based control. **PATIENTS AND METHODS:** We conducted a hospital-based case-control study that included 122 untreated patients with plaque psoriasis and 122 age- and gender-matched controls. **RESULTS:** There was no significant difference in the prevalence of the metabolic syndrome between the patients with psoriasis (24.6 %) and the controls (22.9 %) (OR 1.095, 95 % CI 0.607-1.974). Among the components of the metabolic syndrome only hypertriglyceridemia and abdominal obesity were associated with psoriasis. The psoriatic patients with metabolic syndrome had a higher mean age ($p = 0.001$), and higher mean BMI ($p = 0.001$) compared with the psoriatic patients without metabolic syndrome. The metabolic syndrome was not associated with the severity of psoriasis. **CONCLUSIONS:** Untreated patients with psoriasis have no significantly higher prevalence of the metabolic syndrome than healthy controls. Our data suggest that systemic antipsoriatic drugs may play an important role in the pathogenesis of the metabolic syndrome. PMID: 24267013

Damevska K(1), Gocev G. Multifocal tuberculosis verrucosa cutis of 60 years duration. Int J Infect Dis. 2013 Dec;17(12):e1266-7.

(1)University Clinic of Dermatology, Medical Faculty, Ss. Cyril and Methodius University, Skopje, Republic of Macedonia. Electronic address: kate_damevska@yahoo.com.

No abstract available. PMID: 24094527

Davalieva K(1), Kiprijanovska S(2), Plaseska-Karanfiliska D(2). Fast, reliable and low cost user-developed protocol for detection, quantification and genotyping of hepatitis C virus. J Virol Methods. 2014 Feb;196:104-12.

(1)Research Centre for Genetic Engineering and Biotechnology "Georgi D Efremov", Macedonian Academy of Sciences and Arts, Krste Misirkov 2, 1000 Skopje, Republic of Macedonia. Electronic address: katarina@manu.edu.mk. (2)Research Centre for Genetic Engineering and Biotechnology "Georgi D Efremov", Macedonian Academy of Sciences and Arts, Krste Misirkov 2, 1000 Skopje, Republic of Macedonia.

Early detection and genotyping of HCV infection is important for disease management. It is important to develop fast and cost-effective semi-automated techniques allowing an accurate and reproducible detection, quantification and genotyping of HCV. The proposed protocol includes a real-time RT-PCR assay for HCV detection/quantification and a type-specific one-tube RT-PCR assay for genotyping. Both assays detect genotypes 1-4 as intended. The limit of detection was 112IU/ml for the real-time assay and 600±278IU/ml (mean±SD) for the genotyping assay. Concordance

between the real-time assay and AMPLICOR HCV v2.0 test was 100%. The real-time assay has wide linear dynamic range of detection and quantification and excellent reproducibility with 2% and 0.75% coefficients of variations, for inter- and intra-assays, respectively. The observed correlation with AMPLICOR HCV Monitor v2.0 kit was linear with the correlation coefficient of 0.988. The diagnostic specificity and sensitivity of the genotyping assay, tested on 102 samples, was 100% and 95%, respectively. The overall procedure of HCV diagnosis is completed within 6h in a closed system with minor contamination risk. In addition to being fast and cost-effective, this approach is reproducible and avoids post-PCR enzymatic and hybridization steps while detecting and genotyping HCV with high clinical sensitivity. PMID: 24269794

Dimitrov G(1), Talevska B, Nikolovski S, Micevska M, Panov S, Dimitrov G. HPV status after cold knife conization. Akush Ginekol (Sofia). 2013;52(2):65-8.

(1)University Clinic of Obstetrics & Gynecology, Medical Faculty, Ss. Cyril and Methodius University, Skopje, Republic of Macedonia.

INTRODUCTION: The aim of this study was to determine whether HPV DNA test after cold knife conization is a predictive factor for CIN persistence or recurrence. The study also investigated whether HPV DNA test results should influence post cold knife excision surveillance. **MATERIALS AND METHODS:** A retrospective observation study was performed on 738 patients who underwent cold knife conization for CIN or microinvasive cervical cancer at the University Clinic of Obstetrics & Gynecology, Medical Faculty, Ss. Cyril and Methodius University, Skopje from 1st June 2007 to 1st June 2009. A total of 217 patients met the inclusion criteria and were with complete data. The follow-up HPV DNA testing was performed at 8 months after cold knife conization, after which the patients were followed-up every 4 months till 24 months postoperatively. **RESULTS:** HPV DNA testing after 8 months after conization showed that 44 patients were HPV DNA positive and 199 were HPV DNA negative. Recurrent cytological abnormalities were found in 26 of the 44 HPV DNA positive patients, and in 12 of the 199 HPV DNA negative patients. Analysis showed that a positive HPV DNA result was a risk factor for recurrent/persistent cervical intraepithelial neoplasia. **CONCLUSION:** HPV DNA testing 8 months after conization is important for predicting the risk of disease: persistence or recurrence. In addition, such testing can assist in designing patient management, since HPV DNA negative patients should undergo routine surveillance, while HPV DNA positive patients should undergo frequent and meticulous surveillance. PMID: 23807985

Donev D. Principles and ethics in scientific communication in biomedicine. Acta Inform Med. 2013 Dec;21(4):228-33.

Institute of Social Medicine, Faculty of Medicine, University "Ss Cyril and Methodius" Skopje, Republic of Macedonia.

INTRODUCTION AND AIM: To present the basic principles and standards of scientific communication and writing a paper, to indicate the importance of honesty and ethical approach to research and publication of results in scientific journals, as well as the need for continuing education in the principles and ethics in science and publication in biomedicine. **METHODS:** An analysis of relevant materials and documents, sources from the internet and published literature and personal experience and observations of the author. **RESULTS:** In the past more than 20 years there is an increasingly emphasized importance of respecting fundamental principles and standards of scientific communication and ethical approach to research and publication of results in peer review journals. An advance in the scientific community is based on honesty and equity of researchers in conducting and publishing the results of research and to develop guidelines and policies for prevention and punishment of publishing misconduct. Today scientific communication standards and definitions of fraud in science and publishing are generally consistent, but vary considerably policies and approach to ethics education in science, prevention and penal policies for misconduct in research and publication of results in scientific journals. **CONCLUSION:** It is necessary to further strengthen the capacity for education and research, and raising

awareness about the importance and need for education about the principles of scientific communication, ethics of research and publication of results. The use of various forms of education of the scientific community, in undergraduate teaching and postgraduate master and doctoral studies, in order to create an ethical environment, is one of the most effective ways to prevent the emergence of scientific and publication dishonesty and fraud. PMID: PMC3905721. PMID: 24505166

Dzekova-Vidimliski P(1), Dzikova S, Selim G, Gelev S, Trajceska L, Pushevski V, Sikole A. Ultrasound predictors of compensated liver cirrhosis in hemodialysis patients with hepatitis C. Saudi J Kidney Dis Transpl. 2013 Jan;24(1):30-5.

(1)University Clinic of Nephrology, Skopje, R. Macedonia.

Ultrasound examination was performed in 80 hemodialysis (HD) patients with chronic hepatitis C in order to determine the ultrasound predictors of compensated liver cirrhosis. The ultrasound score (US) was calculated from the morphological parameters (liver size, morphology, surface, echogenicity and spleen volume) and the hemodynamic parameters (portal vein diameter and portal vein mean flow velocity). The US ranged from 0 to 200, with a cut-off value of 66, for discrimination between absence and presence of liver cirrhosis. A logistic regression model with stepwise variable selection was used to determine predictors of the progression of liver disease. According to the calculated US, patients were divided into two groups. The first group consisted of 37 (46.3%) patients with US greater than 66, indicating the presence of compensated liver cirrhosis. The second group included 43 (53.7%) patients without liver cirrhosis, with US equal to or less than 66. The value of liver morphology was significantly higher, but the portal vein flow velocity was significantly lower in patients with compensated liver cirrhosis compared with those without cirrhosis. Furthermore, rounded liver surfaces and increased liver echogenicity were significantly more frequent in patients with compensated liver cirrhosis compared with the non-compensated group. Logistic regression model with stepwise discriminant analysis identified liver morphology, liver echogenicity and portal vein mean flow velocity as independent ultrasound predictors of compensated liver cirrhosis in HD patients with chronic hepatitis C. Ultrasound examination could be used for non-invasive diagnosis of compensated liver cirrhosis, with accurate estimation of the disease severity in HD patients with chronic hepatitis C. PMID: 23354188

Erdem H(1), Inan A(2), Altindis S(3), Carevic B(4), Askarian M(5), Cottle L(6), Beovic B(7), Csomos A(8), Metodiev K(9), Ahmetagic S(10), Harxhi A(11), Raka L(12), Grozdanovski K(13), Nechifor M(14), Alp E(15), Bozkurt F(16), Hosoglu S(16), Balik I(17), Yilmaz G(17), Jereb M(7), Moradi F(18), Petrov N(19), Kaya S(20), Koksall I(20), Aslan T(21), Elaldi N(22), Akkoyunlu Y(21), Moravjevi SA(23), Csato G(24), Szedlak B(25), Akata F(26), Oncu S(27), Grgic S(28), Cosic G(29), Stefanov C(30), Farrokhnia M(31), Müller M(32), Luca C(14), Koluder N(33), Korten V(34), Platikanov V(35), Ivanova P(35), Soltaniipour S(36), Vakili M(37), Farhangiz S(38), Afkhamzadeh A(39), Beeching N(6), Ahmed SS(15), Cami A(40), Shiraly R(41), Jazbec A(42), Mirkovic T(43), Leblebicioglu H(44), Naber K(45). Surveillance, control and management of infections in intensive care units in Southern Europe, Turkey and Iran—a prospective multicenter point prevalence study. J Infect. 2014 Feb;68(2):131-40.

(1)GATA Haydarpasa Training Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey. Electronic address: hakanerdem1969@yahoo.com. (2)Haydarpasa Numune Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey. (3)Sakarya University, Faculty of Management, Department of Health Administration, Sakarya, Turkey. (4)Clinical Center of Serbia (CCS), Department for Hospital Epidemiology, Belgrade, Serbia. (5)Department of Community Medicine, School of Medicine, Medicinal & Natural Products Chemistry Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran. (6)Royal Liverpool University Hospital, United Kingdom. (7)University Medical Centre, Department of Infectious Diseases, Ljubljana, Slovenia. (8)Simmelweis University,

Department of Anaesthesia and Intensive Care, Budapest, Hungary. (9)Medical University, Department of Preclinical and Clinical Sciences, Varna, Bulgaria. (10)University Clinical Center Tuzla, Department for Infectious Diseases, Tuzla, Bosnia and Herzegovina. (11)University Hospital Center of Tirana, Service of Infectious Disease, Tirana, Albania. (12)University of Prishtina, School of Medicine & National Institute of Public Health of Kosova, Prishtina, Kosova, Serbia. (13)University Clinic for Infectious Diseases, Department of Intensive Care, Skopje, Macedonia. (14)Gr. T. Popa University of Medicine and Pharmacy, Department of Pharmacology, Iasi, Romania. (15)Erciyes University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Kayseri, Turkey. (16)Dicle University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Diyarbakir, Turkey. (17)Ankara University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey. (18)Clinical Research Center on Infectious Diseases and Tropical Medicine, Bandar Abbas, Iran. (19)Military Medical Academy, Department Anaesthesiology and Intensive Care, Sofia, Bulgaria. (20)Karadeniz Technical University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Trabzon, Turkey. (21)Bezmi Alem University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey. (22)Cumhuriyet University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Sivas, Turkey. (23)Kashan University of Medical Sciences, Trauma Research Center, Department of Community Medicine, Kashan, Iran. (24)Kenézy Hospital, Department of Anesthesiology and Intensive Care, Debrecen, Hungary. (25)Borsod County Hospital and Teaching Hospital, Department of Anaesthesiology and Intensive Therapy, Miskolc, Hungary. (26)Trakya University, School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Edirne, Turkey. (27)Adnan Menderes University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Aydin, Turkey. (28)University Hospital Clinic for Infectious Diseases, Mostar, Bosnia and Herzegovina. (29)IPH of Vojvodina, Department of Prevention and Control of Diseases, Medical Faculty, University of Novi Sad, Serbia. (30)University Multiprofile Hospital for Active Treatment, Department of Anesthesiology and Intensive Treatment, St. Georgi, Plovdiv, Bulgaria. (31)Kerman University of Medical Sciences, Department of Internal Medicine, Kerman, Iran. (32)Markhot Hospital, Department of Anaesthesiology and Intensive Care, Eger, Hungary. (33)Clinic for Infectious Diseases, Sarajevo, Bosnia and Herzegovina. (34)Marmara University, School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey. (35)University Hospital "St. Marina", Department of Anesthesiology and ICM, Varna, Bulgaria. (36)Guilan University of Medical Sciences, School of Medicine, Department of Community Medicine, Rasht, Iran. (37)Shahid Sadoughi University School of Medicine, Department of Community Medicine, Yazd, Iran. (38)Department of Community Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran. (39)Department of Community Medicine, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran. (40)University Hospital of Pulmonary Disease, Intensive Care Clinic, Tirana, Albania. (41)Ilam University of Medical Sciences, Department of Community Medicine, Yazd, Iran. (42)University Clinical Center Ljubljana, Center for Intensive Internal Medicine, Ljubljana, Slovenia. (43)University Medical Centre Ljubljana, Department of Anesthesiology and Surgical Intensive Care, Ljubljana, Slovenia. (44)Ondokuz Mayıs University School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Samsun, Turkey. (45)Technical University of Munich, Munich, Germany.

OBJECTIVE: We aimed to compare the features of intensive care units (ICUs), their antimicrobial resistance patterns, infection control policies, and distribution of infectious diseases from central Europe to Mid-West Asia. **METHODS:** A cross-sectional point prevalence study was performed in 88 ICUs from 12 countries. Characteristics of ICUs, patient and antibiotic therapy data were collected with a standard form by infectious diseases specialists. **RESULTS:** Out of 749, 305 patients at least with one infectious disease were assessed and 254 patients were reported to have coexistent medical problems. When primary infectious diseases diagnoses of the patients were evaluated, 69 had community-acquired, 61 had healthcare-associated, and 176 had hospital-acquired infections.

Pneumonia was the most frequent ICU infection seen in half of the patients. Distribution of frequent pathogens was as follows: Enteric Gram-negatives (n = 62, 28.8%), *Acinetobacter* spp. (n = 47, 21.9%), *Pseudomonas aeruginosa* (n = 29, 13.5%). Multidrug resistance profiles of the infecting microorganisms seem to have a uniform pattern throughout Southern Europe and Turkey. On the other hand, active and device-associated infection surveillance was performed in Turkey more than Iran and Southeastern Europe (p < 0.05). However, designing antibiotic treatment according to culture results was highest in Southeastern Europe (p < 0.05). The most frequently used antibiotics were carbapenems (n = 92, 30.2%), followed by anti-gram positive agents (vancomycin, teicoplanin, linezolid, daptomycin, and tigecycline; n = 79, 25.9%), beta-lactam/beta lactamase inhibitors (n = 78, 25.6%), and extended-spectrum cephalosporins (n = 73, 23.9%). CONCLUSION: ICU features appears to have similar characteristics from the infectious diseases perspective, although variability seems to exist in this large geographical area. PMID: 24269951

Fustik S. Liver cirrhosis and portal hypertension in cystic fibrosis. Srp Arh Celok Lek. 2013 Nov-Dec;141(11-12):764-9.

University Children's Clinic, Skopje, Republic of Macedonia. stojkaf@yahoo.com

INTRODUCTION: As the expected survival improves in individuals with the cystic fibrosis (CF), so they may be faced with a number of medical complications. OBJECTIVE: The aim of this study was to analyze the prevalence of liver cirrhosis in our CF population as well as the clinical and genetic characteristics of these patients. METHODS: All patients older than 2 years (n = 96) were screened for liver disease. Liver cirrhosis was defined by ultrasonographic findings of distinct heterogeneity of liver parenchyma and nodular liver surface and/or by liver biopsy findings. Enlarged spleen, distended portal vein and abnormal portal venous flow indicated portal hypertension. Clinical and genotype data were analyzed. RESULTS: Sixteen patients were found to have liver cirrhosis, three of them with portal hypertension. All patients had pancreatic insufficiency. Nutritional status expressed as standard deviation score (Z score) for weight, height, and body mass index was as follows: zW = -0.40 +/- 1.24, zH = -0.83 +/- 1.02, and BMI = 20.1 +/- 2.3. CF patients with liver cirrhosis generally had mild-to-moderate lung disease, with average FVC and FEV1 values of 97.1 +/- 16.5% of predicted and 87.9 +/- 23.5% of predicted, respectively. Genetic analysis showed high frequency of F508del mutation in the group with cirrhosis (90.6%). CONCLUSION: The prevalence of liver cirrhosis in our CF population older than 2 years was 16.6%. Patients with pancreatic insufficiency and severe CFTR mutations, especially F508del, were exposed to higher risk of developing liver cirrhosis. Liver cirrhosis has no significant impact on the pulmonary function and the nutritional status, until the end-stage liver disease. PMID: 24502094

Geskovski N(1), Kuzmanovska S, Simonoska Crcarevska M, Calis S, Dimchevska S, Petrushevska M, Zdravkovski P, Goracinova K. Comparative biodistribution studies of technetium-99m radiolabeled amphiphilic nanoparticles using three different reducing agents during the labeling procedure. J Labelled Comp Radiopharm. 2013 Dec;56(14):689-95.

(1)Institute of Pharmaceutical technology, Faculty of Pharmacy, University Ss. Cyril and Methodius, Vodnjanska 17, 1000, Skopje, Macedonia.

Considering the confusing biodistribution data through the literature and few reported alerts as well as our preliminary biodistribution results, we decided to evaluate the interaction and interference of the commonly present (99m) Tc (technetium-99m)-stannic oxide colloid during the direct stannous chloride (99m) Tc-labeling procedure and to assess its influence on the biodistribution pattern of amphiphilic poly(lactic-co-glycolic acid) nanoparticles. In order to confirm our thesis, beside stannous chloride, we employed two different reducing agents that don't form colloidal particles. The use of sodium borohydride was previously reported in the literature, whereas sodium dithionite was adapted for the first time in the (99m) Tc direct labeling procedure for nanoparticles. The results in

our paper clearly differentiate among samples with and without colloidal impurities originating from the labeling procedure with a logical follow up of the radiochemical, physicochemical evaluation, and biodistribution studies clarifying previously reported data on stannic oxide colloidal interference. (99m) Tc-nanoparticle complex labeled with sodium dithionite as reducing agent illustrated appropriate labeling efficacy, stability, and potential for further use in biodistribution studies thus providing solution for the problem of low-complex stability when sodium borohydride is used and colloidal stannic oxide interference for stannous chloride procedure. PMID: 24339006

Giraud G(1), Amblard C, Thiel E, Zaucche-Laniau M, Stojanović Z, Pohar J, Butigan R, Cvetković M, Mugosa B, Kendrovski V, Mora C, Barjolle D. A cross-cultural segmentation of western Balkan consumers: focus on preferences toward traditional fresh cow cheese. J Sci Food Agric. 2013 Nov;93(14):3464-72.

(1)Social Sciences and Humanities Department, AgroSup Dijon, France.

BACKGROUND: Western Balkan countries (WBCs) have a long-standing culinary tradition. The promotion of traditional foods may be a tool for coping with modernisation trends in such transition economies. This paper explores consumer preferences toward food in this region, focusing on a traditional fresh cow cheese locally called 'Mladi Sir'. This product was quoted in all the preliminary focus groups as a common traditional product present in the six WBCs studied: Bosnia-Herzegovina, Croatia, Macedonia, Montenegro, Serbia and Slovenia. RESULTS: After a literature review investigating the concept of traditional food in WBCs and the implementation of focus groups, a survey including a conjoint analysis on preferences for fresh cow cheese was carried out in 2011 to collect data from 1200 respondents. Four clusters of consumers were identified: one focused more on the local origin; one oriented more toward the scale of production (on-farm and small dairy); the third favouring low prices and the fourth preferring high prices and industrial products. CONCLUSION: Policy makers and the supply chain could take these differences in consumer preferences regarding traditional food products into account in order to develop specific strategies. PMID: 23963819

Gjorgieva D(1), Zaidman N, Bosnakovski D. Mesenchymal stem cells for anti-cancer drug delivery. Recent Pat Anticancer Drug Discov. 2013 Sep;8(3):310-8.

(1)Faculty of Medical Sciences, University Goce Delcev Stip, Krste Misirkov bb, 2000 Stip, R. Macedonia.

Self renewal, extensive proliferation and multilineage differentiation ability in vitro and in vivo make mesenchymal stem cells (MSCs) powerful tools for tissue engineering. Beyond their potential uses in regenerative medicine, an emerging field of research aims to utilize MSCs for anti-cancer treatment. These strategies are based on the remarkable ability of MSCs to localize and integrate into tumor stroma and deliver anti-cancer agents (US20100055167, US20120207725, US20120010499). Genetically engineered MSCs can specifically target different tumor types and locally secrete therapeutic proteins such as interferons α and β , interleukins 2 and 12 or chemokine CX3CL1 (US20110027239, US20120087901, WO2012071527). In addition, MSCs have also been engineered to deliver oncolytic viruses, for targeted chemotherapy using enzyme prodrug conversion or for inducing tumor cell apoptosis by delivering tumor necrosis factor-related apoptosis inducing ligand (TRAIL) (WO2012106281). The patent databases FPO and Delphion were used to locate patents that were published between 2005 and 2013. Here, we present the current progress and the most recent patents on MSC anti-cancer drug delivery systems and discuss future directions in the field. PMID: 23688246

Gjorgieva D(1), Kadifkova Panovska T(2), Ruskovska T(1), Bačeva K(3), Stafilov T(3). Mineral nutrient imbalance, total antioxidants level and DNA damage in common bean (*Phaseolus vulgaris* L.) exposed to heavy metals. Physiol Mol Biol Plants. 2013 Oct;19(4):499-507.

(1)Faculty of Medical Sciences, Goce Delčev University, Krste Misirkov str. bb, POB 201, 2000 Štip, Macedonia. (2)Faculty of Pharmacy, Ss. Cyril and Methodius University, Skopje, Macedonia. (3)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Skopje, Macedonia.

The present study aimed to analyze the biological effects induced by bioaccumulation of metals in common bean (*Phaseolus vulgaris* L.). Effects of mineral nutrient imbalance, total antioxidants level and DNA damage induced by accumulation of heavy metals, were investigated in bean seedlings treated with two selected metal concentrations for 7 days. Metal content is analyzed by inductively coupled plasma - atomic emission spectrometer (ICP-AES), for total antioxidants level assessment the Ferric-Reducing Antioxidant Power (FRAP) assay is used and Random Amplified Polymorphic DNA (RAPD) method was applied for investigation of DNA damages. The increasing metal concentration in the treatment medium changed synchronously metal content in samples, and decreased total antioxidant activity in all samples with exception only for samples treated with Ni and Cd. The obtained "DNA fingerprints" demonstrated that the increasing metal concentrations induced changes in RAPD profiles (disappearance and/or appearance of bands in comparison with untreated control samples). The highest number of missing bands was observed in samples treated with zinc (total 4 bands) and nickel (total 4 bands) at both concentrations. These results suggested that mineral nutrient imbalance is involved in changes of antioxidant levels and DNA damages of the seedlings, which may help to understand the mechanism of metal toxicity in plants. PMID: PMC3781285. PMID: 24431518

Gjorgieva D(1), Kadifkova Panovska T, Ruskovska T, Bačeva K, Stafilov T. Influence of heavy metal stress on antioxidant status and DNA damage in *Urtica dioica*. Biomed Res Int. 2013;2013:276417.

(1)Faculty of Medical Sciences, Goce Delčev University, Štip, Macedonia. darinka.gjorgieva@ugd.edu.mk

Heavy metals have the potential to interact and induce several stress responses in the plants; thus, effects of heavy metal stress on DNA damages and total antioxidants level in *Urtica dioica* leaves and stems were investigated. The samples are sampled from areas with different metal exposition. Metal content was analyzed by Inductively Coupled Plasma-Atomic Emission Spectrometer (ICP-AES), for total antioxidants level assessment the Ferric-Reducing Antioxidant Power (FRAP) assay was used, and genomic DNA isolation from frozen plant samples was performed to obtain DNA fingerprints of investigated plant. It was found that heavy metal contents in stems generally changed synchronously with those in leaves of the plant, and extraneous metals led to imbalance of mineral nutrient elements. DNA damages were investigated by Random Amplified Polymorphic DNA (RAPD) technique, and the results demonstrated that the samples exposed to metals yielded a large number of new fragments (total 12) in comparison with the control sample. This study showed that DNA stability is highly affected by metal pollution which was identified by RAPD markers. Results suggested that heavy metal stress influences antioxidant status and also induces DNA damages in *U. dioica* which may help to understand the mechanisms of metals genotoxicity. PMID: PMC3687766. PMID: 23862140

Gjorgievska E(1), Apostolska S, Dimkov A, Nicholson JW, Kaftandzieva A. Incorporation of antimicrobial agents can be used to enhance the antibacterial effect of endodontic sealers. Dent Mater. 2013 Mar;29(3):e29-34.

(1)Department of Paediatric and Preventive Dentistry, Faculty of Dental Medicine, University "Ss Cyril and Methodius", Skopje, Macedonia.

AIM: The antibacterial activity of five endodontic sealers against three different microorganism strains alone and following incorporation of 2% benzalkonium chloride (BC) and 2% cetylpyridinium chloride (CPC) was evaluated. METHODOLOGY:

The agar diffusion method was used to determine the inhibitory effect of the following endodontic sealers: RoekoSeal, Endomethasone N, N2, Apexit Plus and AH plus, on *Streptococcus mutans* - ATCC 25175, *Lactobacillus casei* - ATCC 4646 and *Actinomyces viscosus* - ATCC 19246. Bacterial strains were inoculated into BHIB, and incubated in an anaerobic atmosphere (37 °C). From the bacteria grown in the liquid medium, the density of the inoculum was set to be equivalent to McFarland 2 standard. In Shaedler agar, 350 µL of the bacterial suspension were equally spread. Specimens (4 mm × 6 mm) were prepared from each material without and with addition of 2% BC or 2% CPC. The inhibition zones were determined after 2 days, after 7 days and after 21 days of incubation. RESULTS: The largest inhibition zones were shown at zero time in all cases, with progressively less inhibition at 7 and 21 days. Endomethasone N and N2 showed the most intense antimicrobial activity, while RoekoSeal showed the least antimicrobial effect. The most susceptible microorganism was *A. viscosus*. Greater antimicrobial effects were found following incorporation of BC or CPC, and generally, BC gave greater inhibition zones than CPC. CONCLUSIONS: Adding either BC or CPC has the potential to improve clinical outcomes with endodontic sealers, as these substances enhance the short-term antimicrobial effects of the sealers. PMID: 23107192

Gjorgievska ES(1), Nicholson JW, Slipper IJ, Stevanovic MM. Remineralization of demineralized enamel by toothpastes: a scanning electron microscopy, energy dispersive X-ray analysis, and three-dimensional stereo-micrographic study. Microsc Microanal. 2013 Jun;19(3):587-95.

(1)Faculty of Dental Medicine, University Sts Cyril and Methodius Skopje, Republic of Macedonia. egjorgievska@stomfak.ukim.edu.mk

Remineralization of hard dental tissues is thought to be a tool that could close the gap between prevention and surgical procedures in clinical dentistry. The purpose of this study was to examine the remineralizing potential of different toothpaste formulations: toothpastes containing bioactive glass, hydroxyapatite, or strontium acetate with fluoride, when applied to demineralized enamel. Results obtained by scanning electron microscopy (SEM) and SEM/energy dispersive X-ray analyses proved that the hydroxyapatite and bioactive glass-containing toothpastes were highly efficient in promoting enamel remineralization by formation of deposits and a protective layer on the surface of the demineralized enamel, whereas the toothpaste containing 8% strontium acetate and 1040 ppm fluoride as NaF had little, if any, remineralization potential. In conclusion, the treatment of demineralized teeth with toothpastes containing hydroxyapatite or bioactive glass resulted in repair of the damaged tissue. PMID: 23659606

Gjorgievska ES(1), Nicholson JW, Apostolska SM, Coleman NJ, Booth SE, Slipper IJ, Mladenov MI. Interfacial properties of three different bioactive dentine substitutes. Microsc Microanal. 2013 Dec;19(6):1450-7.

(1)Faculty of Dental Medicine, University "Sts Cyril and Methodius" Skopje 1000, Republic of Macedonia.

Three different bioactive materials suitable as dentine substitutes in tooth repair have been studied: glass-ionomer cement, particulate bioglass, and calcium-silicate cement. On 15 permanent human molars, Class V cavities were prepared and the bottom of each cavity was de-mineralized by an artificial caries gel. After the demineralization, the teeth were restored with: (1) Bioglass®45S5 and ChemFil® Superior; (2) Biodentine™ and ChemFil® Superior; and (3) ChemFil® Superior for a complete repair. The teeth were stored for 6 weeks in artificial saliva, then cut in half along the longitudinal axis: the first half was imaged in a scanning electron microscope (SEM) and the other half was embedded in resin and analyzed by SEM using energy-dispersive X-ray analysis. The glass-ionomer and the bioglass underwent ion exchange with the surrounding tooth tissue, confirming their bioactivity. However, the particle size of the bioglass meant that cavity adaptation was poor. It is concluded that smaller particle size bioglasses may give more acceptable results. In contrast, both the glass-ionomer and the

calcium-silicate cements performed well as dentine substitutes. The glass-ionomer showed ion exchange properties, whereas the calcium silicate gave an excellent seal resulting from its micromechanical attachment. PMID: 24148964

Gjurchinovski A(1), Jüngling T, Urumov V, Schöll E. Delayed feedback control of unstable steady states with high-frequency modulation of the delay. Phys Rev E Stat Nonlin Soft Matter Phys. 2013 Sep;88(3):032912.

(1)Institute of Physics, Faculty of Natural Sciences and Mathematics, Saints Cyril and Methodius University, P.O. Box 162, 1000 Skopje, Macedonia.

We analyze the stabilization of unstable steady states by delayed feedback control with a periodic time-varying delay in the regime of a high-frequency modulation of the delay. The average effect of the delayed feedback term in the control force is equivalent to a distributed delay in the interval of the modulation, and the obtained distribution depends on the type of the modulation. In our analysis we use a simple generic normal form of an unstable focus, and investigate the effects of phase-dependent coupling and the influence of the control loop latency on the controllability. In addition, we have explored the influence of the modulation of the delays in multiple delay feedback schemes consisting of two independent delay lines of Pyragas type. A main advantage of the variable delay is the considerably larger domain of stabilization in parameter space. PMID: 24125330

Glavas-Dodov M(1), Steffansen B, Crcarevska MS, Geskovski N, Dimchevska S, Kuzmanovska S, Goracinova K. Wheat germ agglutinin-functionalised crosslinked polyelectrolyte microparticles for local colon delivery of 5-FU: in vitro efficacy and in vivo gastrointestinal distribution. J Microencapsul. 2013;30(7):643-56.

(1)Institute of Pharmaceutical Technology, Faculty of Pharmacy, University "Ss Cyril and Methodius", Vodnjanska 17, P.O. Box 36, 1000 Skopje, Macedonia.

We have previously reported the development and characterisation of wheat germ agglutinin (WGA)-functionalised chitosan-Ca-alginate (CTS-Ca-ALG) microparticles (MPs) loaded with acid-resistant particles of 5-fluorouracil (5-FU). In the present work, our goal was to evaluate the potential of these carriers for efficient treatment of colon cancer by studying in vitro permeability and cell association of 5-FU and [methyl-³H]thymidine uptake in Caco-2 cells, as well as in vivo gastrointestinal distribution. The amount of 5-FU permeated through Caco-2 cells was 15.1, 7.7 and 6.5% for 5-FU solution, CTS-Ca-ALG MPs and WGA conjugates. The concentration of 5-FU associated with Caco-2 cells was significantly greater when delivered from MPs. By incorporation of 5-FU into MPs and further decoration with WGA, an increased [methyl-³H]thymidine uptake was observed few hours after continuous drug treatment followed by significantly reduced uptake after 6 h. Gastrointestinal distribution was in favour of increased localisation and concentration of the particles in colon region. PMID: 23544879

Goldsmid A(1), Kiemeneij F, Gilchrist IC, Kantor P, Kedev S, Kwan T, Dharma S, Valdivieso L, Wensternberg B, Patel T. Radial artery spasm associated with transradial cardiovascular procedures: results from the RAS registry. Catheter Cardiovasc Interv. 2014 Jan 1;83(1):E32-6.

(1)Department of Interventional Cardiology, Sanatorio Guemes, Buenos Aires, Argentina.

OBJECTIVES: To report the incidence and predictors of moderate/severe radial artery spasm (RAS) in patients undergoing cardiovascular percutaneous procedures through a transradial approach (TRA) in centers with TRA expertise. **BACKGROUND:** Data regarding the actual rate of clinically meaningful RAS are limited due to difference in study designs and operator expertise. **METHODS:** The RAS registry, an international (14 centers from Argentina, Chile, India, Indonesia, Macedonia, The Netherlands and United States of America) registry that included 1,868 patients undergoing TRA cardiovascular procedures (63.5% diagnostic and

56.5% therapeutic). All selected centers used TRA as default strategy in the cardiac catheterization laboratory. Throughout 2012, each center included all consecutive TRA cases (during a 2-month period) into a dedicated database covering clinical characteristics as well as procedural topics related to TRA patterns and RAS occurrence. **RESULTS:** The incidence of moderate/severe RAS was 2.7%. Only 0.7% of patients required crossover (8 to transfemoral and 5 to contralateral TRA). Patients with moderately/severe spasm were more frequently females, had a history of dyslipidemia, received more often a 7F sheath and more puncture attempts than patients without spasm. By multivariate analysis, the need for more than one attempt and the use of a 7 F sheath were independent predictors of the development of moderate/severe RAS. **CONCLUSIONS:** The incidence of moderate/severe RAS is low in centers with a default TRA. Its development appears to be strongly related to the numbers of puncture attempts and the use of large sheaths. PMID: 23785005

Gucev Z(1), Tasic V, Pop-Jordanova N, Jancevska A, Simonaro CM, Schuchmann EH. Two siblings with Niemann-Pick disease (NPD) type B: clinical findings and novel mutations of the acid sphingomyelinase gene. Indian J Pediatr. 2013 Feb;80(2):163-4.

(1)Department of Endocrinology and Genetics, Pediatric Clinic, Medical Faculty Skopje, 50 Divizija BB, 1000, Skopje, Macedonia. gucevz@gmail.com

Acid sphingomyelinase deficiency leads to the accumulation of sphingomyelin in cells, causing Niemann-Pick disease (NPD) types A/B. RF (13.66 y) and HF (3 y) are brother and sister. RF growth was markedly delayed at the age of 12.66 y (123 cm; -3.25 SD), while at the age 3 y his sister is 86 cm (-2.75 SD). The brother had a huge liver (13 cm) and spleen (12 cm). His sister also had an enlarged liver, but presented no other symptoms. The fibroblast cultivation had a reduced sphingomyelinase activity in the fibroblasts (0.68 mkat/kg protein), β -galactosidase (937 mkat/kg) and glucosylceramidase (125.4 mkat/kg) were elevated. Mutational analysis demonstrated the siblings are compound heterozygotes (V112M and H554Y). The mother is carrier of V112M and the father carries H554Y. This is the first report of NPD type B in Macedonia. The novel mutation results in a moderately severe phenotype of NPD type B. PMID: 22367733

Gulaboski R(1), Mirčeski V, Mitrev S. Development of a rapid and simple voltammetric method to determine total antioxidative capacity of edible oils. Food Chem. 2013 May 1;138(1):116-21.

(1)Department of Chemistry, Faculty of Agriculture, University Goce Delčev - Štip, Macedonia. rubin.gulaboski@ugd.edu.mk

In this work we report on a new, rapid and simple voltammetric method to determine the total antioxidant capacity (TAC) of the edible oils. The method explores the ABTS radical (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)) assay as a redox probe and it relays on measuring catalytic voltammetric currents. The electrocatalysis comprises redox regeneration of the electrochemically created ABTS(+) radical either by Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) or by antioxidants present in studied oils. The detection limit of the method is determined to be 0.5 mg/L of Trolox equivalent, being a slightly lower than the corresponding UV-VIS spectrophotometric method. Applying the proposed voltammetric method the total antioxidant capacity of three types of commercially available cold-pressed edible oils are determined, and the results are found to be in a very good agreement with those obtained by UV-VIS spectrophotometry. The reported voltammetric method is cheap, rapid and simple, and it can be used as a sustainable alternative to the UV-VIS methods for the determination of total antioxidant capacity of oils and other liquid lipophilic nutrients. Potent antioxidant capacity of studied oils was also confirmed by electron paramagnetic resonance spectroscopy of superoxide anion produced by macrophages. PMID: 23265464

Hiljadnikova Bajro M(1), Sukarova-Angelovska E, Adélaïde J, Chaffanet M, Dimovski AJ. A new case with 10q23 interstitial

deletion encompassing both PTEN and BMPR1A narrows the genetic region deleted in juvenile polyposis syndrome. J Appl Genet. 2013 Feb;54(1):43-7.

(1)Faculty of Pharmacy, Ss. Cyril and Methodius University, Vodnjanska 17, 1000, Skopje, Republic of Macedonia.

We report on a patient with a contiguous interstitial germline deletion of chromosome 10q23, encompassing BMPR1A and PTEN, with clinical manifestations of juvenile polyposis and minor symptoms of Cowden syndrome (CS) and Bannayan-Riley-Ruvalcaba syndrome (BRRS). The patient presented dysmorphic features as well as developmental delay at the age of 5 months. Multiple polyps along all parts of the colon were diagnosed at the age of 3 years, following an episode of a severe abdominal pain and intestinal bleeding. The high-resolution comparative genomic hybridisation revealed a 3.7-Mb deletion within the 10q23 chromosomal region: 86,329,859-90,035,024. The genotyping with four polymorphic microsatellite markers confirmed a de novo 10q deletion on the allele with a paternal origin, encompassing both PTEN and BMPR1A genes. The karyotype analysis additionally identified a balanced translocation involving chromosomes 5q and 7q, and an inversion at chromosome 2, i.e. 46,XY,t(5;7)(q13.3-q36), inv(2)(p25q34). Although many genetic defects were detected, it is most likely that the 10q23 deletion is primarily the cause for the serious phenotypic manifestations. The current clinical findings and deletion of BMPR1A indicate a diagnosis of severe juvenile polyposis, but the existing macrocephaly and PTEN deletion also point to either CS or BRRS, which cannot be ruled out at the moment because of their clinical manifestation later in life and the de novo character of the deletion. The deletion detected in our patient narrows the genetic region deleted in all reported cases with juvenile polyposis by 0.04 Mb from the telomeric side, mapping it to the region chr10:88.5-90.03Mb (GRCh37/hg19), with an overall length of 1.53 Mb. PMID: 22993021

Ivanovski O(1), Drüeke TB. A new era in the treatment of calcium oxalate stones? Kidney Int. 2013 Jun;83(6):998-1000.

(1)University Clinic of Urology, Medical Faculty, Ss. Cyril and Methodius University, Skopje, Republic of Macedonia. ognen.ivanovski@yahoo.com

Comment on Kidney Int. 2013 Jun;83(6):1144-9.

Calcium oxalate (CaOx) is the most prevalent type of kidney stone. The amount of oxalate excreted in the urine is a major risk factor for CaOx stone formation. The study by Siener et al. makes a substantial contribution to our understanding of how Oxalobacter formigenes affects oxalate metabolism and excretion in humans and hence influences the risk of developing CaOx kidney stones. PMID: 23728004

Ivanovski V(1), Mayerhöfer TG. Vibrational spectra and dispersion analysis of K₂Ni(SeO₄)₂·6H₂O Tutton salt single crystal doped with K₂Ni(SO₄)₂·6H₂O. Spectrochim Acta A Mol Biomol Spectrosc. 2013 Oct;114:553-62.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje, Skopje, Republic of Macedonia. vladimir@pmf.ukim.mk

Dispersion analysis of the polarized IR reflectance spectra of K₂Ni(SeO₄)₂·6H₂O doped with K₂Ni(SO₄)₂·6H₂O has been performed. Vibrational parameters like oscillator strength, attenuation constant and frequency of the transversal phonons for the modes of Au symmetry type plus the orientation of the transition dipole moments for the modes of Bu symmetry type in the ac crystal plane have been obtained. The spectra-structure correlation of the H₂O stretching vibrations show that bands appearing in the spectra for polarization of the external radiation oriented along the b axis are mainly due to the H₂O stretching vibrations of one of the three crystallographically distinct sets of water molecules. The orientation of the transition dipoles of stretching vibrations of the selenate ion differ from the characteristic spectra of the sulfate analog in that no mutually perpendicular transition dipoles are found in the ac crystal plane. Water librational bands masked with the bands of the

v₄(SO₄(2-)) mode in the sulfate analog have now been unveiled and assigned. The ratio between the oscillator strength and the attenuation constant appears to be a helpful tool in the assignment of the sulfate stretching vibrations and water librations. The vibrational and orientational characteristics of the v₄(SeO₄(2-)) modes were obtained. The v₃(SO₄(2-)) frequency region of the isomorphously isolated SO₄(2-) ion in the K₂Ni(SeO₄)₂·6H₂O matrix was investigated in some detail. Contrary to the expected three, four bands can be identified. Three of them were assigned to v₃(SO₄(2-)) based on the orientation of the transition dipole moments. On the basis of the IR, but also Raman spectra of the pure and mixed crystals, a discussion of the influence of the potential field and the hydrogen bonds with the change in the volume of the unit cell is given. PMID: 23796943

Jakovski K(1), Nestorovska AK(2), Labacevski N(1), Dimovski AJ(2). Characterization of the most common CYP2C9 and CYP2C19 allelic variants in the population from the Republic of Macedonia. Pharmazie. 2013 Nov;68(11):893-8.

(1)Department of Preclinical and Clinical Pharmacology and Toxicology, Faculty of Medicine, University Ss Cyril and Methodius, Skopje, Republic of Macedonia. (2)Center for Bimolecular Pharmaceutical Analysis, Faculty of Pharmacy, University Ss Cyril and Methodius, Skopje, Republic of Macedonia.

The aim of this study was to evaluate the most common CYP2C9 and CYP2C19 polymorphisms in the population of Macedonia and compare them with the global geographic data reported from different ethnic populations. In total, 184 healthy volunteers from the general population were included. Genotypes for the CYP2C9 (*2 [rs1799853] and *3[rs1057910]) and CYP2C19 (*2-[rs4244285] and *17 [rs12248560]) polymorphisms were detected by Real-Time PCR using TaqMan SNP genotyping assay. The CYP2C9 wildtype allele (*1) was the most frequent (78.8%) and the non-functional alleles *2 and *3 had a frequency of 13.9% and 7.3%, respectively. Seven subjects (2.97%) were poor metabolites (PMs) for CYP2C9 because of the *2/*2 and *3/*3 genotype. For CYP2C19, the frequencies of the *1 (wild-type) and the non-functional alleles (*2 and *17) were 65.4%, 14.4% and 20.1%, respectively. The *2/*2 genotype, corresponded to the predicted frequency of 2.7% for the CYP2C19 PM phenotype. The total of 59 out of 184 subjects (32.0%) was determined as UMs because of the *1/*17 and *17/*17 genotypes. The compound heterozygote (*2/*17), which is associated with a difficult-to-predict phenotype, was detected in 8 subjects (4.34%). The CYP2C9 and CYP2C19 are polymorphic in the population of the Republic of Macedonia. The frequencies of the most common CYP2C9 and CYP2C19 allelic variants are similar to those reported for Caucasians of European descendant, but differ from those of North America Caucasians. Our results suggest that the genetically determined capacity of CYP2C9 and CYP2C19 has to be taken into account in order to improve the individual risk / benefit ratio of the drug therapy in Macedonia. PMID: 24380239

Jankulovski N(1), Spasevska L, Janevska V, Dukova B. A true epidermotropic apocrine neoplasm in the form of perianal Paget's disease: a case report. J Med Case Rep. 2013 Jun 20;7(1):162.

(1)Institute of Pathology, Medical Faculty, University "St Cyril and Methodius", Skopje, Republic of Macedonia. blagicadr@yahoo.com.

INTRODUCTION: Extramammary Paget's disease is an uncommon intraepithelial neoplasm that arises in areas rich in apocrine glands. Treatment includes wide surgical excision and nonsurgical modalities. We present the case of a patient with perianal Paget's disease with no recurrent disease after wide surgical resection. CASE PRESENTATION: Our patient was a 46-year-old man of Macedonian ethnicity who presented with a pruritic perianal lesion measuring up to 6cm without pain or bleeding. Two biopsies and a perianal wide surgical excision were performed. The tissue specimens were formalin-fixed and the paraffin-embedded samples analyzed according to standard histochemical and immunohistochemical procedures. Surgical perianal skin excision revealed diffuse eczematoid, whitish plaques. Pathohistology showed Paget cells infiltrating his epidermis and adnexal

epithelium, with ulceration. Immunohistochemical analysis revealed positive Paget cell expression for cytokeratin 7, epithelial membrane antigen, carcinoembryonic antigen, androgen receptor and human epidermal growth factor receptor 2, and negative expression for cytokeratin 20 and melan-A. **CONCLUSION:** Paget's disease is a rare disorder that should be considered in the differential diagnosis of perianal lesions. Reporting cases of extramammary Paget's disease is crucial for diagnostic guidelines and different therapeutic options. PMID: 23786719

Jankulovski N(1), Antović S, Petrussevska G, Rusiti K, Kostovski O, Mitevski A, Stojanović A. Laparoscopic versus open splenectomy: a single center eleven-year experience. Acta Clin Croat. 2013 Jun;52(2):229-34.

(1)Department of Abdominal Surgery, Medical Faculty of Skopje, Ss Cyril and Methodius University, 50 Divizija No. 6, 1000 Skopje, Republic of Macedonia. prof.jankulovski@gmail.com

The 11-year experience with open (OS) and laparoscopic (LS) splenectomy at a single center is reported. A total of 201 splenectomies were performed and clinical and demographic data were retrospectively analyzed. Patients were classified according to the type of operation as LS or OS. The mean age of patients was 45.1 +/- 17.1, and 141 patients were male. Out of 43 LS, 40 were done for hematologic causes, and they had a significantly shorter hospital stay compared to OS for hematologic causes (6.87 +/- 2.2 vs. 9.84 +/- 2.9 days; $p = 0.000003$) and significantly less requirement for blood transfusion (26.2 +/- 93.4 vs. 132.4 +/- 252.3 mL; $p = 0.0152$). In the OS group, comparison of patients with trauma and those with hematologic causes showed that significantly more males underwent surgery for trauma causes (35 of 43 vs. 16 of 21), hospital stay was longer (18.9 +/- 27.4 vs. 9.8 +/- 2.9 days) and blood requirement higher (708.1 +/- 603.7 mL vs. 132.4 +/- 252.3 mL; $p = 0.0004$, $p = 0.047$ and $p = 0.000001$, respectively). Laparoscopic splenectomy is a safe procedure for spleen removal. PMID: 24053084

Jashari A(1), Popovski E, Mikhova B, Nikolova RP, Shivachev BL. 3-[2-(5-tert-Butyl-1,2-oxazol-3-yl)hydrazinyl-iden]chroman-2,4-dione. Acta Crystallogr Sect E Struct Rep Online. 2013 Feb 1;69(Pt 2):o258.

(1)Group of Physics & Chemistry, Faculty of Natural Sciences & Mathematics, State University of Tetovo, 1200 Tetovo, Macedonia.

In title compound, C(16)H(15)N(3)O(4), the dihedral angle between the chromane and isoxazole rings [r.m.s. deviations = 0.042 and 0.007 Å, respectively] is 20.33 (12)°. The mol-ecular geometry is stabilized by an intra-molecular N-H...O hydrogen bond. In the crystal, N-H...O hydrogen bonds generate chains along the c-axis direction. The crystal studied was a non-morohedral twin. PMID: PMC3569789. PMID: 23424535

Jeram S(1), Lekaviciute J, Krukle Z, Argalasova-Sobotova L, Ristovska G, Paunovic K, Pawlaczyk-Luszczynska M. Community response to noise: research in Central, Eastern and South-Eastern Europe and Newly Independent States. Noise Health. 2013 Jan-Feb;15(62):12-21.

(1)National Institute of Public Health, Communicable Diseases and Environmental Health Center, Ljubljana, Slovakia. sonja.jeram@ivz-rs.si

The systems of public complaints on environmental noise were reviewed in seven countries of Central and Eastern Europe (CEE), South-East Europe (SEE), and Newly Independent States (NIS). Public complaints remain an important issue due to differences in public sensitivity to noise and due to several cases where a measurement of noise intensity does not give a satisfying solution to the problem. The unresolved problem remaining in the residential neighborhoods is the noise from pubs and restaurants that are open until late in the night. In our review, we compiled information on the institutions responsible for the implementation of environmental

noise legislation and organizations that are responsible for dealing with public complaints. Information on activities for increasing public awareness on hazards rising from environmental noise and the role of civil initiative was explored. In seven countries, and among them, Slovenia, Lithuania, Latvia, Slovakia, The Former Yugoslav Republic of Macedonia, Serbia, and Poland, the responsibilities and duties are shared among different institutions at national and regional levels, depending on the noise source. The problem of gathering information on complaints and using it for improving the wellbeing and health of citizens remains often difficult and unsolved. PMID: 23412576

Karadzinska-Bislimovska J(1), Basarovska V, Mijakoski D, Minov J, Stoleski S, Angeleska N, Atanasovska A. Linkages between workplace stressors and quality of care from health professionals' perspective - Macedonian experience. Br J Health Psychol. 2013 Mar 11. doi: 10.1111/bjhp.12040. [Epub ahead of print]

(1)Institute of Occupational Health of RM, WHO Collaborating Center, Skopje, Republic of Macedonia.

OBJECTIVES: During last two decades, within the process of transition, the socio-economic reforms in Republic of Macedonia reflected on the national health care system. The objective of this article was to identify workplace stressors and factors that influence quality of care, from the perspective of health professionals (HPs), and to understand how they were linked in the context of such social circumstances. **METHODS:** A qualitative research based on focus group (FG) methodology was conducted in a general teaching hospital. Two main topics were the subjects of discussion in FGs: workplace stressors and factors that influence quality of care, from the HPs perspective. Six FGs were conducted with a total of 56 HPs (doctors, nurses, interns, and residents) divided into two sets of three FGs for each topic separately. Two sets of data were processed with thematic analysis, and the obtained results were compared with each other. **RESULTS:** By processing the data, we identified themes relating to factors that generate stress among HPs and factors that influence quality of care, from HPs' perspective. By comparing the two sets of themes, we found that many of them were identical, which means factors that increase workplace stress at the same time reduce quality of care. **CONCLUSIONS:** Implementation of specific organizational interventions in the hospital setting can lead to the prevention of work-related stress and improvement in quality of care. Our research suggests that the prevention of work-related stress will impact positively on the quality of care, which may contribute to establish criteria and recommendations for the improvement in organizational culture and climate in hospitals. **STATEMENT OF CONTRIBUTION:** What is already known on this subject? Psychosocial stress at work among health professionals is often present and well studied, but relations between job stress and quality of care were rarely examined. Job demands-resources model by Demerouti, Bakker, Nachreiner and Schaufeli (2001), for assessment of job stress includes job demands (working environment, work overload, time pressures, recipient contact, shift work) and job resources (feedback, rewards, job control, participation, job security, supervisor support) was applied in different studies. There is scientific evidence that burned-out physicians have shown depersonalization from their patients, they have withdrawn from patients, demonstrated sub-optimal care, and sometimes burnout has been related to serious mistakes and patient death. Different research has shown that some workplace factors contributed to the development of work-related stress and burnout among HPs whereas others contributed protectively. What does this study add? Similar and overlapping workplace factors in hospital setting produce stress in health professionals and influence quality of care. Impact of specific socioeconomic environment in Macedonia as a country in transition and EU candidate country on job stress among health professionals and quality of care. Development of criteria and recommendations for the job stress prevention and improvement of the organizational culture and climate in hospital settings. PMID: 23480487

Kedev S(1), Zafirovska B, Dharma S, Petkoska D. Safety and

feasibility of transulnar catheterization when ipsilateral radial access is not available. Catheter Cardiovasc Interv. 2014 Jan 1;83(1):E51-60.

(1)University Clinic of Cardiology, Medical Faculty, University of St. Cyril & Methodius, Skopje, Macedonia.

OBJECTIVES: We evaluated the safety and feasibility of transulnar approach when ipsilateral radial access was not available. **METHODS AND RESULTS:** From March 2011 until February 2013, 476 consecutive patients who underwent transulnar catheterization were included in a single center prospective registry of effectiveness and safety. Diagnostic coronary angiography accounted for 42% of cases, percutaneous coronary intervention (PCI) for 38%, and 17% underwent carotid artery stenting. A subgroup analysis was done in 240 patients with documented ipsilateral radial artery occlusion (RAO). Procedural success was 97% with a crossover rate of 3% to transfemoral access. Hand ischemia was not observed in any patient on day 1 after procedure and on 1 month follow-up. None of the patients showed ulnar nerve injury. Two patients developed major forearm hematoma that resolved without clinical consequences. Minor access site hematoma occurred in 8%. Severe clinical spasm occurred in two patients. Asymptomatic ulnar artery occlusion at 1 month follow-up was detected in 3.1%. There was no difference between patients with or without RAO in terms of procedural success and any vascular complication. **CONCLUSION:** Transulnar approach is safe and feasible alternative wrist access when performed by experienced radial operators, providing high success rate and low incidence of vascular complications. PMID: 23832623

Kiprijanovska S(1), Davalievka K, Noveski P, Sukarova-Stefanovska E, Plaseska-Karanfilska D. Prevalence of hepatitis C virus genotypes in risk groups in the Republic of Macedonia: a 5 years survey. J Med Virol. 2013 Dec;85(12):2072-8.

(1)Research Center for Genetic Engineering and Biotechnology "Georgi D. Efremov", Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia.

The prevalence of hepatitis C virus (HCV) genotypes depends on geographical location. HCV genotyping is important for epidemiological investigations and treatment management. The aim of this study was to determine the HCV genotype prevalence in the most prominent risk groups in the Republic of Macedonia in the last 5 years and to evaluate its association with patient's age, gender, and mode of transmission. A total of 1,167 HCV positive patients, divided into three risk groups (intravenous drug use, chronic hemodialysis, and other risk factor), were genotyped using an in-house ASO hybridization method with genotype-specific oligonucleotide probes. The genotypes 1, 2, and 3 were present with 52.2%, 0.6%, and 47.0%, respectively. Genotype 1 was most prevalent in hemodialysis (89.0%) and other risk factor group (53.8%). It was found associated independently with hemodialysis, age >40 and female gender. Genotype 3 predominated in intravenous drug users (64.0%) and was associated significantly also with age ≤40 and male gender. Multivariable logistic regression analysis pointed out hemodialysis ($P < 0.0001$, Exp (B) = 12.0) as a positive predictor factor for genotype 1 and age ≤40 ($P = 0.021$, Exp (B) = 1.8) and intravenous drug use ($P < 0.0001$, Exp (B) = 8.4) as a positive predictor factors for genotype 3. In conclusion, the main transmission route of HCV infection in the Republic of Macedonia is intravenous drug use, followed by hemodialysis. HCV genotypes 1 and 3 dominate in these two most prominent risk groups in the Republic of Macedonia. PMID: 23959998

Kohls E(1), Mishev A, Pejov L. Solvation of fluoroform and fluoroform-dimethylether dimer in liquid krypton: a theoretical cryospectroscopic study. J Chem Phys. 2013 Aug 7;139(5):054504.

(1)Institute of Chemistry, Faculty of Science, Ss. Cyril and Methodius University, P.O. Box 162, 1001 Skopje, Republic of Macedonia.

A hybrid, sequential statistical physics-quantum mechanical electronic-quantum mechanical nuclei approach has been applied

to study the C-H stretching frequencies of bare fluoroform dissolved in liquid krypton under cryogenic conditions (at ~130 K), as well as upon blue shifting hydrogen bonding interactions with dimethylether in the same solvent. The structure of the liquid at 130 K was generated by Monte Carlo simulations of cryogenic Kr solutions containing either fluoroform or fluoroform and dimethylether molecules. Statistically uncorrelated configurations were appropriately chosen from the equilibrated MC runs and supermolecular clusters containing solute and solvent molecules (either standalone or embedded in the "bulk" part of the solvent treated as a polarizable continuum) were subjected to quantum mechanical electronic (QMel) and subsequent quantum mechanical nuclei (QMnuc) calculations. QMel calculations were implemented to generate the in-liquid 1D intramolecular C-H stretching vibrational potential of the fluoroform moiety and subsequently in the QMnuc phase the corresponding anharmonic C-H stretching frequency was computed by diagonalization techniques. Finally, the constructed vibrational density of states histograms were compared to the experimental Raman bands. The calculated anharmonic vibrational frequency shifts of the fluoroform C-H stretching mode upon interaction with dimethylether in liquid Kr are in very good agreement with the experimental data (20.3 at MP2 level vs. 16.6 cm^{-1} experimentally). Most of this relatively large frequency blue shift is governed by configurations characterized by a direct C-H...O contact between monomers. The second population detected during MC simulations, characterized by reversed orientation of the monomers, has a minor contribution to the spectral appearance. The experimentally observed trend in the corresponding bandwidths is also correctly reproduced by our theoretical approach. Solvation of the fluoroform monomer, according to experiment, results in small C-H stretching frequency red shift (~2 cm^{-1}), while our approach predicts a blue shift of about 10 cm^{-1} . By a detailed analysis of the anharmonic C-H stretching frequency dependence on the position of the nearest solvent krypton atom and also by analyzing the vibrational Stark effect induced by the local fluctuating field component parallel to the C-H axis, we have derived several conclusions related to these observations. The frequency vs. C...Kr distance dependence shows appreciable fluctuations and even changes in sign at R values close to the maximum of the C...Kr radial distribution function, so that most of the first-shell Kr atoms are located at positions at which the CH frequency shifts acquire either small negative or small positive values. It so happens, therefore, that even the actual sign of the frequency shift is strongly dependent on the correct description of the first solvation shell around CF₃H by the Monte Carlo method, much more than the other in-liquid properties calculated by similar approaches. PMID: 23927267

Kondova IT(1), Milenkovic Z, Marinkovic SP, Bosevska G, Kuzmanovska G, Kondov G, Alabakovska S, Muller CP, Hübschen JM. Measles outbreak in Macedonia: epidemiological, clinical and laboratory findings and identification of susceptible cohorts. PLoS One. 2013 Sep 10;8(9):e74754.

(1)University Clinic of Infectious Diseases and Febrile Conditions, Clinical Centre, Medical Faculty, Skopje, R. Macedonia.

OBJECTIVES: Despite a 92-99% national vaccination coverage since 2000, the former Yugoslav Republic of Macedonia experienced a large measles outbreak between 2010 and 2011. Here we investigate the characteristics of patients hospitalized during this outbreak at the Clinic of Infectious Diseases in Skopje. **METHODS:** Epidemiological, clinical and laboratory data of 284 measles patients, including 251 from Skopje (43.80% of the 573 reported cases) and 33 from elsewhere in Macedonia were collected. **RESULTS:** The most affected age groups were children up to 4 years of age and adolescents/adults of 15 years and older. Most patients were unvaccinated ($n=263$, 92.61%) and many had non-Macedonian nationalities ($n=156$, 54.93%) or belonged to the Roma ethnicity ($n=73$, 25.70%). Bronchopneumonia and diarrhea were the most common complications. Eighty-two out of 86 tested patients (95.35%) had measles-specific IgM antibodies. The outbreak was caused by the measles variant D4-Hamburg. **CONCLUSIONS:** The epidemic identified pockets of susceptibles in Skopje and indicated that additional vaccination opportunities in particular for people with non-Macedonian nationality and traveler

communities are warranted to ensure efficient measles control in Macedonia. The high attack rate among children of less than 1 year suggests that vaccination before 12 months of age should be considered in high risk settings. PMID: PMC3769294. PMID: 24040337

Krsteska R(1), Pejaska VG. The association of poor economic condition and family relations in childhood with late-life depression. Psychiatr Danub. 2013 Sep;25(3):241-7.

(1)Centre for Geriatric Psychiatry, Psychiatric Hospital "Skopje", Proleterska street b.b., 1000 Skopje, R. Macedonia, r_krsteska@yahoo.com.

BACKGROUND: Late-life depression encompasses both patients with late-life onset of depression (>60 years) and older adults with a prior and current history of depression. The aim of the study was to analyze the impact of the economic condition and family relations in childhood as risk factors for late-life depression. **SUBJECTS AND METHODS:** This was an analytical cross-sectional study comprising 120 subjects, 60 patients with unipolar depression and 60 subjects without depressive disorders, diagnosed in accordance with the 10-th International Classification of Mental and Behavioural Disorders. All participants in the study were above the age of 60 and there was no significant statistical difference in the sex proportion in both groups ($p>0.05$). Data for the examination were taken from a self-reported questionnaire designed for our aim. The Geriatric Depression Scale was used to measure depressive symptoms. **RESULTS:** Our results have shown that severe financial difficulties are important events in childhood and are risk factors for depression in the elderly (Chi-square=12.68, $df=2$, $p=0.0018$). Our investigation has found the association of family relations with late-life depression. In fact, conflictual relations in the family were more common in the experimental group than in the control group (Chi-square=14.32, $df=3$, $p=0.0025$). Furthermore, father's addiction to alcohol in childhood was associated with depression in later life ($p=0.013$). The difference in childhood emotional neglect and unequal treatment between siblings in both groups was insufficient to be confirmed statistically, but the examinees with this trauma had a threefold higher chance of having depression later in life (Odds ratio=3.04, 95% CL 0.92 < OR < 10.65; Yates chi-square=3.2, $df=1$, $p=0.07$). Subjects who have estimated their mother ($p=0.019$) or father ($p=0.046$) having personal character traits had a significantly greater risk for development of late-life depression. **CONCLUSIONS:** Negative socio-economic circumstances as well as family conflicts during childhood are associated with late-life depression. Father's addiction to alcohol and parents' negative personal character traits are associated with depression in the elderly. PMID: 24048391

Lazarevik V(1), Spasovski M, Donev D. Between anti-smoking policies and tobacco farming subsidies--the case of Macedonia. Eur J Public Health. 2013 Jun;23(3):354-5.

(1)Institute of Social Medicine, Faculty of Medicine, Ss Cyril and Methodius University, Skopje, Republic of Macedonia.

No abstract available. PMID: 23275476

Madjunkova S(1), Kocheva SA, Plaseska-Karanfilska D. Fanconi Anemia Founder Mutation in Macedonian Patients. Acta Haematol. 2013 Dec 13;132(1):15-21.

(1)Research Center for Genetic Engineering and Biotechnology 'Georgi D. Efremov', Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia.

Background: Fanconi anemia (FA) is a rare autosomal recessive disorder clinically characterized by developmental abnormalities, progressive bone marrow failure (BMF) and profound cancer predisposition. Approximately 65% of all affected individuals have mutation in the FANCA (Fanconi anemia complementation group A) gene. The mutation spectrum of the FANCA gene is highly heterogeneous. FA-A is usually associated with private FANCA mutations in individual families. **Methods:** We describe 3 unrelated

patients with FA with a similar clinical presentation: BMF, renal anomalies and café-au-lait pigmentation without major skeletal abnormality. The molecular analysis of the FANCA gene using the FA MLPA kit P031-A2/P032 FANCA, showed homozygous deletion of exon 3 in all 3 patients. Molecular analysis of the flanking regions of exon 3 precisely defined unique deletion of 2,040 bp and duplication of C (1788_3828dupC). **Discussion/Conclusions:** These are the first 3 patients homozygous for deletion of FANCA exon 3 described to date. Although not related, the patients originated from the same Gypsy-like ethnic population. We conclude that c.190-256_283 + 1680del2040 dupC mutation in the FANCA gene is a founder mutation in Macedonian FA patients of Gypsy-like ethnic origin. Our finding has very strong implications for these patients in formulating diagnostic and carrier-screening strategy for BMF and FA and to enable comprehensive genetic counseling. PMID: 24356203

Makraduli L(1), Crcarevska MS, Geskovski N, Dodov MG, Goracinova K. Factorial design analysis and optimisation of alginate-Ca-chitosan microspheres. J Microencapsul. 2013;30(1):81-92.

(1)Faculty of Pharmacy, Institute of Pharmaceutical Technology, University Ss Cyril and Methodius, Vodnjanska 17, 1000 Skopje, Macedonia.

The purpose of this study was to apply factorial design in order to determine the influence of the formulation factors and their interactions on several responses such as particle size, dissolution behaviour at pH 1.2 and pH 7.4 as well as production yield, during the development of budesonide loaded, chitosan coated Ca-alginate microparticles (MPs) intended for treatment of inflammatory diseases in the gastrointestinal tract. Produced drug-loaded MPs were spherical in shape, had smooth surfaces with low porosity and size range between 5 and 11 μm . Production yield for the formulations from the design varied from 19% to 50%. Optimisation was performed using central composite design setting the targets: particle size at 5.5 μm , maximised yield, suppressed dissolution at pH 1.2 and sustained release at pH 7.4. The optimised batches were identified with a combined desirability value of 0.967. PMID: 22746546

Makreski P(1), Jovanovski S, Pejov L, Kloess G, Hoebler HJ, Jovanovski G. Theoretical and experimental study of the vibrational spectra of sarkinite Mn₂(AsO₄)(OH) and adamite Zn₂(AsO₄)(OH). Spectrochim Acta A Mol Biomol Spectrosc. 2013 Sep;113:37-42.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Arhimedova 5, 1000 Skopje, Macedonia. petremak@pmf.ukim.mk

The arsenate hydroxyl-bearing minerals sarkinite and adamite were studied with vibrational spectroscopic (IR and Raman) and quantum theoretical methods. The observed IR bands in the higher (1100-600 cm^{-1}) and especially lower (600-450 cm^{-1}) frequency region of AsO₄ vibrations could clearly discriminate between the studied analogues. The differences between their crystal structures are much pronounced in both IR and Raman OH-stretching regions. Namely, a single strong band is found in the case of orthorhombic adamite compared to four weaker bands observed in corresponding IR and Raman spectral regions of monoclinic sarkinite. Essentially all bands in the experimental spectra, collected at both room and liquid nitrogen temperature, were tentatively assigned. To support the tentative assignment of bands in the vibrational spectra of the mentioned minerals, periodic pseudopotential plane wave density functional theory calculations were carried out. Geometry optimizations of the 3D periodic systems included both optimizations of the atomic positions within the unit cell and of the unit cell itself. In most cases, the assignments were either supported or implied by the obtained theoretical data. It is worth mentioning that this is the first experimental and theoretical study of the vibrational spectra of the very-rare sarkinite mineral. PMID: 23711395

Malloy PJ(1), Tasic V(2), Taha D(3), Tütüncüler F(4), Ying GS(5),

Yin LK(5), Wang J(1), Feldman D(1). Vitamin D receptor mutations in patients with hereditary 1,25-dihydroxyvitamin D-resistant rickets. *Mol Genet Metab.* 2014 Jan;111(1):33-40.

(1)Department of Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA. (2)Department of Pediatric Nephrology, Clinic for Children's Diseases, University Children's Hospital, Medical School of Skopje, Skopje, Macedonia. (3)Department of Endocrinology, Children's Hospital of Michigan, Detroit, MI 48201, USA. (4)Pediatric Endocrinology, Trakya University, Faculty of Medicine, Edirne, Turkey. (5)Department of Pediatrics, University Children's Medical Institute, National University Hospital, Singapore.

CONTEXT: Hereditary vitamin D resistant rickets (HVDRR), also known as vitamin D-dependent rickets type II, is an autosomal recessive disorder characterized by the early onset of rickets with hypocalcemia, secondary hyperparathyroidism and hypophosphatemia and is caused by mutations in the vitamin D receptor (VDR) gene. The human gene encoding the VDR is located on chromosome 12 and comprises eight coding exons and seven introns. **OBJECTIVES, PATIENTS, AND METHODS:** We analyzed the VDR gene of 5 previously unreported patients, two from Singapore and one each from Macedonia (former Yugoslav Republic), Saudi Arabia and Turkey. Each patient had clinical and radiographic features of rickets, hypocalcemia, and the 4 cases that had the measurement showed elevated serum concentrations of 1,25-dihydroxyvitamin D (1,25(OH)₂D). Mutations were re-created in the WT VDR cDNA and examined for 1,25(OH)₂D(3)-mediated transactivation in COS-7 monkey kidney cells. **RESULTS:** Direct sequencing identified four novel mutations and two previously described mutations in the VDR gene. The novel mutations included a missense mutation in exon 3 causing the amino acid change C60W; a missense mutation in exon 4 causing the amino acid change D144N; a missense mutation in exon 7 causing the amino acid change N276Y; and a 2bp deletion in exon 3 5'-splice site (IVS3Δ+4-5) leading to a premature stop. **CONCLUSIONS:** These 4 unique mutations add to the previous 45 mutations identified in the VDR gene in patients with HVDRR. **PMCID:** PMC3933290. **PMID:** 24246681

Masin-Spasovska J(1), Dohcev S, Stankov O, Stavridis S, Saidi S, Dejanova B, Dejanov P, Hristova-Dimceva A, Dimitrovski K, Spasovski G. Can an increased nitric oxide level be accepted as non-invasive marker for sub/acute rejection of the kidney allograft? *Int J Artif Organs.* 2013 Dec;36(12):907-12.

(1)Department of Nephrology, Faculty of Medicine, University of Skopje - Macedonia.

BACKGROUND: Subclinical and acute rejections (SAR/AR) continue to have a negative impact on graft survival. The aim of our study was to analyze allograft rejection and nitric oxide (NO) levels in patients with protocol- and clinically-indicated biopsies in relationship with other causes of allograft dysfunction, and to evaluate the clinical impact of NO measurement as non-invasive marker for early diagnosis of SAR/AR. **METHODS:** In 45 living-related kidney transplants, serum NO levels were measured at: 20 min after reperfusion (NO1); on days 1 (NO2), 5 (NO3), and 14 (NO4); and at the first (NO5) and sixth (NO6) months after transplantation (Tx). Protocol biopsies (Bx) were performed at the first and sixth months after Tx. **RESULTS:** 38 (42.2%) Bx showed histological features of (SAR), 4 (4.5%) Bx showed mild tubulointerstitial rejection, while 48 (53.3%) Bx had no histological signs of SAR/AR. Significantly higher (NO3) levels were found in patients with AR and (NO5)/(NO6) in SAR as compared to other causes of allograft dysfunction occurred within the first posttransplant month (delayed graft function, urinary tract infection, and cyclosporine toxicity). Sensitivity/specificity for cut-off NO level of 70 μmol/l were 69.2% and 88.4% in AR, and 78.9% and 75.4% for the level of 50 μmol/l in SAR patients, respectively. **CONCLUSIONS:** Our study reports significantly higher serum NO levels at day 5 and a gradual decrease at day 14 (prior to and at the time of clinically manifested AR), and at 1- and 6-month protocol biopsies in SAR patients as compared to all other causes of renal dysfunction. NO measurement may have a satisfactorily diagnostic performance as a useful non-invasive marker not only for AR, but also for SAR patients. **PMID:** 24362900

Masin-Spasovska J(1), Dimitrovski K, Stavridis S, Stankov O, Dohcev S, Saidi S, Jakovski K, Balkanov T, Labacevski N, Stankov V, Lekovski L, Spasovski G. Acute fulminant hepatitis in kidney transplant recipient after repeated sevoflurane anesthesia—a case report and literature review. *Curr Drug Saf.* 2013 Apr;8(2):141-4.

(1)University Department of Nephrology, Ss Cyril and Methodius University, Skopje, Republic of Macedonia.

INTRODUCTION: A liver dysfunction induced by halogenated volatile anaesthetics is considered as a significant diagnostic problem. The aim of our report was to describe the first case of lethal hepatic failure in a female patient undergoing kidney transplantation (KTx) from a living donor after repeated sevoflurane anaesthesia. **CASE PRESENTATION:** A 47-year-old hypertensive and diabetic female patient received kidney from her 70-year-old mother. There was an immediate graft function and around 800 ml of blood loss on the abdominal drains, which gradually decreased after the erythrocyte and fresh frozen plasma (FFP) substitution. On the first postoperative (p.o.) day she gradually became anuric and overweighted at the next day undergoing dialysis. Because of prolonged hypotension and somnolence she required reintubation. The second day transaminases increased (AST&ALT>700, LDH>1200 U/L). On the third p.o. day she was urgently reoperated because of a sudden excessive bleeding. However, there was a rather slow flow of tears from the whole operative field that was even more excessive after the operation with signs of a consumptive coagulopathy. She was adequately substituted until the bleeding stopped more than 24 hrs after its onset. The new laboratory results showed further increase in transaminases (3300 U/L-ALT, 5100-AST, 8900-LDH) and ultrasound investigation confirmed an extensive toxic hepatic lesion. On the fourth p.o. night the patient was stable, diuresis rate was at 100 ml/hour, but in the morning she became hyposaturated because of an increased bronchial secretion. The dialysis could not improve the cardio-respiratory insufficiency and she died 30min later. **CONCLUSIONS:** This case report suggests that sevoflurane can lead to a severe hepatotoxicity in at-risk individuals with repeated sevoflurane anaesthesia, having renal failure, in those with a preoperative known history of cardiovascular disorders, as well as in those with excessive extracellular volume. A particular precaution should be considered in cases of an elective surgery including organ transplantation. **PMID:** 23845191

Maver PJ(1), Seme K, Korač T, Dimitrov G, Döbrössy L, Engle L, Iljazović E, Kesic V, Kostova P, Laušević D, Maurina A, Nicula FA, Panayotova Y, Primic Žakelj M, Repše Fokter A, Romejko-Wolniewicz E, Smailtyé G, Šuteu O, Świdarska-Kiec J, Tachezy R, Valerianova Z, Veerus P, Viberger I, Znaor A, Zubor P, Poljak M. Cervical cancer screening practices in central and eastern Europe in 2012. *Acta Dermatovenerol Alp Panonica Adriat.* 2013;22(1):7-19.

(1)Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.

The burden of cervical cancer in central and eastern Europe is generally higher compared to western or northern Europe due to a history of mostly opportunistic cervical cancer screening practices and due to the strong influence of political and economic changes in post-communist transition. This article describes the current cervical cancer screening practices, organizational plans for the future, and main obstacles that need to be overcome in 16 countries in central and eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia and The former Yugoslav Republic of Macedonia. Unfortunately, only a few countries have managed to establish an organized and well-functioning cervical cancer screening program in recent years, whereas most countries in the region are still struggling with implementation-related issues of organized cervical cancer screening. Encouragingly, even in the countries where only opportunistic screening is performed, well-prepared plans and strategies have been established for switching to organized screening in the near future. **PMID:** 23674180

Mikton C(1), Power M(2), Raleva M(3), Makoe M(4), Al Eissa M(5), Cheah I(6), Cardia N(7), Choo C(8), Almuneef M(9). The assessment of the readiness of five countries to implement child maltreatment prevention programs on a large scale. Child Abuse Negl. 2013 Dec;37(12):1237-51.

(1)Department of Violence and Injury Prevention and Disability, World Health Organization, Switzerland. (2)University of Edinburgh, Edinburgh, UK. (3)University of St. Cyril and Methodius Clinical Center, Skopje, The Former Yugoslav Republic of Macedonia. (4)Human Sciences Research Council, Cape Town, South Africa. (5)King Saud bin Abdulaziz University for the Health Sciences, Riyadh, Saudi Arabia. (6)Kuala Lumpur Hospital, Kuala Lumpur, Malaysia. (7)University of Sao Paulo, Sao Paulo, Brazil. (8)University of Malaya, Kuala Lumpur, Malaysia. (9)National Guard Health Affairs, Riyadh, Saudi Arabia.

This study aimed to systematically assess the readiness of five countries - Brazil, the Former Yugoslav Republic of Macedonia, Malaysia, Saudi Arabia, and South Africa - to implement evidence-based child maltreatment prevention programs on a large scale. To this end, it applied a recently developed method called Readiness Assessment for the Prevention of Child Maltreatment based on two parallel 100-item instruments. The first measures the knowledge, attitudes, and beliefs concerning child maltreatment prevention of key informants; the second, completed by child maltreatment prevention experts using all available data in the country, produces a more objective assessment readiness. The instruments cover all of the main aspects of readiness including, for instance, availability of scientific data on the problem, legislation and policies, will to address the problem, and material resources. Key informant scores ranged from 31.2 (Brazil) to 45.8/100 (the Former Yugoslav Republic of Macedonia) and expert scores, from 35.2 (Brazil) to 56/100 (Malaysia). Major gaps identified in almost all countries included a lack of professionals with the skills, knowledge, and expertise to implement evidence-based child maltreatment programs and of institutions to train them; inadequate funding, infrastructure, and equipment; extreme rarity of outcome evaluations of prevention programs; and lack of national prevalence surveys of child maltreatment. In sum, the five countries are in a low to moderate state of readiness to implement evidence-based child maltreatment prevention programs on a large scale. Such an assessment of readiness - the first of its kind - allows gaps to be identified and then addressed to increase the likelihood of program success. PMID: 23962585

Minov JB(1), Karadzinska-Bislimovska JD, Vasilevska KV, Stoleski SB, Mijakoski DG. Exercise-related respiratory symptoms and exercise-induced bronchoconstriction in industrial bakers. Arch Environ Occup Health. 2013;68(4):235-42.

(1)Department for Respiratory Functional Diagnostics, Institute for Occupational Health of R. Macedonia, Skopje, The Former Yugoslav Republic of Macedonia. minovj@hotmail.com

In order to assess prevalence and characteristics of exercise-related respiratory symptoms (ERRS) and exercise-induced bronchoconstriction (EIB) in industrial bakery, the authors performed a cross-sectional study including 57 bakers and an equal number of office workers studied as a control. Evaluation of examined subjects included completion of a questionnaire, skin prick tests to common inhalant and occupational allergens, spirometry, and exercise and histamine challenge. The authors found a similar prevalence of ERRS and EIB in both bakers and controls. EIB was significantly associated with atopy, asthma, family history of asthma, and positive histamine challenge in either group, whereas in bakers it was closely related to sensitization to occupational allergens ($p = .032$). Bronchial reaction to exercise was significantly higher in bakers with EIB (25.7% vs 19.2%; $p = .021$). These findings suggest that occupational exposure in industrial bakery may accentuate bronchoconstrictive response to exercise. PMID: 23697696

Mirceski V(1), Laborda E, Guziejewski D, Compton RG. New approach to electrode kinetic measurements in square-wave

voltammetry: amplitude-based quasireversible maximum. Anal Chem. 2013 Jun 4;85(11):5586-94.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss Cyril and Methodius University, P.O. Box 162, 1000 Skopje, Republic of Macedonia. valentin@pmf.ukim.mk

The influence of the potential pulse height of square-wave voltammetry (SWV) (i.e., the SW amplitude) is studied for a variety of quasireversible electrode mechanisms, including a simple solution-phase electrode reaction at a planar or spherical electrode, a solution phase electrode reaction coupled with a reversible follow-up chemical reaction, and a diffusionless surface confined electrode reaction. The electrode kinetics of all the electrode mechanisms depends critically on the SW amplitude, and the quasireversible kinetic region is a function of both frequency-related electrode kinetic parameters and the SW amplitude. Thus, a novel methodology for electrode kinetics measurements is proposed by altering the SW amplitude only, at a fixed frequency of the SW potential modulation, that is, at a constant scan rate of the voltammetric experiment. Electrode kinetic measurements at a constant SW frequency are of exceptional importance especially when complex electrode mechanisms are studied, which depend on several frequency-related kinetic parameters. The electrode kinetic measurements are based on a novel feature termed the "amplitude-based quasireversible maximum", manifested as a parabolic dependence of the amplitude-normalized net SW peak current versus the SW amplitude. The position of the amplitude-based quasireversible maximum depends on the standard rate constant of the electrode reaction, enabling estimation of this important kinetic parameter in a simple and fast procedure. The novel quasireversible maximum is attributed to all studied electrode mechanisms, implying that it is a general feature of most electrode mechanisms under conditions of SWV. PMID: 23642036

Mitic K(1), Popovska M, Pandilova M, Jovanovic R, Spasovski G, Nikolov V. The role of inflammation and apoptosis in cyclosporine A-induced gingival overgrowth. Bosn J Basic Med Sci. 2013 Feb;13(1):14-20.

(1)Dental Clinical Center St. Pantelejmon, Clinic for Periodontology, Faculty of Dentistry, Skopje 1000, Macedonia. 3mkristina@gmail.com

Cyclosporin A(CsA) - induced gingival overgrowth(GO) is a current problem of tissue-specific mechanism which is still incompletely explained. The apoptotic process has been of particular interest like a new concept in the etiology of this unwanted effect. The aim of our study was to detect the level of apoptosis, expression bcl-2 and p53, associated with the different doses of CsA. in gingival stroma. A cohort of 84 kidney transplant recipients was divided into four subgroups based on average daily dose of therapeutically applied CsA (Neoral®), (100 mg, 125 mg, 150 mg and 175 mg). The control group consisted of 21 patients, clinically diagnosed with periodontitis, who were not subjected to any medicamentous treatment causing gingival overgrowth. The following indexes were analyzed: plaque index (PI), index of gingival inflammation (GI) according to Loe-Silnes, and gingival overgrowth index (GOI) according to MacGaw et al. The tissue samples were subjected to a semiquantitative analysis to detect apoptotic cells and immunohistochemically stained to detect the expression of the bcl-2 and p53 proteins. The difference in percentage of apoptotic cells between the group taking 175 mg and other subgroups, as well as the control group was statistically significant ($p < 0.05$). There was a significant difference in percentage of expression bcl-2 between the 175 mg group compared to the other three subgroups and the control ($p = 0.001$). However, a statistically significant positive correlation between the medicament dose, p53, apoptosis, and bcl-2 was registered ($p < 0.05$). Inflammation plays the most important role in the induction of apoptosis and proliferation in gingival tissues. PMID: 23448605

Nakov N(1), Mladenovska K, Labacevski N, Dimovski A, Petkovska R, Dimitrovska A, Kavrakovski Z. Development and validation of automated SPE-LC-MS/MS method for determination of indapamide in human whole blood and its

application to real study samples. Biomed Chromatogr. 2013 Nov;27(11):1540-6.

(1)Faculty of Pharmacy, University of 'Ss Cyril and Methodius', Skopje, Republic of Macedonia.

A fast and simple liquid chromatography-electrospray ionization tandem mass spectrometry method for determination of indapamide in human whole blood was developed and validated. The sample extraction of indapamide from human whole blood was achieved using automated solid-phase extraction. Chromatographic separation was performed on Kinetex C18 column (100 × 2.1 mm, 1.7 µm particle size) using acetonitrile and 2 mM ammonium formate in ratio 90:10 (v/v) as a mobile phase. The mass spectrometer was operated in the multiple reaction monitoring mode using positive electrospray ionization for indapamide and the internal standard (zolpidem tartarate). The total run time was 2.5 min. The present method was found to be linear in the concentration range of 1-50 ng/mL with the coefficient of determination 0.9987. The absolute recoveries of indapamide were 90.51-93.90%. The method was validated according to the recommendations for validation of bioanalytical methods of European Medicines Agency guideline and was successfully used to analyze human whole blood samples for application in a pharmacokinetic study. PMID: 23798332

Nikolovska J. Oral health care provision systems in the black sea countries part 14: the Republic of Macedonia. Oral Health Dent Manag. 2013 Jun;12(2):61-4.

University of St Cyrilus and St Methodius, Skopje, Republic of Macedonia. julijanikolovska@yahoo.com

This paper gives an overview of the development of health insurance and some aspects of the oral health care in the Republic of Macedonia since it became independent in 1991. First, it describes the provision of oral health care and treatments funded by the public health care system. The dental educational system and available epidemiological data are then described. Generally, few data are available about the dental workforce in recent years, especially regarding dental epidemiology. There are various specialisations in dentistry recognised in Macedonia, as well as three subspecialisations: implantology, maxillofacial and reconstructive prosthodontics, and prosthodontics for children. One aspect of particular interest is that there are many dental faculties in Macedonia and many dentists, relative to the population and the country's requirements. PMID: 23756420

Noveski P(1), Madjunkova S, Maleva I, Sotiroska V, Petanovski Z, Plaseska-Karanfilska D. A Homozygous Deletion of the DPY19L2 Gene is a Cause of Globozoospermia in Men from the Republic of Macedonia. Balkan J Med Genet. 2013 Jun;16(1):73-6.

(1)Macedonian Academy of Sciences and Arts, Research Center for Genetic Engineering and Biotechnology "Georgi D. Efremov", Skopje, Republic of Macedonia.

Globozoospermia is a rare but severe teratozoospermia, characterized by ejaculates consisting completely of round-headed spermatozoa that lack an acrosome or, in partial globozoospermia, containing a variable proportion (20.0-90.0%) of acrosomeless spermatozoa. Men that are affected with total globozoospermia are infertile, and even the application of intracytoplasmic sperm injection (ICSI) has met with disappointingly low success rates. In humans, several case reports of globozoospermia have demonstrated that two or more siblings were affected in each family, which suggested a genetic component to this disease. Currently, three genes are known to be associated with total globozoospermia in humans, SPATA16, PICK1 and DPY19L2 genes. Mutations in SPATA16 and PICK1 are rare causes of globozoospermia, found in only one patient each. Several studies have suggested that DPY19L2 mutations are the major cause of globozoospermia in patients from different ethnic origins and different geographic regions. The most common DPY19L2 mutation is the 200 kb deletion arising from a nonallelic homologous recombination (NAHR) between the flanking low copy repeats

(LCRs). Here we describe the presence of a homozygous deletion of the DPY19L2 gene in two infertile Macedonian patients with 100.0% round headed spermatozoa, thus suggesting that this deletion represents a major cause of globozoospermia among Macedonian men. PMID: 24265589

Ognenovski V(1), Arsovska-Nalbanti M, Chichikj D, Calovski J. Improving rheumatologic care and education in the Republic of Macedonia: model for rheumatologic education and care in a developing country--ILAR Initiative. Clin Rheumatol. 2013 Nov;32(11):1669-71.

(1)University of Michigan Health Center, 300 North Ingalls Building, Room 7C27, Ann Arbor, MI, 48109-5422, USA, vognen@umich.edu.

No abstract available. PMID: 23780635

Petreska Stanoeva J(1), Stefova M. Assay of urinary excretion of polyphenols after ingestion of a cup of mountain tea (Sideritis scardica) measured by HPLC-DAD-ESI-MS/MS. J Agric Food Chem. 2013 Nov 6;61(44):10488-97.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Arhimedova 5, 1000 Skopje, Republic of Macedonia.

Flavonoids and phenolic acid metabolites excreted in human urine after ingestion of Sideritis scardica decoction with characterized polyphenolic composition were studied. A feeding study was carried out with 10 human volunteers, and urine samples were collected for 24 h after ingestion of the Sideritis decoction. Polyphenol metabolites were identified and quantified in urine samples by HPLC with tandem mass spectrometric detection. Thirty-one different metabolites of hypolaetin, methylhypolaetin, isoscutellarein, methylisoscutellarein, and apigenin and 32 phenolic acid metabolites were detected and quantified using a method validated for this purpose. The urinary excretion of polyphenol metabolites corresponded to 5% (n/n) of the intake of polyphenols from the Sideritis decoction. Flavonoid metabolites were dominant in urine samples with 87-94% of total polyphenolic metabolites content. The most abundant metabolites were methylhypolaetin and methylisoscutellarein glucuronides. Urinary excretion of isoscutellarein (35.61%) was 10 times higher than that of hypolaetin (3.67%). Apigenin also showed high urinary excretion (32.46%). PMID: 24102372

Picard-Meyer E(1), Mrenoshki S, Milicevic V, Ilieva D, Cvetkovikj I, Cvetkovikj A, Krstevski K, Dzhadzhovski I, Robardet E, Gagnev E, Iliev E, Plavsic B, Kirandjiski T, Cliquet F. Molecular characterisation of rabies virus strains in the Republic of Macedonia. Arch Virol. 2013 Jan;158(1):237-40.

(1)French Agency for Food, Environmental and Occupational Health and Safety (ANSES), Nancy Laboratory for Rabies and Wildlife, European Union Reference Laboratory for rabies, European Union Reference Laboratory for rabies serology, OIE Reference Laboratory for rabies, WHO Collaborating centre for research and management in zoonoses control, Technopôle agricole et vétérinaire, BP 40009, 54 220 Malzéville Cedex, France. evelyne.picard-meyer@anses.fr

Rabies, a worldwide zoonosis, remains a public-health concern despite oral wildlife vaccination in Europe. After a ten-year break, Macedonia reported eight rabies cases in 2011-2012. Two countries (Serbia and Bulgaria) bordering Macedonia are reporting cases in domestic and wild animals. This report describes the genetic characterisation of eight isolates from Macedonia compared with representative samples from neighbouring countries. All of the isolates tested belong to the Eastern European group, with a high degree of nucleotide sequence identity in the nucleoprotein gene. The close genetic relationship between isolates from the three bordering countries suggests that wildlife is responsible for rabies movements in the region. PMID: 23001721

Pieroni A(1), Rexhepi B, Nedelcheva A, Hajdari A, Mustafa B, Kolosova V, Cianfaglione K, Quave CL. One century later: the folk botanical knowledge of the last remaining Albanians of the upper Reka Valley, Mount Korab, Western Macedonia. J Ethnobiol Ethnomed. 2013 Apr 11;9:22.

(1)University of Gastronomic Sciences, Cuneo, Italy. a.pieroni@unisg.it

BACKGROUND: Ethnobotanical surveys of the Western Balkans are important for the cross-cultural study of local plant knowledge and also for obtaining baseline data, which is crucial for fostering future rural development and eco-tourism initiatives in the region. The current ethnobotanical field study was conducted among the last remaining Albanians inhabiting the upper Reka Valley at the base of Mount Korab in the Mavrovo National Park of the Republic of Macedonia. The aims of the study were threefold: 1) to document local knowledge pertaining to plants; 2) to compare these findings with those of an ethnographic account written one century ago and focused on the same territory; and 3) to compare these findings with those of similar field studies previously conducted in other areas of the Balkans. **METHODS:** Field research was conducted with all inhabitants of the last four inhabited villages of the upper Reka Valley (n=17). Semi-structured and open interviews were conducted regarding the perception and use of the local flora and cultivated plants. **RESULTS AND CONCLUSION:** The uses of ninety-two plant and fungal taxa were recorded; among the most uncommon uses, the contemporary use of young cooked potato (*Solanum tuberosum*) leaves and *Rumex patientia* as a filling for savory pies was documented. Comparison of the data with an ethnographic study conducted one century ago in the same area shows a remarkable resilience of original local plant knowledge, with the only exception of rye, which has today disappeared from the local foodscape. Medicinal plant use reports show important similarities with the ethnobotanical data collected in other Albanian areas, which are largely influenced by South-Slavic cultures. PMID: PMC3648429. PMID: 23578063

Pollozhani A(1), Kosevska E(2), Petkovski K(3), Memeti S(1), Limani B(4), Kasapinov B(2). Some Aspects of Culturally Competent Communication in Health Care in the Republic of Macedonia. Mater Sociomed. 2013 Dec;25(4):250-254. Epub 2013 Nov 24.

(1)Institute of Public Health of the Republic of Macedonia, Skopje, Republic of Macedonia. (2)Institute of Public Health of the Republic of Macedonia, Skopje, Republic of Macedonia ; Medical Faculty, University Ss. Cyril and Methodius, Skopje, Republic of Macedonia. (3)University of Kliment Ohridski, Bitola, Republic of Macedonia. (4)Institute of Political and Intercultural Studies, Skopje, Republic of Macedonia.

AIM: To examine the existing situation, barriers and consequences of the intercultural communication in health institutions and to offer training models for strengthening and improving communication skills of health professionals in the Republic of Macedonia. **METHODS:** A cross-sectional survey was conducted to assess the relationship between patients and health professionals. A total of 813 health professionals (302 physicians and 511 other medical staff) from different healthcare institutions, and 1016 patients participated in cross-sectional survey performed in autumn 2010. **RESULTS:** The research has showed that each third examined patient thought that his/her physician or the other medical personnel had no understanding for his/her emotions and gave no answer to all of his/her questions. From the other side, 60% of the physicians declare that they have a good communication with patients speaking other language than their mother tongue. Only 60% of physicians said that they know good the culture of their patient and 52% of the other medical staff said that they adjusted the treatment to the patient culture (religion, attitudes, language, life style). **CONCLUSION:** There are some gaps in current provision of health care practice in an aspect of effective interactions and communication skills of health professionals to meet patient needs in a multicultural and multilingual setting. A training model is proposed for strengthening communication skills of health professionals. PMID: PMC3914747. PMID: 24511268

Pop-Jordanova ND(1), Polenakovic MH. Psychological characteristics of patients treated by chronic maintenance hemodialysis. Int J Artif Organs. 2013 Feb;36(2):77-86.

(1)Department for Psychophysiology, Faculty of Medicine, University of Skopje, Skopje - Republic of Macedonia. popjordanova.nadica@gmail.com

Studies related to psychological aspects of dialysis patients show that depression and anxiety are the most common characteristics. The aim of our study was to analyze the personality profile in patients on chronic maintenance dialysis and to evaluate more specifically the level of depression. The total number of patients was 68 (30 females and 38 males), with mean age 62.3 and 56.5 for females and males respectively. Mean duration of dialysis was 6.73 years for females and 6.68 years for men (the period varied from 0.5 to 18 years). For the evaluation of psychological characteristics, we used two psychometric instruments: Minnesota Multiphase Personality Inventory (MMPI- 201) and Beck Depression Inventory. The obtained results confirmed the presence of depression in patients treated with hemodialysis. The level of depression is variable (minimal is present in 21.43%; mild in 35.71%; moderate in 17.85% and severe in 14.28% of patients). The depression is significantly positively correlated with age ($p<0.05$) as well as with educational level, and negatively with the duration of dialysis. Specific characteristics of personality obtained with MMPI are hypersensitivity, depressive mood, and withdrawal from friends and relatives. More specific emotional traits are the accentuated anxiety, low level of hostility, but very high passive aggression which destroys their social communications. Some response measures for depression such as relaxation training, psychological support, music therapy, or peripheral biofeedback are recommended. PMID: 23335381

Popovska-Jankovic K(1), Tasic V, Bogdanovic R, Miljkovic P, Golubovic E, Soylu A, Saraga M, Pavicevic S, Baskin E, Akil I, Gregoric A, Lilova M, Topaloglu R, Sukarova Stefanovska E, Plaseska-Karanfilska D. Molecular characterization of cystinuria in south-eastern European countries. Urolithiasis. 2013 Feb;41(1):21-30.

(1)Macedonian Academy of Science and Arts, Research Centre for Genetic Engineering and Biotechnology "Georgi D. Efremov", 1000, Skopje, Republic of Macedonia.

Cystinuria is an autosomal recessive disorder caused by defective transport of cystine and dibasic amino acids in the proximal renal tubules and small intestine. So far, more than 128 mutations in SLC3A1 gene, and 93 in SLC7A9 gene have been described as a cause of cystinuria. We present a molecular characterization of the cystinuria in 47 unrelated south-east European families. The molecular methodology included direct sequencing, single strand conformational polymorphism, and restriction fragment length polymorphism. A total of 93 (94.9 %) out of 98 unrelated cystinuric chromosomes have been characterized. Mutations in SLC3A1 gene account for 64.3 % and in SLC7A9 gene for 30.6 % of the cystinuric chromosomes. Ten different mutations in SLC3A1 gene were found, and two of them were novel (C242R and L573X), while in SLC7A9 gene seven mutations were found, of which three were novel (G73R, V375I and c.1048_1051delACTC). The most common mutations in this study were T216M (24.5 %), M467T (16.3 %) and R365L (11.2 %) in SLC3A1 and G105R (21.4 %) in SLC7A9 gene. A population specificity of cystinuria mutations was observed; T216M mutation was the only mutation present among Gypsies, G105R was the most common mutation among Albanians and Macedonians, and R365L among Serbs. The results of this study allowed introduction of rapid, simple and cost-effective genetic diagnosis of cystinuria that enables an early preventive care of affected patients and a prenatal diagnosis in affected families. PMID: 23532419

Qarri F(1), Lazo P, Stafilov T, Frontasyeva M, Harmens H, Bekteshi L, Baceva K, Goryainova Z. Multi-elements atmospheric deposition study in Albania. Environ Sci Pollut

Res Int. 2014 Feb;21(4):2506-18.

(1)Department of Chemistry, University of Vlora, Vlora, Albania.

For the first time, the moss biomonitoring technique and inductively coupled plasma-atomic emission spectrometric (ICP-AES) analytical technique were applied to study multi-element atmospheric deposition in Albania. Moss samples (*Hypnum cupressiforme*) were collected during the summer of 2011 and September-October 2010 from 62 sites, evenly distributed over the country. Sampling was performed in accordance with the LRTAP Convention-ICP Vegetation protocol and sampling strategy of the European Programme on Biomonitoring of Heavy Metal Atmospheric Deposition. ICP-AES analysis made it possible to determine concentrations of 19 elements including key toxic metals such as Pb, Cd, As, and Cu. Cluster and factor analysis with varimax rotation was applied to distinguish elements mainly of anthropogenic origin from those predominantly originating from natural sources. Geographical distribution maps of the elements over the sampled territory were constructed using GIS technology. The median values of the elements in moss samples of Albania were high for Al, Cr, Ni, Fe, and V and low for Cd, Cu, and Zn compared to other European countries, but generally were of a similar level as some of the neighboring countries such as Bulgaria, Croatia, Kosovo, Macedonia, and Romania. This study was conducted in the framework of ICP Vegetation in order to provide a reliable assessment of air quality throughout Albania and to produce information needed for better identification of contamination sources and improving the potential for assessing environmental and health risks in Albania, associated with toxic metals. PMID: 24081920

Ristevska-Dimitrovska G(1), Shishkov R, Gerazova VP, Vujovik V, Stefanovski B, Novotni A, Marinov P, Filov I. Different serum BDNF levels in depression: results from BDNF studies in FYR Macedonia and Bulgaria. Psychiatr Danub. 2013 Jun;25(2):123-7.

(1)Higher Medical School Bitola, University, St. Kliment Ohridski, Bitola, Vasko Karadjolevski bb, 7000 Bitola, FYR Macedonia. gordana.md@gmail.com

BACKGROUND: A growing body of evidence shows that brain-derived neurotrophic factor (BDNF) plays a role in depressive disorder. Serum BDNF levels are lower in depressed patients and they increase after a long course of antidepressant treatment. Our study aims to test the effect of antidepressant treatment on serum BDNF levels in patients with a depressive episode, after they have achieved remission in two studies in Macedonia and Bulgaria. **SUBJECTS AND METHODS:** In the Macedonian study 23 patients were included (11 female, 12 male) diagnosed with a first depressive episode according to ICD-10, as well as 23 control subjects age- and sex-matched without a history of psychiatric disorder. In the Bulgarian study 10 female patients with depression and 10 control subjects were included. We have applied the Hamilton Depression Rating Scale (HDRS) to assess depression severity. Blood samples were collected before antidepressant treatment and after remission was achieved (decrease to 7 points or less on HDRS). **RESULTS:** In the Macedonian study, mean serum BDNF level at baseline was 13.15 ± 6.75 ng/ml and the mean HDRS score was 28.52 ± 4.02 . Untreated depressed patients showed significantly lower serum BDNF levels compared to the control group (25.95 ± 9.17 ng/ml). After remission was achieved, the mean serum BDNF level was 24.73 ± 11.80 ng/ml whereas the mean HDRS score was 7.04 ± 3.15 . After 8 weeks of treatment there was no statistically significant difference in the serum BDNF levels between the two groups. In the Bulgarian study, baseline mean serum BDNF levels were 26.84 ± 8.66 ng/ml, after 3 weeks treatment and remission was achieved mean serum BDNF levels were 30.33 ± 9.25 ng/ml and in the control group mean serum BDNF levels were 25.04 ± 2.88 ng/ml. Integrated results showed baseline mean serum BDNF levels of 17.30 ± 9.66 ng/ml, after achieved remission 26.43 ± 11.25 ng/ml and in the control group mean serum BDNF levels of 25.68 ± 7.76 ng/ml. **CONCLUSION:** The Bulgarian results showed no statistical difference between the depressed group and controls. The Integrated results and the Macedonian study supported previous findings of low BDNF levels in untreated

depressive patients compared to healthy controls, and that those levels increase after antidepressant treatment. These results may suggest that low serum levels of BDNF are a state abnormality that is evident during depression and normalizes during remission. PMID: 23793275

Ristovska G(1), Lekaviciute J. Environmental noise and sleep disturbance: research in Central, Eastern and South-Eastern Europe and Newly Independent States. Noise Health. 2013 Jan-Feb;15(62):6-11.

(1)Institute of Public Health, Department for Environmental Health, Skopje, the Former Yugoslav Republic of Macedonia. drgordana@sonet.com.mk

Countries from South-East Europe (SEE), Central and Eastern Europe (CEE) and Newly Independent States (NIS) are in the process of harmonization with European environmental noise legislation. However, research work on noise and health was performed in some countries independently of harmonization process of adoption and implementation of legislation for environmental noise. Aim of this review is to summarize available evidence for noise induced sleep disturbance in population of CEE, SEE and NIS countries and to give directions for further research work in this field. After a systematic search through accessible electronic databases, conference proceedings, PhD thesis, national reports and scientific journals in English and non-English language, we decided to include six papers and one PhD thesis in this review: One paper from former Yugoslavia, one paper from Slovakia, one paper from Lithuania, two papers from Serbia and one paper, as also one PhD thesis from The Former Yugoslav Republic of Macedonia. Noise exposure assessment focused on road traffic noise was mainly performed with objective noise measurements, but also with noise mapping in case of Lithuanian study. Sleep disturbance was assessed with the questionnaire based surveys and was assumed from dose-effect relationship between night-time noise indicator (L_{night}) for road traffic noise and sleep disturbance (for Lithuanian study). Although research evidence on noise and sleep disturbance show to be sufficient for establishing dose response curves for sleep disturbance in countries where studies were performed, further research is needed with particular attention to vulnerable groups, other noise sources, development of laboratory research work and common methodology in assessment of burden of diseases from environmental noise. PMID: 23412575

Rosenthal VD(1), Richtmann R, Singh S, Apisarnthanarak A, Kübler A, Viet-Hung N, Ramirez-Wong FM, Portillo-Gallo JH, Toscani J, Gikas A, Dueñas L, El-Kholy A, Ghazal S, Fisher D, Mitrev Z, Gamar-Elanbya MO, Kanj SS, Arreza-Galapia Y, Leblebicioglu H, Hlinková S, Memon BA, Guanache-Garcell H, Gurskis V, Alvarez-Moreno C, Barkat A, Mejia N, Rojas-Bonilla M, Ristic G, Raka L, Yuet-Meng C; International Nosocomial Infection Control Consortium. Collaborators: Tome S, Rodrigues T, Baltieri SR, Camolesi F, Silva Cde A, Onzi-Siliprandi EM, dos Santos RP, Sánchez TE, Valente R, Apolinário D, Moreira M, Stadlober GF, Cavaglieri AG, Pérez-Fernandez AM, Pinilla-Martínez IF, Martínez-Saleg PA, León-Vega Y, Luengas EL, Quintero J, Sierra P, Chapeta-Parada E, Mindiola-Roche AE, Linares C, Yepes-Gomez D, Gómez BM, Ruiz MG, Morales-Pérez C, Severino R, Delgado M, Pérez Y, Tolari G, Sánchez T, Marei T, Balbaa Y, Sami G, El Banna A, Bran de Casares AC, Machuca Lde J, Chaniotaki K, Tsioutis C, Bampalis D, Radhakrishnan K, Chakravarthy M, Gokul B, Sukanya R, Leema P, Nainan-Myatra S, Pramesh C, Shrikhande SV, Gulia A, Puri A, Moiyadi A, Divatia J, Kelkar R, Biswas S, Raut S, Sampat S, Dwivedy A, Shetty S, Binu S, Bagasrawala I, Munshi N, Singhal T, Shah S, Naik R, Singhal T, Panigrahi B, Sharma B, Sood S, Verma N, Kumar-Nair P, Shah M, Chacko SF, Baftiu N, Spahija G, Zahreddine N, Alamuddin L, Kanafani Z, Molaeb B, Gailiene G, Grinkeviciute D, Kevalas R, Dagys A, Kondratas T, Anguseva T, Ampova V, Guroska ST, Bogovska-Miteva Z, Manikavasagam J, Tan LH, Lim J, Aguilera-Almazán F, Miramontes GI, Vázquez-Olivas Mdel R, Sánchez-Chávez A, Espinoza YA, Miranda-Navales MG, Lugo IZ, Sánchez M, Ayala-Gaytan J, Culebro-Burguete MC, Arteaga-Troncoso G, Guerra-

Infiante FM, Morales-Méndez I, Ortiz-Juárez VR, Bouazzaoui NL, Meyrem K, Abouqal R, Madani N, Zeggwagh AA, Abidi PK, Dendane T, Bhutto GH, Luciani K, Gisela González C, Díaz Tavera ZR, Ulloa JC, Ramirez E, Atencio-Espinoza T, Sarmiento López F, Torres-Zegarra SL, Silva Astete N, Campos Guevara F, Bazan Mendoza C, Valencia Ramirez A, Soto Pastrana J, Navoa-Ng JA, Villanueva VD, Tolentino MC, Mendoza MT, Riego Javier A, Belmonte LS, Duszynska W, Kaiser T, Szmaj B, Hakawi A, Tambyah PA, Kubacka I, Lesnakova A, Ali IM, Satti AA, Jamulitrat S, Thamlikitkul V, Erben N, Ozgunes I, Usluer G, Sener A, Uzun C, Senol G, Ersoz G, Kaya A, Kaya Z, Kuyucu N, Demirdal T, Duygu F, Willke A, Meric M, Azak E, Esen S, Ulger F, Dilek A, Yilmaz H, Sirmatel F, Oztoprak N, Koksali I, Yilmaz G, Kaya S, Ulusoy H, Oncul O, Haznedaroglu T, Gorenek L, Acar A, Gurbuz Y, Tutuncu E, Tuna N, Turgut H, Sacar S, Sungurtekin H, Uğurcan D, Nevzat-Yalcin A, Turhan O, Gunay N, Gumus E, Dursun O, Ozdemir D, Geyik MF, Yildirim M, Erdogan S, Kendirli T, Ince E, Çiftçi E, Özdemir H, Aslan T, Anh NQ, Thu TA, Le TA, Trang DT, Nga TK, Zruong PH. Surgical site infections, International Nosocomial Infection Control Consortium (INICC) report, data summary of 30 countries, 2005-2010. *Infect Control Hosp Epidemiol.* 2013 Jun;34(6):597-604.

(1)International Nosocomial Infection Control Consortium, Buenos Aires, Argentina. victor_rosenthal@inicc.org

OBJECTIVE: To report the results of a surveillance study on surgical site infections (SSIs) conducted by the International Nosocomial Infection Control Consortium (INICC). **DESIGN:** Cohort prospective multinational multicenter surveillance study. **SETTING:** Eighty-two hospitals of 66 cities in 30 countries (Argentina, Brazil, Colombia, Cuba, Dominican Republic, Egypt, Greece, India, Kosovo, Lebanon, Lithuania, Macedonia, Malaysia, Mexico, Morocco, Pakistan, Panama, Peru, Philippines, Poland, Salvador, Saudi Arabia, Serbia, Singapore, Slovakia, Sudan, Thailand, Turkey, Uruguay, and Vietnam) from 4 continents (America, Asia, Africa, and Europe). **PATIENTS:** Patients undergoing surgical procedures (SPs) from January 2005 to December 2010. **METHODS:** Data were gathered and recorded from patients hospitalized in INICC member hospitals by using the methods and definitions of the Centers for Disease Control and Prevention National Healthcare Safety Network (CDC-NHSN) for SSI. SPs were classified into 31 types according to International Classification of Diseases, Ninth Revision, criteria. **RESULTS:** We gathered data from 7,523 SSIs associated with 260,973 SPs. SSI rates were significantly higher for most SPs in INICC hospitals compared with CDC-NHSN data, including the rates of SSI after hip prosthesis (2.6% vs. 1.3%; relative risk [RR], 2.06 [95% confidence interval (CI), 1.8-2.4]; $P < .001$), coronary bypass with chest and donor incision (4.5% vs. 2.9%; RR, 1.52 [95% CI, 1.4-1.6]; [$P < .001$); abdominal hysterectomy (2.7% vs. 1.6%; RR, 1.66 [95% CI, 1.4-2.0]; $P < .001$); exploratory abdominal surgery (4.1% vs. 2.0%; RR, 2.05 [95% CI, 1.6-2.6]; $P < .001$); ventricular shunt, 12.9% vs. 5.6% (RR, 2.3 [95% CI, 1.9-2.6]; $P < .001$, and others. **CONCLUSIONS:** SSI rates were higher for most SPs in INICC hospitals compared with CDC-NHSN data. PMID: 23651890

Rosenthal VD(1), Pawar M, Leblebicioglu H, Navoa-Ng JA, Villamil-Gómez W, Armas-Ruiz A, Cuéllar LE, Medeiros EA, Mitrev Z, Gikas A, Yang Y, Ahmed A, Kanj SS, Dueñas L, Gurskis V, Mapp T, Guanche-Garcell H, Fernández-Hidalgo R, Kübler A. Impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional hand hygiene approach over 13 years in 51 cities of 19 limited-resource countries from Latin America, Asia, the Middle East, and Europe. *Infect Control Hosp Epidemiol.* 2013 Apr;34(4):415-23.

(1)International Nosocomial Infection Control Consortium, Buenos Aires, Argentina. victor_rosenthal@inicc.org

OBJECTIVE: To assess the feasibility and effectiveness of the International Nosocomial Infection Control Consortium (INICC) multidimensional hand hygiene approach in 19 limited-resource countries and to analyze predictors of poor hand hygiene compliance. **DESIGN:** An observational, prospective, cohort, interventional, before-and-after study from April 1999 through

December 2011. The study was divided into 2 periods: a 3-month baseline period and a 7-year follow-up period. **SETTING:** Ninety-nine intensive care unit (ICU) members of the INICC in Argentina, Brazil, China, Colombia, Costa Rica, Cuba, El Salvador, Greece, India, Lebanon, Lithuania, Macedonia, Mexico, Pakistan, Panama, Peru, Philippines, Poland, and Turkey. **PARTICIPANTS:** Healthcare workers at 99 ICU members of the INICC. **METHODS:** A multidimensional hand hygiene approach was used, including (1) administrative support, (2) supplies availability, (3) education and training, (4) reminders in the workplace, (5) process surveillance, and (6) performance feedback. Observations were made for hand hygiene compliance in each ICU, during randomly selected 30-minute periods. **RESULTS:** A total of 149,727 opportunities for hand hygiene were observed. Overall hand hygiene compliance increased from 48.3% to 71.4% ([Formula: see text]). Univariate analysis indicated that several variables were significantly associated with poor hand hygiene compliance, including males versus females (63% vs 70%; [Formula: see text]), physicians versus nurses (62% vs 72%; [Formula: see text]), and adult versus neonatal ICUs (67% vs 81%; [Formula: see text]), among others. **CONCLUSIONS:** Adherence to hand hygiene increased by 48% with the INICC approach. Specific programs directed to improve hand hygiene for variables found to be predictors of poor hand hygiene compliance should be implemented. PMID: 23466916

Ruskovska T(1), Bernlohr DA. Oxidative stress and protein carbonylation in adipose tissue - implications for insulin resistance and diabetes mellitus. *J Proteomics.* 2013 Oct 30;92:323-34.

(1)Faculty of Medical Sciences, Goce Delcev University, Stip, Former Yugoslav Republic of Macedonia. Electronic address: tatjana.ruskovska@ugd.edu.mk.

While historically considered simply as a depot for excess energy, white adipose tissue is a dynamically active endocrine organ capable of responding to a variety of efferent stimuli resulting in the synthesis and secretion of peptides, proteins and metabolites that serve as signal transducers to the peripheral and central circulation. Such regulation controls a variety of physiological processes including energy expenditure, food intake, reproductive capacity and responsiveness to insulin. Indeed, the accumulation of inflammatory cells in white adipose tissue is considered to be causative in the development of insulin resistance and eventually type 2 diabetes mellitus. A large body of evidence suggests that oxidative stress in adipose tissue not only correlates with insulin resistance but is also causative in its development. Moreover, using the available plasma oxidative stress biomarkers, many clinical studies have shown the presence of systemic oxidative stress in obese insulin resistant subjects, and its decrease after the successful treatment of obesity. In this review we emphasize the role of protein carbonylation in dysfunctional obese white adipose tissue and its metabolic implications. We focus on glutathione S-transferase A4 as the key enzyme for trans-4-hydroxy-2-nonenal and trans-4-oxo-2-nonenal removal from the cell, thus preventing protein carbonylation. This article is part of a Special Issue entitled: Posttranslational Protein modifications in biology and Medicine. PMID: PMC3769464. PMID: 23584148

Seme K(1), Maver PJ, Korač T, Canton A, Částková J, Dimitrov G, Filippova I, Hudecová H, Iljazović E, Kaič B, Kesić V, Kuprevičienė N, Laušević D, Molnár Z, Perevoščikovs J, Spaczyński M, Stefanova V, Učakar V, Poljak M. Current status of human papillomavirus vaccination implementation in central and eastern Europe. *Acta Dermatovenerol Alp Panonica Adriat.* 2013;22(1):21-5.

(1)Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.

We present a review of the current implementation status of vaccination against human papillomaviruses (HPV) and available data concerning the burden of HPV infection and HPV type-specific distribution in 16 central and eastern European countries: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Estonia, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia,

and The Former Yugoslav Republic of Macedonia. At least one current HPV prophylactic vaccine is registered in all central and eastern European countries except Montenegro. Six countries-Bulgaria, the Czech Republic, Latvia, Romania, Slovenia, and Former Yugoslav Republic of Macedonia-have integrated the HPV vaccination into their national immunization program and currently provide routine vaccination free of charge to the primary target population. Ten countries have not integrated HPV vaccination into the national immunization program. The key reasons for lack of implementation of HPV vaccination into the national immunization program are the high vaccine cost and negative public perception. Vaccination of males is not recommended in any country in the region. PMID: 23674181

Simonoska Crcarevska M(1), Geskovski N, Calis S, Dimchevska S, Kuzmanovska S, Petruševski G, Kajžanoska M, Ugarkovic S, Goracinova K. Definition of formulation design space, in vitro bioactivity and in vivo biodistribution for hydrophilic drug loaded PLGA/PEO-PPO-PEO nanoparticles using OFAT experiments. Eur J Pharm Sci. 2013 Feb 22;49(1):65-80.

(1)Institute of Pharmaceutical Technology, Faculty of Pharmacy, University of "Ss. Cyril & Methodius", Vodnjanska 17, 1000 Skopje, Macedonia. Electronic address: msimonoska@ff.ukim.edu.mk.

Modified nanoprecipitation method was used for improved incorporation of hydrophilic drug (irinotecan hydrochloride) into the PLGA/PEO-PPO-PEO blended and blended/adsorbed nanoparticles. One factor at a time (OFAT) variation experiments were conducted in order to determine key formulation factors (concentration and volume of drug solution, evaporation rate and PLGA/PEO-PPO-PEO ratio) influencing nanoparticle properties (particle size and size distribution, encapsulation efficiency, drug content, zeta potential, drug dissolution rate, as well as protein binding capacity). The insight into in vivo behavior of prepared nanoparticles and their potential for effective anticancer treatment was gained by performing biodistribution and cell culture studies as part of OFAT experiments. The mean particle size, mainly dependent upon PLGA/PEO-PPO-PEO ratio, was in the range of 112-125nm, with narrow unimodal distribution (PDI~0.1). Encapsulation efficiency (32-63%) was impacted by evaporation rate and PLGA/PEO-PPO-PEO ratio. Drug content (0.2-1.51%) and controlled release properties were related to the influence of all tested formulation factors. Structural information for the studied nanoparticles was obtained using DSC and FT-IR spectroscopy. Zeta potential values indicated that presence of PEO-PPO-PEO in the formulations shielded the high surface negative charge of PLGA. PEO-PPO-PEO surface coverage of PLGA/PEO-PPO-PEO blended as well as blended/adsorbed nanoparticles depended upon amount of used PEO-PPO-PEO during preparation procedure and was related to the protein resistant characteristics of nanoparticles. Results from in vivo studies evidenced prolonged blood circulation time of the prepared nanoparticles, while cell culture studies indicated higher in vitro bioefficacy compared to free drug. Performed experiments defined possible design space and justified further optimization of formulation using experimental design studies. PMID: 23439240

Smilkov K(1), Petreska Ivanovska T, Petrushevska Tozi L, Petkovska R, Hadjieva J, Popovski E, Stafilov T, Grozdanov A, Mladenovska K. Optimization of the formulation for preparing Lactobacillus casei loaded whey protein-Ca-alginate microparticles using full-factorial design. J Microencapsul. 2014;31(2):166-75.

(1)Faculty of Medical Sciences, University "Goce Delčev", Krste Misirkov bb, POB 201, 2000 Stip, Macedonia.

Abstract Context: This article presents specific approach for microencapsulation of Lactobacillus casei using emulsion method followed by additional coating with whey protein. Methods: Experimental design was employed using polynomial regression model at 2nd level with three independent variables, concentrations of alginate, whey protein and CaCl₂. Physicochemical, biopharmaceutical and biological properties were investigated.

Results: In 11 series generated, negatively charged microparticles were obtained, with size 6.99-9.88 μm, Ca-content 0.29-0.47 mg per 10 mg microparticles, and viability of the probiotic 9.30-10.87 log₁₀CFU/g. The viability after 24 hours in simulated gastrointestinal conditions was between 3.60 and 8.32 log₁₀CFU/g. Discussion: Optimal formulation of the microparticles that ensures survival of the probiotic and achieves controlled delivery was determined: 2.5% (w/w) alginate, 3% (w/w) CaCl₂ and 3% (w/w) whey protein. Conclusion: The advantageous properties of the L. casei-loaded microparticles make them suitable for incorporation in functional food and/or pharmaceutical products. PMID: 23919399

Spasovski D(1), Latifi A(2), Marina N(1), Calovski J(1), Kafedziska I(1), Božinovski G(1), Percinkova S(1), Slaninka-Micevska M(3), Balkanov T(3), Dejanova B(4), Alabakovska S(5), Krstevska-Balkanov S(2), Spasovski G(6), Spasovski D(7). Symmetric dimethyl arginine and N-acetyl-β-D-glucosaminidase lysozymuria of proximal renal tubules as a target for nephrotoxicity in patients with rheumatoid arthritis treated with disease modifying antirheumatic drugs. J Nephropathol. 2013 Jan;2(1):36-52.

(1)Department of Rheumatology. (2)Department of Hematology. (3)Department of Preclinic Farmacology. (4)Department of Physiology. (5)Institutes of preclinical biochemistry. (6)Department of Nephrology. (7)Department of Rheumatology, University Clinical Centre, Skopje, Republic of Macedonia.

BACKGROUND: The aim of this study was to determine the effect of initial therapy with some disease modifying antirheumatic drugs (DMARDs) (Methotrexate and Ketoprofen) on glomerular and tubular integrity in patients with Rheumatoid arthritis (RA). OBJECTIVES: OBJECTIVES: To determine whether there is a change in clinical and laboratory indicators of renal function in course of the follow up of treatment and whether that change correlates with the dynamics of the quantity of enzymes excreted in urine and reactants of the acute phase. MATERIALS AND METHODS: Using colorimetric method for determination of NAG, samples of 70 participants were examined (35 RA patients treated with Ketoprofen only, 35 RA patients treated with combined use of Methotrexate and Ketoprofen). The follow up was 5 time-intervals in the course of 24 weeks. RESULTS: There was moderate correlation between NAG and microalbuminuria (r=0,34) in the group of patients treated with Ketoprofen only, while statistically significant correlation (r=0,21) was seen in group of patients with combined use of Methotrexate and Ketoprofen. NAG enzymuria in size, number of patients registered, and time of appearance were greater and appears earlier in the group with the combined use of Methotrexate and Ketoprofen compared with the mono-therapy with Ketoprofen. Mean urinary NAG induction was increasing with the concomitant use of Methotrexate and Ketoprofen. CONCLUSIONS: Methotrexate is more potent NAG inductor than Ketoprofen and provokes greater tubular enzymuria than Ketoprofen. PMID: 24475424

Spasovski D(1), Latifi A, Osmani B, Krstevska-Balkanov S, Kafedziska I, Slaninka-Micevska M, Dejanova B, Alabakovska S, Balkanov T. Determination of the diagnostic values of asymmetric dimethylarginine as an indicator for evaluation of the endothelial dysfunction in patients with rheumatoid arthritis. Arthritis. 2013;2013:818037.

(1)Department of Rheumatology, University Clinical Centre, Skopje, Macedonia.

Introduction. To compare the diagnostic values of laboratory variables, to present evaluations of the diagnostic test for asymmetric dimethyl arginine (ADMA), rheumatoid factor (RF), C-reactive protein (CRP), and DAS28 index, and to define the effect of untreated rheumatoid arthritis on endothelial function. In order to determine whether ADMA changes depending on the disease evolution, ADMA was used as an indicator for endothelial dysfunction. Methods. Using an ELISA technology of DLD-Diagnostika-GMBH for the detection of ADMA, the samples of serum and urine have been examined in 70 participants (35 RA who were not treated, 35 healthy controls). RF was defined with the

test for agglutination (Latex RF test) in the same participants. Results. Out of 35 examined patients with RA, RF appeared in 17 patients (sensitivity of the test, 51.42%). In 20 of the 35 examined patients with RA, we found the presence of ADMA (sensitivity of the test, 57.14%). Anti-CCP antibody was present in 24 examined patients with RA (sensitivity of the test, 68.57%). Conclusion. ADMA has equal or very similar sensitivity and specificity to RF in untreated RA (sensitivity of 57.14% versus 48.57%, specificity of 88.57% versus 91.42%) in the detection of asymptomatic endothelial dysfunction in untreated RA. PMCID: PMC3671235. PMID: 23762554

Spiroski M(1), Milenkovic Z, Petlichkovski A, Ivanovski L, Topuzovska IK, Djulejic E. Killer cell immunoglobulin-like receptor genes in four human West Nile virus infections reported 2011 in the Republic of Macedonia. Hum Immunol. 2013 Mar;74(3):389-94.

(1)Institute of Immunobiology and Human Genetics, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Macedonia. mspiroski@yahoo.com

West Nile virus (WNV) is a neurotropic, arthropod-borne flavivirus that is maintained in an enzootic cycle between mosquitoes and birds, but can also infect and cause disease in horses and humans. The aim of this study was to examine KIR gene polymorphisms by determining the frequencies of 16 KIR genes and pseudogenes and KIR genotypes in Macedonian patients with West Nile virus infection, and to compare with healthy Macedonians. The studied sample consists Republic of Macedonia, hospitalized at the University Clinic of Infective Diseases between September 2011 and October 2011, and reported through WHO. For KIR genotyping, commercially available PEL-FREEZ KIR genotyping SSP kit (DynaL Biotech, Brown Deer, WI) was used. The population genetics analysis package, Arlequin, was used for analysis of the data. We found that all 16 KIR genes were observed in the studied individuals and framework genes (KIR3DL3, KIR3DP1, KIR2DL4, and KIR3DL2) were present in all individuals. Comparison of KIR frequencies between Macedonian patients with West Nile virus infection and healthy Macedonian population reveals several significant differences in the inhibitory group (KIR2DL2), and in the non-inhibitory group (KIR2DS1, KIR2DS2, KIR2DS5, and KIR3DS1). The single most frequent genotypes in the Bx group were genotypes ID71 and ID89 with statistically significant difference compared to healthy Macedonians. Our results suggest that specific KIR genotypes could be connected with West Nile virus infection. PMID: 23220498

Stankov A(1), Jakovski Z, Pavlovski G, Muric N, Dwork AJ, Cakar Z. Air gun injury with deadly aftermath--case report. Leg Med (Tokyo). 2013 Jan;15(1):35-7.

(1)Institute of Forensic Medicine, Criminalistic and Medical Deontology, Ss. Cyril and Methodius University, School of Medicine, Skopje, Republic of Macedonia. astankov@medf.ukim.edu.mk

In Republic of Macedonia the use of air guns is quite widespread. They are used mainly for target practice. They are regulated by the Law of Arms, where they are defined as pneumatic weapons. There is no legal limit on type or quantity of ammunition that one may possess. Our Institute performs at least 90% of the forensic autopsies in Macedonia. In this report we describe the only fatality by pneumatic weapon to come to our attention over the past 10 years. A 6-year-old girl was accidentally wounded by her brother when he and his father were trying a new air gun, a 4.5mm single shot, break barrel, spring piston air rifle manufactured in China under the brand "Westlake". She died within minutes. Autopsy showed cardiac tamponade due to penetration of the aorta. A 0.5g metal projectile, 4.5mm in diameter, with a pointed, conical shape, was recovered from the pericardial sac. PMID: 23017978

Stefkov G(1), Miova B(2), Dinevska-Kjovkarovska S(3), Stanoeva JP(3), Stefova M(3), Petrusevska G(4), Kulevanova S(1). Chemical characterization of Centaurium erythraea L. and

its effects on carbohydrate and lipid metabolism in experimental diabetes. J Ethnopharmacol. 2014 Feb 27;152(1):71-7.

(1)Faculty of Pharmacy, Ss. Cyril and Methodius University, Vodnjanska 17, 1000 Skopje, R. Macedonia. (2)Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Gazi Baba bb, 1000 Skopje, Republic of Macedonia. Electronic address: bmiova@yahoo.com. (3)Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Gazi Baba bb, 1000 Skopje, Republic of Macedonia. (4)Faculty of Medicine, Ss. Cyril and Methodius University, Vodnjanska 17, 1000 Skopje, Republic of Macedonia.

ETHNOPHARMACOLOGICAL RELEVANCE: Centaurium erythraea L. fam. Gentianaceae (CE) has been traditionally used for centuries in folk medicine of Balkans as a bitter medicinal herb for digestive complications and for treating febrile conditions and diabetes. The aim of this study was to gain insight into the chemical composition and underlying biochemical mechanism of action of the antihyperglycemic and antilipidemic activities of the dry extract of Centaurium erythraea L., widely growing and traditionally used medicinal plant in the Republic of Macedonia. MATERIALS AND METHODS: An ultrasonic methanol maceration of the aerial parts of the dried plant was performed and the extract was freeze-dried. HPLC-DAD-ESI-MS(n) was carried out on 150mm×4.6mm, 5µm RP-18 Eclipse XDB column, at 40°C. Mobile phase: water with 1% formic acid (A) and methanol (B) with linear gradient starting with 10% B was used to reach 15% at 5min, 40% B at 25min, 55% of B at 50min and 100% at 60min, with flow rate of 0.4mLmin⁻¹. Normal and streptozotocin (STZ) hyperglycemic Wistar rats were used for assessment of the antihyperglycemic and antilipidemic activity by measurement of the key carbohydrate-related enzymes and substrates, as well as lipid state of the organism. RESULTS: HPLC-DAD-ESI-MS(n) analyses revealed presence of four different secoiridoids, seven flavonoid glycosides and seven xanthenes in the freeze-dried extract of CE representing 53%, 25% and 22% of all compounds, respectively. The short-term (12 days) treatment of the STZ-diabetic rats with CE-extracts resulted in a 74% reduction of the produced hyperglycemia, which is only 6% less than the reduction caused by glibenclamide (GLB, positive control). The CE-extract had a significant impact on the hepatic carbohydrate metabolism enhancing the direct synthesis of glycogen, normalizing phosphorylase a activity and reducing the activity of glucose-6-phosphatase, which further causes reduction in production of blood glucose level. The long-term (45 days) treatment showed that the HbA1c in CE-treated group of animals was even lower than in the GLB-treated groups. The antilipidemic assessment of the CE-extract revealed decrease of total cholesterol, triglycerides, HDL and LDL level in the blood of the normal and STZ-hyperglycemic rats. CONCLUSION: The obtained results indicate that treatment with CE extract in STZ-diabetic rats regulates the elevated level of blood glucose and carbohydrate-related disturbances slightly better than the effect of glibenclamide. There was also regulation of the serum lipid status in diabetic rats. Identified groups of bitter compounds in the extract (flavonoides, iridoids and xanthenes) probably have influence on the expressed antihyperglycaemic effect. PMID: 24321864

Stojanovski G(1), Stankovski M. Comparison of predictive control methods for high consumption industrial furnace. ScientificWorldJournal. 2013 Nov 10;2013:279042.

(1)Department of Automation and System Engineering, Faculty of Electrical Engineering and Information Technologies, Saints Cyril and Methodius University in Skopje, ul. Ruger Boskovic bb., 1000 Skopje, Macedonia.

We describe several predictive control approaches for high consumption industrial furnace control. These furnaces are major consumers in production industries, and reducing their fuel consumption and optimizing the quality of the products is one of the most important engineer tasks. In order to demonstrate the benefits from implementation of the advanced predictive control algorithms, we have compared several major criteria for furnace control. On the basis of the analysis, some important conclusions have been drawn. PMCID: PMC3844168. PMID: 24319354

Stojkovski V(1), Hadzi-Petrushev N, Ilieski V, Sopi R, Gjorgoski I, Mitrov D, Jankulovski N, Mladenov M. Age and heat exposure-dependent changes in antioxidant enzymes activities in rat's liver and brain mitochondria: role of alpha-tocopherol. *Physiol Res.* 2013;62(5):503-10.

(1)Faculty of Natural Sciences and Mathematics, Institute of Biology, "Sts, Cyril and Methodius" University, Skopje, Macedonia. mitkom@pmf.ukim.mk.

To investigate the role of mitochondrial antioxidant capacity during increased susceptibility to heat accompanied by the aging, young and aged Wistar rats were exposed on heat for 60 min. After heat exposure, hepatic and brain mitochondria were isolated. Our results revealed changes in antioxidant enzyme activities in liver and brain mitochondria from young and to a greater extent in aged rats. Our measurements of MnSOD, GPx and GR activity indicate greater reactive oxygen species production from the mitochondria of aged heat exposed in comparison to young heat exposed rats. Also in the aged rats, the effect of alpha-tocopherol treatment in the prevention of oxidative stress occurred as a result of heat exposure, is less pronounced. Taken together, our data suggest that mitochondria in aged rats are more vulnerable and less able to prevent oxidative changes that occur in response to acute heat exposure. PMID: 24020814

Sulejmani E(1), Hayaloglu AA(2), Rafajlovska V(3). Study of the chemical composition, proteolysis, volatile compounds, and textural properties of industrial and traditional Beaten (Bieno sirenje) ewe milk cheese. *J Dairy Sci.* 2014 Mar;97(3):1210-24.

(1)Department of Food Technology and Nutrition, State University of Tetova, 1200, Tetovo, Republic of Macedonia; Department of Food Engineering, Inonu University, 44280 Malatya, Turkey. Electronic address: erhan.sulejmani@unite.edu.mk. (2)Department of Food Engineering, Inonu University, 44280 Malatya, Turkey. (3)Department of Food Technology and Biotechnology, Ss. Cyril and Methodius University in Skopje, 1000 Skopje, Republic of Macedonia.

The objective of this study was to determine the gross composition, proteolysis, and volatile and texture profiles during ripening of industrial (IND) and traditional (TRD) Beaten (Bieno sirenje) cheeses made by using ewe milk. In the course of the analyses, statistical differences were determined in some physicochemical parameters, nitrogen fractions, and total free amino acid levels between TRD and IND types of cheese. Higher levels of proteolysis were observed in IND cheeses than in TRD cheeses during ripening. Levels of residual β - and α s-caseins were 72.2 and 48.7%, respectively, in 180-d-old TRD cheeses. However, the residual levels were 52.8% for β -casein and 18% for α s-casein in IND cheeses. Similar differences were noted for the reversed-phase HPLC peptide profiles of 2 types of cheeses. Also, higher concentrations of peptides were eluted in IND cheeses than in TRD cheeses during ripening. A total of 73 volatile compounds, including alcohols (16), esters (17), acids (14), terpenes (7), ketones (5), aldehydes (4), and miscellaneous (10) were identified. The IND cheeses contained higher levels of carboxylic acids, esters, alcohols, and terpenes than the TRD cheeses; however, the same levels of methyl ketones were determined in the 2 types of cheeses at the end of ripening. These may be due to some differences (e.g., pasteurization and scalding temperature, among other factors) in the manufacture of the 2 types of Beaten cheeses. The textural profile of Beaten cheeses showed that TRD production method resulted in firmer, less fracturable, and stiffer cheeses than the IND production method. In conclusion, the results suggest that the use of industrial production method (pasteurization of cheese milk and curd scalding at 70°C) in the manufacture of Beaten ewe milk cheese enriched the volatile profile of the cheese. PMID: 24377800

Suturkova L(1), Brezovska K, Poceva-Panovska A, Grozdanova A, Knežević Apostolski S, Basta I. Antibodies to Glycoproteins Shared by Human Peripheral Nerve and *Campylobacter jejuni* in Patients with Multifocal Motor Neuropathy. *Autoimmune Dis.*

2013;2013:728720.

(1)Faculty of Pharmacy, Ss. Cyril and Methodius, University Skopje, Macedonia.

We have tested serum samples from 24 patients with multifocal motor neuropathy (MMN) for reactivity to ganglioside GM1 and to Gal(β 1-3)GalNAC-bearing glycoproteins isolated from human peripheral nerve and from *Campylobacter jejuni* (Cj) serotype O:19. IgM anti-GM1 antibodies were detected by ELISA in 11 patients (45.8%) with MMN and in only one subject (4%) from the control group. Western blots showed positive reactivity of sera from 6 patients (25%) with MMN to several Gal(β 1-3)GalNAC-bearing glycoproteins from human peripheral nerve and from Cj O:19 isolates. Sera from three patients (12.5%) with MMN showed positively reactive bands with similar electrophoretic mobility in all isolates (60-62 kDa, 48-51 kDa, 42 kDa, and 38 kDa). All six patients showed positive reactivity to 48-52 kDa protein isolated from human peripheral nerve. Increased titer of IgG antibodies to 60-62 kDa protein isolated from Cj O:19 associated with Guillain-Barré syndrome was detected in three patients, and their serum showed also IgG positive reactivity to peripheral nerve antigen with the same electrophoretic mobility. One of these patients had a previous history of Cj infection which suggests the possibility that Cj may be also involved in the pathogenesis of MMN. PMID: PMC3666391. PMID: 23762534

Tenev A(1), Markovska-Simoska S, Kocarev L, Pop-Jordanov J, Müller A, Candrian G. Machine learning approach for classification of ADHD adults. *Int J Psychophysiol.* 2013 Jan 27. pii: S0167-8760(13)00023-8.

(1)Faculty for Computer Science and Engineering, University of Skopje, Former Yugoslav Republic of Macedonia. Electronic address: aleksandar.tenev@finki.ukim.mk.

Machine learning techniques that combine multiple classifiers are introduced for classifying adult attention deficit hyperactivity disorder (ADHD) subtypes based on power spectra of EEG measurements. The analyzed sample includes 117 adults (67 ADHD, 50 controls). The measurements are taken for four different conditions: two resting conditions (eyes open and eyes closed) and two neuropsychological tasks (visual continuous performance test and emotional continuous performance test). We divide the sample into four data sets, one for each condition. Each data set is used for training of four different support vector machine classifiers, while the output of classifiers is combined using logical expression derived from the Karnaugh map. The results show that this approach improves the discrimination between ADHD and control groups, as well as between ADHD subtypes. PMID: 23361114

Tozija F, Jankulovski N. Strategy to improve quality in emergency medical services: from assessment to policy. *Arh Hig Rada Toksikol.* 2013 Dec;64(4):567-79.

The aim of this paper was to present the strategic approach applied for improvement of quality in emergency medical services (EMS) in the Republic of Macedonia. This approach was accomplished through three stages: (I) assessment and recommendations for policies; (II) development of innovative evidence-based programmes; and (III) policy implementation. Strategic assessment of EMS was performed by applying WHO standard methodology. A survey was conducted in 2006/2007 on the national level in fifteen general hospitals, four university hospitals, and sixteen pre-hospital EMS. The overall evaluation was based on a hospital emergency department (ED) questionnaire, information on the general characteristics of the pre-hospital dispatch centre, review of ED medical records, and the patient questionnaire. The key findings of the assessment showed that EMS required extensive changes and improvements. Pre-hospital EMS was not well-developed and utilised. Hospital EDs were not organised as separate divisions ran by a head medical doctor. The diagnostic and treatment capacities were insufficient or outdated. Most of the surveyed hospitals were capable of providing essential diagnostic tests in 24 h or less. There was no follow-up of the EMS patients or an appropriate link between the hospital EDs and primary health care facilities. The

main findings of the assessment, recommendations, and proposals for action served as the basis for new policies and integrated into Macedonia's official strategy for emergency medical services 2009-2017. PMID: 24384764

Trajanovska AS(1), Vujovic V, Ignjatova L, Janicevic-Ivanovska D, Cibisev A. Sexual dysfunction as a side effect of hyperprolactinemia in methadone maintenance therapy. Med Arh. 2013;67(1):48-50.

(1)Day Hospital for Drug Addiction, Psychiatric Hospital Skopje, R. Macedonia.

Although endocrine abnormalities are recognized in opiate users, very little is known about the range of hormones affected, their pathophysiology and their clinical relevance. Various endocrine abnormalities have been reported in these patients including, increased prolactin levels and abnormalities in sexual hormone. Pathophysiological mechanism postulated does explain these findings including direct action of heroin or methadone at the hypothalamic pituitary level. The aim of this study was to explore the effects of heroin and methadone maintenance treatment on the plasma prolactin levels and sexual function. Material and methods: We evaluated 20 male narcotic addicts maintained of methadone more than 3 years on oral high dose methadone 60-120 mgr/day. Patients taking neuroleptic therapy were excluded from the study because neuroleptic-included hyperprolactinemia. We also evaluated group of twenty male heroin addicts on the street heroin. The prolactin plasma levels were assayed using the chemiluminescent immunometric assay (CLIA)--high sensitive methods. The normal range of prolactin levels was 1,5-17 ng/ml (53-360 nmol/l) for men and 1,90-25,0 ng/ml for women. The sexual function was assessed using a Questionnaire: International Index of Erectile Function (IIEF) with 15 items in four levels of sexual function. The differences between two examination groups were determined by a student's t test. The results show that street heroin addicts (55% of them have high level of prolactin) have significantly higher plasma prolactin levels ($p = 0.006$) than the group of methadone maintenance patients (only 15% of them have high prolactin level). In our study, when we compared sexual dysfunction in examination groups in some domains, we did not find statistical significant results (sexual desire $p = 0.52$ and overall satisfaction $p = 0.087$). But in domains of erectile function $p = 0.011$ and orgasm function $p = 0.033$ we got statistical significant results. PMID: 23678840

Tusevski O(1), Petreska Stanoeva J(2), Stefova M(2), Simic SG(1). Phenolic Profile of Dark-Grown and Photoperiod-Exposed *Hypericum perforatum* L. Hairy Root Cultures. ScientificWorldJournal. 2013 Dec 26;2013:602752.

(1)Department of Plant Physiology, Institute of Biology, Faculty of Natural Sciences and Mathematics, "Ss. Cyril and Methodius" University, P.O. Box 162, 1000 Skopje, Macedonia. (2)Department of Analytical Chemistry, Institute of Chemistry, Faculty of Natural Sciences and Mathematics, "Ss. Cyril and Methodius" University, P.O. Box 162, 1000 Skopje, Macedonia.

Hypericum perforatum L. is a medicinal plant considered as an important natural source of secondary metabolites with a wide range of pharmacological attributes. Hairy roots (HR) were induced from root segments of in vitro grown seedlings from *H. perforatum* after cocultivation with *Agrobacterium rhizogenes* A4. Investigations have been made to study the production of phenolic compounds in dark-grown (HR1) and photoperiod-exposed (HR2) cultures. The chromatographic analysis of phenolic acids, flavonols, flavan-3-ols, and xanthenes revealed marked differences between HR1 and HR2 cultures. The production of quinic acid, kaempferol, and seven identified xanthenes was increased in HR2. Moreover, HR2 showed a capability for de novo biosynthesis of two phenolic acids (3-p-coumaroylquinic acid and 3-feruloylquinic acid), three flavonol glycosides (kaempferol hexoside, hyperoside, and quercetin acetylglucoside), and five xanthenes (tetrahydroxy-one-methoxyxanthone, 1,3,5-trihydroxy-6-methoxyxanthone, 1,3,5,6-tetrahydroxy-2-prenylxanthone, paxanthone, and banaxanthone E). On the other side, HR1 cultures were better producers of flavan-3-

ols (catechin, epicatechin, and proanthocyanidin dimers) than HR2. This is the first comparative study on phenolic profile of *H. perforatum* HR cultures grown under dark and photoperiod conditions. PMID: 24453880

Velickova E(1), Winkelhausen E, Kuzmanova S, Moldão-Martins M, Alves VD. Characterization of multilayered and composite edible films from chitosan and beeswax. Food Sci Technol Int. 2013 Nov 27. [Epub ahead of print]

(1)Department of Food Technology and Biotechnology, University Ss. Cyril and Methodius, Republic of Macedonia.

Chitosan-based edible films were prepared and subjected to cross-linking reactions using sodium tripolyphosphate and/or to beeswax coating on both films interfaces. In addition, chitosan-beeswax emulsion-based films were produced. The goal of these modifications of the chitosan films was the improvement of their barrier to water vapor and to decrease their affinity to liquid water maintaining or improving the mechanical and optical properties of the original chitosan films. The cross-linking with tripolyphosphate decreased both the water vapor permeability and the water absorption capacity to about 55% and 50% of that of the original chitosan films, respectively. However, there was an increase in the films stiffness, revealed by the increased Young modulus from 42 kPa up to 336 kPa. The multilayered wax-chitosan-wax films exhibited a similar improvement of the barrier properties to water vapor, with the advantage of maintaining the mechanical properties of the original chitosan films. However, these wax-coated films showed a higher water absorption capacity, which is believed to be a consequence of water entry into small pores between the film and the wax layers. Regarding the film samples subjected to cross-linking and further coating with beeswax, a similar behavior as the uncoated cross-linked films was observed. The emulsion-based composite films were characterized by a substantial decrease of the water vapor permeability (40%), along with a decrease in their stiffness. Regarding the optical properties, all films presented a yellowish color with similar values of lightness, chroma, and hue. PMID: 24285830

Veljanoska-Sarafiloska EM(1), Jordanoski M, Stafilov T. Presence of DDT metabolites in water, sediment and fish muscle tissue from Lake Prespa, Republic of Macedonia. J Environ Sci Health B. 2013;48(7):548-58.

(1)Hydrobiological Institute, Ohrid, Republic of Macedonia.

Organochlorine pesticides were determined in water and sediment samples collected from the littoral zone of Lake Prespa, as well as from its three main tributaries (the rivers Golema, Brajinska and Kranska), during the period 2004 to 2006. In addition, muscle tissue samples of barbus fish (*Barbus prespensis* Karaman, 1928) collected from the littoral zone of Lake Prespa were also analysed. The obtained results give an overview of the contamination levels of these problematic compounds at their potential sources in the river mouths, in the potentially affected, species-rich littoral section of the lake and in the muscle tissue of one selected fish species, collected near the rivers' deltas. Special attention was paid to the presence of some DDT metabolites (1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (p,p'-DDE); (1,1-dichloro-2,2-bis(p-chlorophenyl)ethane (p,p'-DDD) and 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (p,p'-DDT). The extraction of pesticides from water samples was done by liquid-liquid partition in dichloromethane. For the sediment and fish tissue we used solid-liquid extraction. The extracted residues were analyzed on a gas chromatograph equipped with an electron capture detector (GC-ECD). The results of the respective studies indicated the presence of DDT metabolic forms in the samples of the three analysed matrices. The highest levels of presence for these pollutants were found in the muscle tissue of the fish samples. The total DDTs content in the analysed muscle tissue samples range from 11.67 to 13.58 $\mu\text{g kg}^{-1}$ of fresh tissue. The average total DDTs content for the sediment samples were within the range of 2.32 to 4.17 $\mu\text{g kg}^{-1}$ of dry sediment. Higher DDT metabolites content were found in the sediments collected from the rivers than in the samples from the littoral zone. The lowest average total concentrations of DDTs, on

the other hand, were recorded in the water samples and ranged between 0.036 and 0.057 $\mu\text{g L}^{-1}$. The obtained results indicated that the dominant metabolic form in the samples of the three investigated matrixes (water, sediment and fish tissue) from Lake Prespa was p,p'-DDE. There was a very good linear correlation in this study between the content of DDT's (total DDT metabolites) detected and the percentage of total organic material in the sediment. The detected concentrations are clearly below the toxicity thresholds; consequently, severe effects on the endemic species of Lake Prespa are not very likely. PMID: 23581687

Vlaski E(1), Stavric K, Seckova L, Kimovska Hristova M, Isjanovska R. The self-reported density of truck traffic on residential streets and the impact on asthma, hay fever and eczema in young adolescents. Allergol Immunopathol (Madr). 2013 Jan 23. pii: S0301-0546(12)00303-5.

(1)Department of Pulmonology and Allergology, University Children's Clinic, Skopje, The Former Yugoslav Republic of Macedonia. Electronic address: vlaskie@sonet.com.mk.

BACKGROUND: Conflicting results have been reported, mostly in developed countries, on the relationship between exposure to traffic and allergic diseases. This study aims to examine the impact of truck traffic on asthma, rhinitis and eczema in early adolescence in Skopje, the capital of the Republic of Macedonia, as a developing country with a lower middle rate of high truck traffic exposure and low prevalence rates of allergic diseases. **METHODS:** Self-reported data was used, obtained through the International Study of Asthma and Allergies in Childhood Phase 3 written questionnaires, from 3026 adolescents aged 13-14 years from Skopje. Truck traffic density on the street of residence on weekdays was correlated to current and ever-diagnosed asthma, rhinitis and eczema by odds ratios (OR, 95% CI) in binary logistic regression, with and without adjustments for potential confounding factors separately and for their joint effect. **RESULTS:** A positive association of truck traffic density appeared to be limited to current dry night cough (aOR: 1.63; 1.07-2.47; aOR: 2.17; 1.40-3.35; and aOR: 2.33; 1.43-3.79 for truck traffic seldom, frequently through the day, and almost the whole day, respectively) with an exposure-response relationship and to current wheeze only for truck traffic almost the whole day (aOR: 1.87; 1.02-3.42). **CONCLUSION:** The findings suggest an aggravating effect of truck traffic on current asthma symptoms, but not on asthma, allergic rhinitis and eczema diagnoses. It seems that it probably has an impact as a direct respiratory irritant in early adolescence. PMID: 23352596

Vrhovnik P(1), Arrebola JP, Serafimovski T, Dolenc T, Smuc NR, Dolenc M, Mutch E. Potentially toxic contamination of sediments, water and two animal species in Lake Kalimanci, FYR Macedonia: relevance to human health. Environ Pollut. 2013 Sep;180:92-100.

(1)Faculty of Natural Sciences and Engineering, University of Ljubljana, Department of Geology, Aškerčeva Cesta 12, 1000 Ljubljana, Slovenia. petra.vrhovnik@ntf.uni-lj.si

The objectives of the research were: (1) to examine the concentrations of metals in *Vimba melanops* and *Rana temporaria* and (2) to evaluate the potential risks of the contaminated organisms to human health in Makedonska Kamenica region. Analyses identified high levels of Cr, Hg, Ni and Pb in studied animals, which also exceeded their permissible levels in food. In sediment and soil samples, levels of Cd, Cu, Cr, Pb, Zn and As were perceived, while Cd, Cu, Ni, Pb, Se and As were increased in water samples. Results of transfer factor revealed that the examined animals had higher bioaccumulation rate from surrounding waters than from sediments or soils. The accomplished Health Risk Index disclosed that studied animals can have considerably high health risks for inhabitants. Conclusively, they could be considered as highly contaminated with metals and can consequently harm human health, especially children in their early development stages. PMID: 23747817

Vučković I(1), Špirić Z, Stafilov T, Kušan V, Bačeva K. The

study on air pollution with nickel and vanadium in Croatia by using moss biomonitoring and ICP-AES. Bull Environ Contam Toxicol. 2013 Oct;91(4):481-7.

(1)Faculty of Natural Sciences and Mathematics, Institute of Chemistry, Ss. Cyril and Methodius University, POB 162, 1000, Skopje, Macedonia.

Moss samples were collected from 121 sampling sites all over Croatia during the summer and autumn of 2010. They were totally digested by using microwave digestion system and analysed by using atomic emission spectrometry with inductively coupled plasma (ICP-AES). Descriptive statistics and maps of distribution were made. The data obtained in this study were compared with those from the study in 2006 and additionally with the data obtained in the similar studies in neighbouring countries and Norway as pristine area. The median value of nickel is 3.16 mg kg⁻¹ and the content varies from 1.04 to 14.66 mg kg⁻¹. The content of vanadium ranges between 0.23 and 37.26 mg kg⁻¹ with the median value of 2.55 mg kg⁻¹. High contents of these elements are found in the vicinity of Rijeka, Zagreb and Sisak as a result of their emission from oil refinery, thermal power plant and industrial processes. PMID: 23884171

Vučković I(1), Spirić Z, Stafilov T, Kušan V. Moss biomonitoring of air pollution with chromium in Croatia. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2013;48(7):829-34.

(1)Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Skopje, Macedonia.

The purpose of this study was to determine the atmospheric deposition of chromium in Croatia by using moss biomonitoring technique and atomic emission spectrometry with inductively coupled plasma (ICP-AES). Moss samples (*Hylocomium splendens*, *Hypnum cupressiforme*, *Brachythecium rutabulum* and *Homalothecium Sericeum*) were collected from 121 sampling sites evenly distributed over the country, during the summer and autumn of 2010. Collected samples were air dried, then cleaned and digested by using microwave digestion system. The median value obtained in this study (1.94 mg kg⁻¹) compared with the median value of previous investigation performed in 2006 (2.75 mg kg⁻¹) shows that the content of chromium decreased. Higher contents of chromium were found in moss samples collected in the regions of Central Croatia, in/near the cities of Zagreb, Sisak and Kutina, which, in the most of the cases, are result of anthropogenic activities. In Coastal Croatia, higher values have a natural origin due to the significantly higher content of Cr in soil from this region. The results were compared with those from similar studies in neighboring and other Balkan countries. It was established that the content of chromium in Croatia is lower than in the most of these countries. PMID: 23445426

Walfisch A(1), Nikolovski S, Talevska B, Hallak M. Fetal growth restriction and maternal smoking in the Macedonian Roma population: a causality dilemma. Arch Gynecol Obstet. 2013 Jun;287(6):1131-6.

(1)Department of Obstetrics and Gynecology, Hillel Yaffe Medical Center, Hadera, Israel. asnatwalfisch@yahoo.com

PURPOSE: Macedonia is one of the top five countries globally in reported smoking rates. Over 10 % of the population consists of the underprivileged Roma minority. We aimed to determine whether Roma ethnicity is an independent risk factor for adverse pregnancy outcome or merely mediating maternal smoking. **METHODS:** Maternal data were retrieved from the perinatal computerized database for all deliveries during 2007-2011 at the only Clinical Hospital in Bitola, Macedonia. Multivariable regression models were constructed to control for confounders. **RESULTS:** Of nearly 7,000 deliveries, 8.65 % were of maternal Roma ethnicity and 40 % of the Romani women admitted to regularly smoke during pregnancy. Both Roma ethnicity and maternal smoking were significantly associated with the absence of maternal education, history of abortions and intra uterine growth restriction (IUGR) in the univariate analysis. Both maternal Roma ethnicity (OR 2.46, 95 %

CI 1.79-3.38) and smoking status (OR 1.37, 95 % CI 1.02-1.85) were found to be independent predictors of IUGR using the multivariate analysis. Lower birthweight and smaller head circumference were both independently associated with Roma ethnicity and smoking. CONCLUSIONS: Underprivileged ethnic background is a significant risk factor for IUGR, independent of maternal smoking status. To the best of our knowledge, this is the first publication focusing on pregnancy outcome in Romani Macedonian parturients. PMID: 23361458