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Abstract

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

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Competing Interests: The authors have declared that no competing interests exist.

We present abstracts of published papers in international journals deposited in PubMed. Search details were: ((Macedonia[Affiliation] NOT Greece[Affiliation]) NOT "Prilozi"[Journal]) AND ("2012/01/01"[PDAT] : "2012/12/31"[PDAT]), dated September 01, 2013. A total number of 88 papers were selected in PubMed during 2012 year, two of which were not from Republic of Macedonia (one from Greece and one from Kosovo) and were excluded.

A total number of 86 papers are included in 2012 year in Pubmed from Republic of Macedonia from which one paper (Mile B, Valerija K, Krsto G, Ivan V, Ilir D, Nikola L. Doxycycline-rifampin versus doxycycline-rifampin-gentamicin in treatment of human brucellosis. *Trop Doct.* 2012 Jan;42(1):13-7.) was indexed with the names instead of surnames. Authors of this paper should contact Editorial Board of the Journal *Trop Doct* in order to correct the errors. Six 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.

Acevska J, Stefkov G, Petkovska R, Kulevanova S, Dimitrovska A. Chemometric approach for development, optimization, and validation of different chromatographic methods for separation of opium alkaloids. *Anal Bioanal Chem.* 2012 May;403(4):1117-29.

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The excessive and continuously growing interest in the simultaneous determination of poppy alkaloids imposes the development and optimization of convenient high-throughput methods for the assessment of the qualitative and quantitative profile of alkaloids in poppy straw. Systematic optimization of

two chromatographic methods (gas chromatography (GC)/flame ionization detector (FID)/mass spectrometry (MS) and reversed-phase (RP)-high-performance liquid chromatography (HPLC)/diode array detector (DAD)) for the separation of alkaloids from *Papaver somniferum* L. (Papaveraceae) was carried out. The effects of various conditions on the predefined chromatographic descriptors were investigated using chemometrics. A full factorial linear design of experiments for determining the relationship between chromatographic conditions and the retention behavior of the analytes was used. Central composite circumscribed design was utilized for the final method optimization. By conducting the optimization of the methods in very rational manner, a great deal of excessive and unproductive laboratory research work was avoided. The developed chromatographic

methods were validated and compared in line with the resolving power, sensitivity, accuracy, speed, cost, ecological aspects, and compatibility with the poppy straw extraction procedure. The separation of the opium alkaloids using the GC/FID/MS method was achieved within 10 min, avoiding any derivatization step. This method has a stronger resolving power, shorter analysis time, better cost/effectiveness factor than the RP-HPLC/DAD method and is in line with the "green trend" of the analysis. The RP-HPLC/DAD method on the other hand displayed better sensitivity for all tested alkaloids. The proposed methods provide both fast screening and an accurate content assessment of the six alkaloids in the poppy samples obtained from the selection program of Papaver strains. PMID: 22318699

Acevska J, Dimitrovska A, Stefkov G, Brezovska K, Karapandzova M, Kulevanova S. Development and validation of a reversed-phase HPLC method for determination of alkaloids from Papaver somniferum L. (Papaveraceae). J AOAC Int. 2012 Mar-Apr;95(2):399-405.

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An HPLC method for the separation of six target alkaloids from Papaver somniferum L. (morphine, codeine, oripavine, thebaine, papaverine, and noscapine) was developed, optimized, and validated. The chromatographic behavior of these alkaloids was investigated using a reversed-phase chromatography at acidic and alkaline pH. The effects of ion-pairing agents, pH value of the mobile phase, concentration of the buffer components, mobile phase organic modifier, and column temperature were studied. Regardless of the large differences in their pKa values, all alkaloids were separated within a close retention window, and good peak shape was achieved for each of the six alkaloids. The proposed method has adequate selectivity, linearity, accuracy, precision, and reproducibility and is applicable for poppy straw. PMID: 22649926

Alabakovska SB, Tosheska KN, Spiroski MZ, Krstevska MA, Jovanova S, Labudovic DD. Low density lipoprotein size in relation to carotid intima-media thickness in coronary artery disease. Bratisl Lek Listy. 2012;113(2):87-91.

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OBJECTIVE: With increasing interest in the role of non-traditional lipid risk factors in coronary artery disease, we undertook this study to relate LDL subclass size and carotid intima-media thickness of

the common carotid artery in coronary artery disease patients. **METHODS:** The study was conducted in 106 patients during their first visit (study group I) and after 12 months (study group II). Intima-media thickness of the common carotid artery was determined using B-mode ultrasound. Separation of LDL subclasses was performed by 3-31 % polyacrylamide gradient gel electrophoresis. **RESULTS:** LDL3 was the dominant subclass in both study groups, but there was statistically significant difference in the distribution of dominant LDL subclasses ($p < 0.01$). The mean carotid intima-media thickness was significantly increased ($p < 0.001$) in coronary artery disease patients after 12 months period. There was significant negative correlation between intima-media thickness and LDL size in both study groups ($p < 0.05$). Intima-media thickness was not significantly correlated with plasma lipid concentrations. Multiple regression analyses show that strongest independent predictor of the intima-media thickness variation was diastolic blood pressure, followed by LDL size and age, and accounted for 29 % of the observed variability in intima-media thickness. **CONCLUSION:** LDL particle size is independently associated with carotid intima-media thickness in coronary artery disease patients with normal levels of traditional lipid risk. These results imply that small, dense LDL subclasses are an important indicator for assessing atherosclerosis and its progression. PMID: 22394037

Antovska P, 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.

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 V. Outcome Assessment of the Marshall Coughing Test during Cervix Reposition Maneuver in Women with Urinary Stress Incontinence with/without Genital Prolapse. ISRN Urol. 2012;2012:109858.

Department for Urogynaecology and Pelvic Floor Disorders, University Clinic for Gynaecology and Obstetrics, Medical Faculty, University "Saint Cyril and Methodius", Vodnjanska 17, 1000 Skopje, Macedonia.

Objectives. Outcome assessment of the Marshall coughing test (MT) during cervix reposition maneuver (CRM) in women with urinary stress incontinence (USI) with/without genital prolapse (GP). Study Design. 268 patients, divided into USIg (n = 132) with isolated USI and USIGPg (n = 136) with USI and GP stage I/II, additionally divided into USIGP(A) (n = 78) with USI and GP stage I and USIGP(B) (n = 58) with USI and GP stage II, were evaluated with pelvic organ prolapse quantification (POPQ), MT, and CRM. Results. (a) 7.58% had (+) MT with CRM in USIg; (b) in up to 96.15% MT became negative during CRM in USIGP(A); (c) in 51.72% MT became positive only during CRM, as a sign for occult USI in USIGP(B); (d) point Aa (POPQ), which is bladder neck(BN) projection on the anterior vaginal wall, was situated higher in rest position (RP), but moved lower during the Valsalva maneuver (VM) in USIg versus USIGPg (P < 0.05). Conclusion. CRM could be useful arm in selection of (1) patients with isolated USI and great chance for postoperative failure; (2) patients with USI+GP stage I, who need GP repair during antistress surgery; (3) patients with USI + GP stage II, who need antistress procedure during vaginal hysterectomy. PMID: PMC3302208. PMID: 22523712

Antovska VS. Ultrasound Characteristics of Patients with Urinary Stress Incontinence with or without Genital Prolapse. Korean J Urol. 2012 Oct;53(10):691-8.

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

PURPOSE: The study purpose was to evaluate the clinical and ultrasound characteristics of women with urinary stress incontinence (USI) with or without genital prolapse (GP). MATERIALS AND METHODS: A total of 268 patients who underwent ultrasound perineal evaluation were divided into two groups: isolated USI (n=132) and USIGP (n=136) with USI/GP stage I/II. The latter group was additionally divided into two subgroups: USIGP(A) (n=78) with USI/GP

stage I and USIGP(B) (n=58) with USI/GP stage II. RESULTS: Point Aa (pelvic organ prolapse quantification system), which is the projection of the bladder neck (BN) on the anterior vaginal wall, was situated higher in the rest position (RP) but moved lower during a Valsalva maneuver (VM) in the USI group than in the USIGP group (p<0.05). The ultrasound parameters α -angle and the distance Sy-BN (symphysis-bladder neck) decreased, whereas distance H increased, in the USIGP group during VM. The ultrasound parameters that gave the best insight into the range of BN movements were as follows: distance R→V and angle of rotation (ρ), which were significantly higher in the USI group than in the USIGP group during VM. CONCLUSIONS: According to the clinical and ultrasound findings, we can conclude that the BN is situated higher during the RP but moved lower during a VM in patients with isolated USI compared with those with concomitant USI/GP, which could be explained by the cystocele-immobilizing effect on the BN during the VM in the latter group but also by the deteriorated pubo-urethral ligaments in the former group. PMID: PMC3490089. PMID: 23136629

Atanasovska B, Bozhinovski G, Plaseska-Karanfilska D, Chakalova L. Efficient detection of Mediterranean β -thalassemia mutations by multiplex single-nucleotide primer extension. PLoS One. 2012;7(10):e48167.

Research Center for Genetic Engineering and Biotechnology, Macedonian Academy of Sciences and Arts, Skopje, Former Yugoslav Republic of Macedonia.

β -Thalassemias and abnormal hemoglobin variants are among the most common hereditary abnormalities in humans. Molecular characterization of the causative genetic variants is an essential part of the diagnostic process. In geographic areas with high hemoglobinopathy prevalence, such as the Mediterranean region, a limited number of genetic variants are responsible for the majority of hemoglobinopathy cases. Developing reliable, rapid and cost-effective mutation-specific molecular diagnostic assays targeting particular populations greatly facilitates routine hemoglobinopathy investigations. We developed a one-tube single-nucleotide primer extension assay for the detection of eight common Mediterranean β -thalassemia mutations: Codon 5 (-CT); CCT(Pro)->C-, Codon 6 (-A); GAG(Glu)->G-G, Codon 8 (-AA); AAG(Lys)->-G, IVS-I-1 (G->A), IVS-I-6 (T->C), IVS-I-110 (G->A), Codon 39 (C->T), and IVS-II-745 (C->G), as well as the hemoglobin S variant beta 6(A3) Glu>Val. We validated the new assay using previously genotyped samples obtaining 100% agreement between independent genotyping methods. Our approach, applicable in a range of Mediterranean countries, offers a combination of high accuracy and rapidity exploiting standard techniques and widely available

equipment. It can be further adapted to particular populations by including/excluding assayed mutations. We facilitate future modifications by providing detailed information on assay design. PMID: PMC3482202. PMID: 23110203

Atanasovska-Stojanovska A, Trajkov D, Popovska M, Spiroski M. IL10 -1082, IL10 -819 and IL10 -592 polymorphisms are associated with chronic periodontitis in a Macedonian population. Hum Immunol. 2012 Jul;73(7):753-8.

Dental Clinical Center, Department of Oral Pathology and Periodontology, Faculty of Stomatology, University Ss Cyril and Methodius, Skopje, Republic of Macedonia.

Genetic polymorphisms in the interleukin 10 (IL10) gene have been reported to influence the host response to microbial challenge by altering levels of cytokine expression. We analyzed nucleotide polymorphisms in the promoter region of the IL10 gene and its relation with periodontal disease in a Macedonian population. The study population consisted of 111 unrelated subjects with chronic periodontitis and 299 healthy controls. DNA was isolated and IL10 genotyping performed by PCR-SSP (Heidelberg kit) for the alleles and genotypes of IL10 -1082, IL10 -819 and IL10 -592. Frequencies of IL10 haplotypes and the haplotype zygotes were also examined. Comparisons between groups were tested using the Pearson's p-value. After Bonferroni adjustment, significant associations were detected between subjects with chronic periodontitis and IL10 genotypes (IL10 -1082/A:G was negative or protective and IL10 -1082/G:G was positive or susceptible). Cytokine polymorphism on the IL10 gene appears to be associated with susceptibility to chronic periodontitis in Macedonians. PMID: 22537751

Avramovski P, Sikole A. The progression of bone mineral density loss in dialysis patients compared with the general population. Korean J Intern Med. 2012 Dec;27(4):436-42.

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BACKGROUND/AIMS: The aim of this study was to compare the progression of bone mass loss in chronic hemodialysis patients (CHPs) with that in general population patients (GPPs) over an 18-month period. **METHODS:** The control group consisted of 60 patients (aged 57.5 ± 10.9 years) with a glomerular filtration rate > 60 mL/min/1.73 m²). The study group included 80 patients undergoing hemodialysis (aged 59.3 ± 11.8 years; duration of dialysis 5.47 ± 5.16 years). Bone mineral density (BMD) testing was conducted in both groups using dual energy X-ray absorptiometry at hip and lumbar spine regions at

baseline and after 18 months. Biochemical parameters (albumin, C-reactive protein, calcium, ionized calcium, alkaline phosphatase, and parathyroid hormone) were determined in all participants using standard laboratory procedures. **RESULTS:** The mean values of BMD (average hip + lumbar spine) were 0.900 ± 0.14 g/cm²) and 0.866 ± 0.14 g/cm²) in the GPP and 0.823 ± 0.16 g/cm²) and 0.769 ± 0.13 g/cm²) in the CHP groups at baseline and 18 months, respectively. The statistical significance (p value) of hip bone loss progression over 18 months was 0.0577 for GPP and 0.0002 for CHP, whereas that of lumbar spine bone loss progression was 0.6820 for GPP and 0.5389 for CHP. **CONCLUSIONS:** The of progression bone mass loss was significantly greater in CHP than in GPP. Bone mass loss was evident even over 1 month, albeit in only the CHP with accelerated osteoporosis. PMID: PMC3529243. PMID: 23269885

Bajro MH, Josifovski T, Panovski M, Jankulovski N, Nestorovska AK, Matevska N, Petrusevska N, Dimovski AJ. Promoter length polymorphism in UGT1A1 and the risk of sporadic colorectal cancer. Cancer Genet. 2012 Apr;205(4):163-7.

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Uridine diphosphoglucuronate glucuronosyltransferase 1A1 (UGT1A1) is the key hepatic detoxification enzyme involved in the biotransformation of many carcinogens implicated in the development of colon, breast, and prostate cancers in humans. A polymorphism in the UGT1A1 promoter containing a TA-repeat element [(TA)₅₋₈TAA] is involved in the modulation of UGT1A1 transcriptional activity. The wild-type activity is associated with the (TA)₆TAA allele (UGT1A1*1), whereas UGT1A1 expression decreases with the increase of the TA-repeat number. We hypothesize that the low-activity allele UGT1A1*28 with seven TA repeats is associated with a higher risk for colorectal cancer. Our study involved 168 patients with histopathologically confirmed sporadic colorectal cancer and a control group of 96 individuals with no personal history of colorectal cancer. We detected a higher frequency of UGT1A1*28 than the wild-type UGT1A1*1 allele in colorectal cancer patients as compared with that of controls (odds ratio [OR] = 1.55, 95% confidence interval [CI] = 1.07-2.26, P = 0.021). The frequency of genotypes containing the UGT1A1*28 allele in the homozygous or heterozygous state was significantly higher than the frequency of the wild-type UGT1A1*1/*1 genotype in colorectal cancer patients as compared with controls (OR = 2.0, 95% CI = 1.19-3.34, P = 0.007). Our results indicate that the UGT1A1*28 allele is a risk factor for colorectal cancer in the Macedonian male population, whereas no significant risk was detected among women. PMID: 22559977

Barandovski L, Frontasyeva MV, Stafilov T, Sajn R, Pavlov S, Enimiteva V. Trends of atmospheric deposition of trace elements in Macedonia studied by the moss biomonitoring technique. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2012;47(13):2000-15.

Institute of Physics, Faculty of Science, Ss. Cyril and Methodius University, Skopje, Macedonia.

In 2002 and 2005 the moss biomonitoring technique was applied to air pollution studies in the Republic of Macedonia in the framework of the International Cooperative Programme on Effects of Air Pollution on Natural Vegetation and Crops under the auspices of the United Nations Economic Commission for Europe (UNECE-ICP Vegetation) Convention on Long-Range Transboundary Air Pollution (LRTAP). In August 2005 samples of the terrestrial mosses *Homolothecium lutescens* and *Hypnum cupressiforme* were collected at 72 sites evenly distributed over the territory of the country, in accordance with the sampling strategy of the European moss survey programme. A total of 41 elements (Na, Mg, Al, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Br, Rb, Sr, Zr, Mo, Cd, Sb, I, Cs, Ba, La, Ce, Sm, Eu, Tb, Dy, Hf, Ta, W, Hg, Pb, Th, and U) were determined by instrumental epithermal neutron activation analysis and atomic absorption spectrometry. Principal component analysis was used to identify and characterize different pollution sources. Distributional maps were prepared to point out the regions most affected by pollution and to relate this to known sources of contamination. A few areas, as in 2002, are experiencing particular environmental stress: Veles, Skopje, Tetovo, Radoviš and Kavadarci-Negotino, whereas the agricultural regions in the south, south-west, and south-east show median European values for most elements of mainly pollution origin. A significant increase in the content of Ni is noticed in the 2005 moss survey compared with 2002, due to the increased production of the ferro-nickel smelter in Kavadarci. A higher content of Cd, Hg, and Pb in 2005 relative to 2002 can be explained by pollution from the lead-zinc smelter in Veles, as well as the pollution that comes from the open slag waste dump of this smelter. Protection activities on the dump of slag from the former ferrochromium smelter located near Tetovo resulted in a lower content of Cr in the 2005 moss survey. PMID: 22870997

Bačeva K, Stafilov T, Sajn R, Tănăselia C. Moss biomonitoring of air pollution with heavy metals in the vicinity of a ferronickel smelter plant. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2012;47(4):645-56.

Institute of Chemistry, Faculty of Science, Ss. Cyril and Methodius University, Skopje, Macedonia.

The purpose of this study was to establish the atmospheric deposition of various elements in the Kavadarci region, Republic of Macedonia (known for

its ferronickel mining and metallurgical activities) using moss biomonitoring, and to determine whether the deposition is anthropogenic or from geogenic influences. The sampling network includes 31 moss samples evenly distributed over a territory of about 600 km². A total of 46 elements (Ag, Al, As, Au, Ba, Be, Ca, Cd, Ce, Co, Cr, Cs, Cu, Dy, Er, Eu, Fe, Ga, Gd, Ge, Hg, Ho, K, La, Li, Lu, Mg, Mn, Mo, Na, Nb, Ni, P, Pb, Rb, Sb, Sm, Sr, Tb, Th, Ti, U, V, Yb, Zn, Zr) were determined by mass spectrometry with inductively coupled plasma (ICP-MS). Based on a distribution pattern of elements determined in moss, two anthropogenic geochemical associations (Co-Cr-Cu-Fe-Mg-Ni and As-Cd-Cu-Hg-Pb-Zn), were detected. The distribution of these elements shows an increased content (especially Ni, Co and Cr) in the moss samples from the surroundings of the smelter plant compared to the rest of the samples. Thus, the median value of Ni in moss samples from the whole region (40 mg kg⁻¹) is much higher than the median for Macedonia (5.82 mg kg⁻¹). Moreover, the median content of Ni in the moss samples from the polluted area (around the smelter) is 178 mg kg⁻¹ with an enrichment ratio in the moss samples of almost 5.5 times higher than the unpolluted areas (32 mg kg⁻¹). This fact confirms the influence of the dust from the ferronickel plant to the air pollution in this region. PMID: 22375548

Boev B, 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.

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

Bosevska G, Panovski N, Kuzmanovska G, Coneva E, Memeti S, Cekovska Z, Celevska B, Zahariev I, Mikik V. The first survey about the antibiotic usage in the Republic of Macedonia. Med Glas (Zenica). 2012 Aug;9(2):393-6.

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Development of antibiotic resistance represents a major global and Macedonian public health problem. To assess the opinion and knowledge of the citizens of Macedonia about the usage of antibiotics, voluntary and anonymous survey was realized. A total of 239 persons (age 10-67 years) were interviewed. Following information was obtained: 73.64% get antibiotics with a medical prescription; and 87.03% receiving the antibiotic on time, dosage and prescribed duration. When asked about knowledge about antibiotics, 38% of the interviewed persons gave the right answer, 43.1% of respondents made false statements that antibiotics are effective against viral infections and 25.52% did not express any opinion. PMID: 22926383

Bosevski M, 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.

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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, Soedamah-Muthu SS. Blood urea level and diabetes duration are independently associated with ankle-brachial index in type 2 diabetic patients. *Diabetes Metab Syndr*. 2012 Jan-Mar;6(1):32-5.

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AIM: The purpose of the study was to determine factors of ankle-brachial index (ABI) in a population of patients with type 2 diabetes and coronary artery disease. MATERIAL AND METHODS: 370 patients (mean age 60.3 ± 8.3 years and diabetes duration 8.6 ± 6.2 years) with type 2 diabetes and coronary artery disease were enrolled in a cross sectional study

during 2006-2007. Multivariable linear regression analysis was conducted to determine the factors of ABI, considering systolic and diastolic blood pressure, weight, body mass index, waist circumference, glycemia, urea, creatinin, triglycerides, total cholesterol, LDL- and HDL-cholesterol. RESULTS: Peripheral arterial disease was detected in 82.35% (280 pts). Mean ABI value of 0.97 ± 0.33, and its minimal value of 0.95 ± 0.38 was detected in this study population. Regression analysis demonstrated that mean and minimal values of ABI were independently associated with diabetes duration (β 0.120, 95% CI -0.014, -0.001) and blood urea level (β -0.126, 95% CI -0.020, -0.002). CONCLUSION: Results might have clinical implications for patients with type 2 diabetes and coronary artery disease in defining those with a long diabetes duration and a higher blood urea level to have greater probability of detecting pathological ankle-brachial index. PMID: 23014252

Brezovska K, Panovska AP, Grozdanova A, Suturkova L, Basta I, Apostolski S. Authors' reply. *J Neurosci Rural Pract*. 2012 Jan;3(1):104-5.

Faculty of Pharmacy, University Ss. Cyril and Methodius, Skopje, Macedonia, Serbia. PMID: 22346219

Chibishev A, Pareska Z, Chibisheva V, Simonovska N. Clinical and epidemiological features of acute corrosive poisonings. *Med Arh*. 2012;66(3 Suppl 1):11-5.

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BACKGROUND: the ingestion of chemical agents, of caustic nature, represents a serious problem for clinical toxicology. If the ingestion doesn't cause death during the acute period, it will most often cause severe side effects in the upper gastrointestinal tract during the chronic phase. AIMS: The purpose of this study is to show the clinical, epidemiological and socio-economical characteristics seen in acute corrosive poisonings such as ingested caustic agents, causes for abuse and most consequential complications. MATERIAL AND METHODS: a ten year medical data was constructed and collected (2000-2009) from patients with acute corrosive poisonings who were hospitalized and treated in the University Clinic of toxicology and urgent internal medicine in Skopje, Republic of Macedonia. The variables included were: age, sex, type of poisonings and percentage of late post-corrosive complications. RESULTS: In the study, 735 patients files were analyzed, collected in a period often years. The mean age of patients is 32.9 +/- 15.6 years. Majority of patients ingested hydrochloric acid (HCl; n = 354; 48,16%). CONCLUSION: Demographic, diagnostic and therapeutic findings in acute corrosive poisonings

are found to be similar to the findings observed in the referenced literature. Conclusively, women between 14 and 30 years old represent a high risk group; hydrochloric acid is the most often abused agent; and high percentage of post-corrosive complications are. PMID: 22937683

Chibishev A, Pereska Z, Chibisheva V, Simonovska N. Corrosive poisonings in adults. Mater Sociomed. 2012;24(2):125-30.

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Ingestion of corrosive substances may cause severe to serious injuries of the upper gastrointestinal tract and the poisoning can even result in death. Acute corrosive intoxications pose a major problem in clinical toxicology since the most commonly affected population are the young with psychic disorders, suicidal intent and alcohol addiction. The golden standard for determination of the grade and extent of the lesion is esophagogastroduodenoscopy performed in the first 12-24 hours following corrosive ingestion. The most common late complications are esophageal stenosis, gastric stenosis of the antrum and pylorus, and rarely carcinoma of the upper gastrointestinal tract. Treatment of the acute corrosive intoxications include: neutralization of corrosive agents, antibiotics, anti-secretory therapy, nutritional support, collagen synthesis inhibitors, esophageal dilation and stent placement, and surgery. PMID: 23678319

Davalieva K, Kiprijanovska S, Broussard C, Petrushevska G, Efreimov GD. Proteomic analysis of infiltrating ductal carcinoma tissues by coupled 2-D DIGE/MS/MS analysis. Mol Biol (Mosk). 2012 May-Jun;46(3):469-80.

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There is a growing interest in protein expression profiling aiming to identify novel diagnostic markers in breast cancer. Proteomic approaches such as two-dimensional differential gel electrophoresis coupled with tandem mass spectrometry analysis (2-D DIGE/MS/MS) have been used successfully for the identification of candidate biomarkers for screening, diagnosis, prognosis and monitoring of treatment response in various types of cancer. Identifying previously unknown proteins of potential clinical relevance will ultimately help in reaching effective ways to manage the disease. We analyzed breast cancer tissues from five tumor and five normal tissue samples from ten breast cancer subjects with infiltrating ductal carcinoma (IDC) by 2-D DIGE using two types of immobilized pH gradient (IPG) strips: pH

3-10 and pH 4-7. From all the spots detected, differentially expressed ($p < 0.05$ and ratio > 2) were 50 spots. Of these, 39 proteins were successfully identified by MS, representing 29 different proteins. Ten proteins were overexpressed in the tumor samples. The 2-D DIGE/MS/MS analysis revealed an increase in the expression levels in tumor samples of several proteins not previously associated with breast cancer, such as: macrophage-capping protein (CAPG), phosphomannomutase 2 (PMM2), ATPase ASN1, methylthioribose-1-phosphate isomerase (MRI1), peptidyl-prolyl cis-trans isomerase FKBP4, cellular retinoic acid-binding protein 2 (CRABP2), lamin B1 and keratin, type II cytoskeletal 8 (KRT8). Ingenuity Pathway Analysis (IPA) revealed highly significant ($p = 10^{-26}$) interactions between the identified proteins and their association with cancer. These proteins are involved in many diverse pathways and have established roles in cellular metabolism. It remains the goal of future work to test the suitability of the identified proteins in samples of larger and independent patient groups. PMID: 22888636

Davalieva K, Kiprijanovska S, Noveski P, Plaseski T, Kocevaska B, Broussard C, Plaseska-Karanfilska D. Proteomic analysis of seminal plasma in men with different spermatogenic impairment. Andrologia. 2012 Aug;44(4):256-64.

Research Centre for Genetic Engineering and Biotechnology, Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia.

Seminal plasma is a potential source of biomarkers for many disorders of the male reproductive system including male infertility. The identification and characterisation of differentially expressed proteins in seminal plasma of man with normal and impaired spermatogenesis can help in the elucidation of the molecular basis of male infertility. We compared the protein expression profiles of seminal plasma from four different groups of men as follows: normozoospermic, asthenozoospermic, oligozoospermic and azoospermic groups, using two-dimensional differential gel electrophoresis (2-D DIGE). We found eight proteins with statistically significant increased expression in azoospermia compared with at least one of the other studied groups. The differentially expressed spots were fibronectin, prostatic acid phosphatase (PAP), proteasome subunit alpha type-3, beta-2-microglobulin, galectin-3-binding protein, prolactin-inducible protein and cytosolic nonspecific dipeptidase. Notably, PAP was increased in patients with azoospermia compared with that of all other groups. We have observed no statistically significant differences in protein expression between three of the groups: normozoospermic, oligozoospermic and asthenozoospermic. We suggest that the identified panel of proteins in our study especially PAP have a strong potential to be used as azoospermia markers. However, further investigations will be necessary to validate these markers in samples of larger and

independent patient cohorts and to clarify their role in the pathogenesis of male infertility. PMID: 22288839

Davceva N, Janevska V, Ilievski B, Spasevska L, Popeska Z. Dilemmas concerning the diffuse axonal injury as a clinicopathological entity in forensic medical practice. J Forensic Leg Med. 2012 Oct;19(7):413-8.

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Dilemmas and discussions concerning the diffuse axonal injury (DAI) and still existing in forensic medical practice are as it follows: 1. Whether the occurrence of DAI can indicate the type of traumatic event that has caused the head trauma, 2. Whether the presence of axonal damage in cases of hypoxia, ischaemia and other pathological conditions casts a shadow on the post-mortem pathological diagnosis of DAI and totally negates it, or there are certain clues in the findings that can point to the aetiology of the axonal damage. This paper discusses our findings based on neuropathological examination of 60 forensic cases of closed head injury. The neuropathological examination included: a macroscopic examination of the coronal sections and a microscopic examination involving an immunohistochemical method with antibody against β -amyloid precursor protein. Our findings indicate that DAI, as a clinicopathological entity, is undoubtedly an acceleration-deceleration injury, predominant in road traffic accidents as it is classically outlined, and cases of falling from a considerable height. Our findings point to a certain difference between the features of traumatic and ischaemic axonal damage. In this paper we also investigate the correlation between pathological grades of DAI and the impairment of the brain function before death. PMID: 22920765

Davceva N, Janevska V, Ilievski B, Petrushevska G, Popeska Z. The occurrence of acute subdural haematoma and diffuse axonal injury as two typical acceleration injuries. J Forensic Leg Med. 2012 Nov;19(8):480-4.

Institute of Forensic Medicine, Criminology and Medical Deontology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Vodnjanska No 19, 1000 Skopje, Macedonia. drdavcevamk@yahoo.com

Closed head injuries have already been classified into contact injuries and acceleration-deceleration injuries. Two typical acceleration-deceleration injuries and at the same time, the two worst head injuries are acute subdural haematoma (ASDH) and diffuse axonal injury (DAI), and that is where they got their medico-legal importance. Using experiments, it has been shown that acceleration with an impact time of more

than 20-25 min (which occurs in traffic accidents in real life) causes DAI, whereas an impact time of 5-10 min is more likely to produce acute subdural haematoma. The aim of this research is to show that not all, but some types of traffic accidents are more typical for the occurrence of DAI, as well as that the ASDH is not a common feature for all types of fall. The analysis conveyed covered 80 cases of closed head injuries (traffic accidents, falls and assaults) where a complete forensic medical autopsy has been undertaken, followed by a complete forensic-neuropathological examination. For the purpose of diagnosing DAI, immunohistochemistry using antibody against β -amyloid precursor protein has been involved. Results show that ASDH is more likely to occur in cases of simple fall, assaults and cyclists and DAI is more typical for vehicular traffic accidents and cases of falling from a considerable height. The paper also comprises discussion about some open questions regarding the diagnosis of DAI in the medico-legal practice. PMID: 23084313

Davceva N, Janevska V, Ilievski B, Jovanovic R. The importance of the detail forensic-neuropathological examination in the determination of the diffuse brain injuries. Soud Lek. 2012 Jan;57(1):2-6.

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According to the contemporary classification, traumatic brain damage is divided on focal and diffuse brain injuries, and primary and secondary brain damage. The aim of this paper is to emphasize the necessity of the forensic-neuropathological examination in the determination of the diffuse brain injuries. In those injuries frequently neither the most sophisticated clinical-investigation techniques like CT and MRI, nor the routine post-mortem forensic pathological examination, give any results with discovering an intracranial mass lesion, despite the fact that patients had manifested a serious brain failure. In a series of 80 cases with closed head injuries where forensic-neuropathological examination has been undertaken (examination of a fixed brain tissue and immunohistochemistry using monoclonal antibodies against β -amyloid precursor protein), the occurrence of the diffuse brain injuries in the absence of any other massive intracranial lesion has been established in 14 (17,7%) of the cases. Hence, forensic-neuropathological examination has been the only way to establish the diagnosis of the brain injury that caused a serious brain failure and in most of them occurred as a concrete cause of death. This method has already been affirmed in the forensic medicine science and has been implemented in a Recommendation No 99 of the Council of Europe where medico-legal autopsy rules are given, thus, establishing it as an unavoidable part of the daily forensic medicine practice. PMID: 22724588

Dimitrova G, Kato S, Nagahara M. Body posture during colour Doppler imaging of the eye and orbit. Acta Ophthalmol. 2013 Aug;91(5):e406.

Department of Ophthalmology, Neuromedica Polyclinic, Skopje, Macedonia; Department of Ophthalmology, University of Tokyo Hospital, Tokyo, Japan.

PMID: 22989099

Dimovska S, Stafilov T, Sajn R. Radioactivity in soil from the city of Kavadarci (Republic of Macedonia) and its environs. Radiat Prot Dosimetry. 2012 Jan;148(1):107-20.

Republic Institute for Health Protection, 50 Divizija 6, 1000 Skopje, Macedonia.

The activity concentrations and distribution of natural and anthropogenic radionuclides in soils from the city of Kavadarci, Republic of Macedonia, and its environs were investigated. The purpose of the study, the first of this kind in this region was to evaluate the environmental radioactivity and radiological health hazard, as well as to determine the connection between the concentration of natural radionuclides and the geology of the terrain. A total of 45 surface soil samples were collected from evenly distributed sampling sites. Gross alpha and gross beta activity measurements were made using a gas flow proportional counter, while the activity concentrations of gamma emitting radionuclides were measured using a high purity germanium detector. The average activity concentrations of ^{40}K , ^{226}Ra , ^{232}Th and ^{137}Cs were found to be 546 ± 118 , 38.8 ± 14.6 , 43.7 ± 18.4 and 41.5 ± 40 Bq kg^{-1} , respectively. The mean values of gross alpha and gross beta activities were 522 ± 192 and 681 ± 146 Bq kg^{-1} . The mean total absorbed dose rate in air calculated from the concentration of the natural radionuclides was 67.1 ± 20.9 nGy h^{-1} , and the corresponding annual effective dose rate outdoors was 0.082 ± 0.026 mSv y^{-1} . The results of the analysis show strong correlation between the abundance of the natural radionuclides in soils and their geological origin. PMID: 21335627

Gjorgieva D, Kadifkova-Panovska T, Mitrev S, Kovacevik B, Kostadinovska E, Bačeva K, Stafilov T. Assessment of the genotoxicity of heavy metals in *Phaseolus vulgaris* L. as a model plant system by Random Amplified Polymorphic DNA (RAPD) analysis. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2012;47(3):366-73.

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Impact assessments of environmental pollutants are important in eco-genotoxicology. A random amplified polymorphic DNA (RAPD) technique was used to detect genotoxicity-induced DNA damage in

Phaseolus vulgaris L. from heavy metals at two different concentrations. The results from six 10-base pair (bp) random RAPD primers with 60-70% GC content used, showed a total of 295 RAPD fragments of 700-4000 bp in molecular size in the seedlings of untreated and treated samples, of which only 163 fragments were polymorphic. Polymorphisms became evident as the disappearance and/or appearance of DNA fragments in treated samples compared to the control. A dendrogram constructed using the Numerical Taxonomy and Multivariate Analysis System (NTSYSps), showed that the control group merged with groups treated with $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (150 mg L^{-1}) and $\text{MnSO}_4 \cdot \text{H}_2\text{O}$ (150 mg L^{-1}) in a separate cluster. These groups were linked with all of the other samples treated with metals at concentrations of 150 mg L^{-1} and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ and $\text{Cd}(\text{NO}_3)_2$ at concentrations of 350 mg L^{-1} . Finally, the samples treated with metals at concentrations of 350 mg L^{-1} together with NiSO_4 at the concentration of 150 mg L^{-1} , clustered separately. The DNA polymorphism detected by RAPD analysis offered a useful biomarker assay for the detection of toxic chemicals genotoxicity in plant model systems. PMID: 22320688

Gjorgievska E, 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.

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 \times 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 E, Nicholson JW, Grcev AT. Ion migration from fluoride-releasing dental restorative materials into dental hard tissues. J Mater Sci Mater Med. 2012 Jul;23(7):1811-21.

Department of Paediatric and Preventive Dentistry, Faculty of Dental Medicine, University Ss. Cyril and Methodius Skopje, Skopje, Republic of Macedonia.

This study was carried out in order to determine the extent to which ions released from fluoride-containing dental restoratives migrated through the enamel and dentine of extracted teeth. A total of 40 permanent human 3rd molars were used. They were extracted for orthodontic reasons, and employed within 1 month of extraction. A cervical (Class V) cavity was prepared in each tooth, then filled with one of: a conventional glass-ionomer, a resin-modified glass-ionomer, a polyacid-modified composite resin ("compomer") or a fluoride-releasing resin composite. Ten samples were prepared per material. After 1 month, five specimens per material were prepared and examined under SEM/EDX. Concentrations of sodium, aluminium, strontium, fluorine, magnesium, silicon, phosphorus and calcium were determined within the tooth. After 18 months, the remaining five specimens for each material were prepared and studied in the same way. The greatest extent of ion migration into the tooth was found with the conventional glass-ionomer and least migration was found for the fluoride-releasing composite, which showed no evidence of fluoride migration at all. Levels of migrating ions were generally higher in the 18 month specimens than in the 1 month specimens, and also higher in the dentine than in the enamel. Ions released by restorative dental materials have been shown conclusively for the first time to be capable of migrating into the enamel and dentine surrounding the restoration. The conventional glass-ionomer showed the highest level of ion migration whereas the fluoridated composite resin showed little if any ion migration. This suggests that the conventional glass-ionomer has the greatest caries inhibiting effects of all the materials tested, and the fluoridated composite the least. PMID: 22532098

Gligeroska JP, Manchevska S. The effect of physical activity on cognition - physiological mechanisms. Mater Sociomed. 2012;24(3):198-202.

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The presumption that physical activity, i.e. exercise,

as an independent and separated factor influences different aspects of cognitive mechanisms is substantially supported by the literature. The investigations of the influence of physical activity on cognitive functioning have offered several mechanisms which could explain this relationship. Physiological mechanisms including increased cerebral blood flow, changes in neurotransmitter release, structural changes in central nervous system and altered arousal levels are based on physical changes that occur in the body as a consequence of the physical activity. There is evidence that physical training selectively increases angiogenesis, synaptogenesis and neurogenesis. The role of central (BDNF) and peripheral (estrogens, corticosteroids, growth hormone, IGF-1) factors in mediation of the effects of physical exercise on brain functions, has been promoted. Also, there is convergent data on molecular and cellular level, as well as on behavioral and systemic level which support the presumption that physical activity is beneficial to cognition. These data emphasizes the importance of promotion of physical activity during the life span for the prevention of contemporary (obesity, diabetes and cardiovascular) diseases and cognitive decline in humans. PMID: 23678325

Grozdanovski K, Milenkovic Z, Demiri I, Spasovska K. Prediction of outcome from community-acquired severe sepsis and septic shock in tertiary-care university hospital in a developing country. Crit Care Res Pract. 2012;2012:182324.

Department of Intensive Care, University Clinic for Infectious Diseases, Vodnjanska 17, 1000 Skopje, Macedonia.

Our aim was to determine the risk factors on mortality in adult patients with community-acquired severe sepsis and septic shock. The main outcome measure was hospital mortality. This prospective single centre study was conducted from January 1, 2008 to December 31, 2010, and included 184 patients, of whom 135 (73.4%) were with severe sepsis and 49 (26.6%) had septic shock. Overall, ninety-five (51.6%) patients have died, 60 (44.4%) in severe sepsis and 35 (71.4%) patients with septic shock. The lung was the most common site of infection 121 (65.8%), and chronic heart failure was the most frequent comorbidity 65 (35.3%). Logistic multivariate analysis identified three independent risk factors for mortality in patients with severe sepsis: positive blood culture (odds ratio, 2.39; 95% confidence interval, 1.13-5.06; P = 0.02), three or more organ dysfunctions (odds ratio, 3.93; 95% confidence interval, 1.62-9.53; P = 0.002), and Simplified Acute Physiology Score (SAPS) II (odds ratio, 1.02; 95% confidence interval, 1.00-1.04; P = 0.01). In addition to SAPS II, positive blood culture, and three or more organ dysfunctions are important independent risk factors for mortality in patients with severe sepsis and septic shock. PMID: 23678325

PMC3483665. PMID: 23119151

Gucev Z, 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.

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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 -galaktosidase (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

Gucev Z, Tasic V, Pop-Jordanova N, Riepe FG. Aldosterone synthase deficiency type II with hypospadias. Indian Pediatr. 2012 Apr;49(4):318-20.

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Aldosterone synthase deficiency (ASD) type II was diagnosed in a 3 week old boy with severe dehydration. Elevated plasma renin activity, low-normal aldosterone, increased levels for 18-OH corticosterone (18-OHB) and 18-OH-deoxycorticosterone were measured. Sequencing revealed a homozygous mutation for c554C > T in exon 3 (p.T185I) (CYP11B2). Hypospadias has so far not been reported in ASD. PMID: 22565077

Gucev Z, Tasic V, Saranac L, Stobbe H, Kratzsch J, Klammt J, Pfäffle R. A novel GH1 mutation in a family with isolated growth hormone deficiency type II. Horm Res Paediatr. 2012;77(3):200-4.

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BACKGROUND: Four distinct familial types of isolated

GH deficiency (IGHD) have been described so far. OBJECTIVE: We report a novel nonsense GH1 mutation in a father and a son. PATIENTS: Father's height was 137.3 cm (-6.79 SDS); mother's height was 157.3 cm (-1.86 SDS). By the age of 8.25 years, his height was 104.3 cm (-4.82 SDS) and his weight was 18.3 kg (-3.35 SDS). GH stimulation tests had low peak GH value of 6.5 ng/ml (proband) and 6.3 ng/ml (father). Other pituitary hormones and magnetic resonance imaging (MRI) of the pituitary region was normal in both patients. The proband received recombinant human GH (rhGH) treatment (30 μ g/kg/day) and he grew 15.4 cm in 15 months. RESULTS: Sequencing of the GH1 gene revealed a novel heterozygous nonsense mutation in both the father and the son (c.199A>T), which introduces a stop codon in exon 3. CONCLUSION: We present a family with IGHD II, with severe short stature, no phenotypic characteristics of GHD and a novel nonsense mutation in exon 3 of the GH1 gene. As fibroblasts were unavailable, we used computer analysis and we propose a unique mechanism that combines aberrant splicing and derogated GH release from the pituitary with residual secretion of a bioinactive truncated GH peptide. PMID: 22188748

Gulaboski R, 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.

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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'-azinobis(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 capacitance 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, Sukarova-Angelovska E, Adélaide 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.

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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

Hiljadnikova-Bajro M, Josifovski T, Panovski M, Dimovski AJ. A novel germline MLH1 mutation causing Lynch Syndrome in patients from the Republic of Macedonia. Croat Med J. 2012 Oct;53(5):496-501.

Faculty of Pharmacy, Ss. Cyril and Methodius University, Vodnjanska 17, Skopje, Republic of Macedonia.

AIM: To implement molecular analysis in the clinical diagnosis and management of Lynch syndrome (LS). METHODS: We analyzed the mutations in MLH1 and MSH2 in the selected LS families from the Republic of

Macedonia. RESULTS: We performed the very first genetic identification of LS families and characterized a novel mutation. The novel nonsense germline point mutation c.392C>G in the codon 131 of MLH1(S131X) was identified as the underlying genetic cause of LS in three families. The haplotype analysis suggested a founder effect of this mutation in our population. CONCLUSION: We expect to detect the mutation in other LS patients from the region, and recommend cost-effective screening for this mutation by restriction fragment length polymorphism-polymerase chain reaction or DNA sequencing of MLH1 Exon5 prior to full genetic testing in all LS suspects of Macedonian ancestry. PMID: 23100212

Ivanova V, Vojnoski B, Stefova M. Effect of winemaking treatment and wine aging on phenolic content in Vranec wines. J Food Sci Technol. 2012 Apr;49(2):161-72.

Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss Cyril and Methodius University, Arhimedova 5, 1000 Skopje, Republic of Macedonia; Department for Enology, Institute of Agriculture, Ss Cyril and Methodius University, Aleksandar Makedonski bb, Skopje, Republic of Macedonia.

Phenolic compounds and colour stability of red wines produced from Vranec *Vitis vinifera* L. grape variety were investigated by means of different maceration times (3, 6 and 10 days), two doses of SO₂ (30 and 70 mg/L SO₂), two yeasts for fermentation (Vinalco and Levuline), temperature of storage and time of aging (3, 6 and 16 months). In general, maceration time influenced the phenolics extraction from the grapes into the wine. Highest concentrations of phenolic components were observed in the wines produced with 6 days of maceration, except for the flavan-3-ols which were present in highest amounts in the wines macerated for 10 days. Higher doses of SO₂ increased the extraction of polyphenols, preventing the wines from oxidation, while the effect of yeast on phenolics extraction was not significant. Wine aging affected the phenolic content of wines produced with 3 days of maceration and caused intensive decrease of anthocyanins during the storage period. Wines aged at higher temperature showed lower anthocyanin levels and less intense coloration. Principal component analysis revealed that separation of the wines was performed according to the hue value in correlation with the maceration time and time of wine aging. PMID: 23572838

Ivanovska-Adjievska B, Boskurt S, Semiz F, Yuzer H, Dimovska-Jordanova V. Treatment of idiopathic macular hole with silicone oil tamponade. Clin Ophthalmol. 2012;6:1449-54.

European Eye Hospital, Skopje, Macedonia.

PURPOSE: We analyzed the anatomical and visual outcomes after surgical treatment of idiopathic macular holes with pars plana vitrectomy, internal limiting membrane (ILM) peeling using Brilliant Blue dye, and silicone oil tamponade without postoperative posturing. **METHODS:** This was a retrospective interventional study of 10 eyes in eight patients who underwent surgical treatment of idiopathic macular holes using pars plana vitrectomy, ILM peeling using Brilliant Blue dye, and silicone oil tamponade without postoperative posturing. The preoperative staging of macular holes and postoperative anatomic outcomes were assessed using spectral-domain optical coherence tomography. **RESULTS:** All patients were women with a mean age of 66.86 ± 4.8 years. In two patients, bilateral macular holes were present and both eyes were operated on. Stage 2 macular hole was diagnosed in three eyes, three eyes had stage 3, and four eyes had stage 4 macular holes. Anatomical success and closure of the macular hole was achieved in nine eyes (90%) after one operation. In one eye, the macular hole was closed after reoperation. The preoperative mean best-corrected visual acuity (BCVA) was 0.15 decimal units (0.8 logMAR units). Until the end of the follow-up period, BCVA was 0.25 decimal units (0.6 logMAR units). Visual acuity was improved in seven patients (70%). In two patients (20%), visual acuity remained at the same level, and in one eye (10%), visual acuity decreased. Postoperatively, all patients reported a significant reduction of metamorphopsia. **CONCLUSION:** Initial results after 20G pars plana vitrectomy with peeling of the ILM, use of dye (Brilliant Blue), and tamponade with silicone oil without postoperative posturing gave good anatomical and functional outcome in terms of visual acuity and reduction of metamorphopsia. Taking into account the age of the patients, this method, which does not require prolonged postoperative face-down posturing, was well tolerated by the patients. Because the anatomical and visual outcome as well as the rate of postoperative complications are comparable to those when gas is used as a tamponading agent, silicone oil tamponade can also be safely used as a first option in surgery of macular holes. However, a longer period of follow-up of the operated eyes, as well as a larger group of operated eyes, will be required to identify long-term outcomes of this surgical treatment. PMCID: PMC3460698. PMID: 23055662

Ivanovski M, Damcevski N, Radevska B, Doicev G. The influence of the depth of embryo replacement into the uterine cavity on in vitro fertilization outcome. Akush Ginekol (Sofia). 2012;51(3):59-67.

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OBJECTIVE: The aim of our study was to investigate the influence of the depth of embryo replacement into the uterine cavity on the implantation rate after embryo transfer carried out under transabdominal

ultrasound guidance. **METHODS:** This was a prospective observational study at the St Lazar Hospital, Skopje; spisan patients with an indication for IVF or ICSI according to departmental protocol underwent controlled ovarian hyperstimulation followed by IVF/ICSI and embryo transfer. The highest quality embryos were selected for transfer, with quality being assessed based on cell number and number of cytoplasmic fragments. On the day of ET under direct transabdominal ultrasound guidance, the transfer catheter was advanced through the endocervical canal into the lower uterine segment. Immediate identification of the catheter tip was essential to minimize motion of the catheter and avoid any impact on the endometrium. The transfer catheter then was advanced to a defined distance from the uterine fundus, up to the point estimated for transfer: 10 ± 2.5 mm and 15 ± 2.5 mm respectively in A and B group. This measurement was verified by using the calipers prior to injection of the embryos. **RESULTS:** In total, 106 patients, aged 24-42 years were included in the study. The patients were divided into two groups according to the distance between the tip of the catheter and the uterine fundus at the time of embryo deposition in the cavity: group A: 10 ± 2.5 mm; group B: 15 ± 2.5 mm. Of the patients studied, 47.16% were less than 35 years old, with only 11.3% more than age 40 years. The majority (66.9%) of patients had either none or one previous transfer. In only 3.7% transfers was blood noted on the catheter tip; and 77.4% of transfers were rated as easy compared to 5.6% rated as difficult. The remaining transfers were moderately difficult. The mean number of embryos transferred per cycle was 2.32. A mean E2 levels on HCG day was 2120 pg/ml. Overall clinical pregnancy were 37.7%. There were not significantly differences between the two groups in term of embryo transfer characteristics (full bladder, ease of transfer, use of tenaculum, bleeding). Our results show that there was not significantly differences between two groups in term of gonadotropin ampoules administered (30 ± 12.2 in group A vs. 3633 ± 868 in group B); Estradiol levels on the day of HCG day (1897 ± 761 in group A vs 29.2 ± 10.8 in group B), mean of oocytes retrieval and embryo transferred (ET) (8.5 ± 6.7 vs 10.9 ± 6.9 ; 1.9 ± 1.1 vs 2.3 ± 1.2 respectively in group A and B), and grade of ET. Analysis of our results demonstrated that pregnancy rate is significantly influenced by transfer distance from the fundus where the pregnancy rate decreases from 46.2% in group B to 28.8% in group A ($p < 0.05$). There was not significantly difference in abortion rate between the two groups. **CONCLUSION:** In conclusion, our results suggest that depth of embryo replacement inside the uterine cavity may influence the pregnancy rates and should be considered as an important factor to improve the success of IVF cycles. PMID: 23236668

Ivanovski M, Damcevski N, Radevska B, Doicev G. Assessment of uterine artery and arcuate artery

blood flow by transvaginal color Doppler ultrasound on the day of human chorionic gonadotropin administration as predictors of pregnancy in an in vitro fertilization program. Akush Ginekol (Sofia). 2012;51(2):55-60.

Department of Human reproduction, St Lazar Hospital, Skopje. R. Macedonia.

OBJECTIVE: To investigate whether success rates of IVF/ICSI could be predicted by using the Color Doppler technique by measuring the uterine artery and arcuate artery pulsatility (PI), resistance (RI), and velocity (Vs) indices on the day of hCG injection. **METHODS:** This was a prospective observational study at the St Lazar Hospital, Skopje; 106 patients with an indication for IVF or ICSI according to departmental protocol underwent controlled ovarian hyperstimulation followed by IVF/ICSI and embryo transfer. Using Color Doppler in the two-dimensional (2D) mode, flow velocity waveforms were obtained from the ascending main branch of the uterine artery on the right and left sides of the cervix in a longitudinal plane and arcuate arteries, before they entered the uterus. The PI, RI and peak systolic velocity (PSV) of the uterine arteries and arcuate arteries were calculated electronically when similar consecutive waveforms of good quality were obtained and results were compared between patients who conceived and those who did not. **RESULTS:** In total, 106 patients, aged 24-42 years were included in the study. The patients were divided into two groups according to successful outcome, defined as pregnancy and failure of implantation, where no pregnancy was detected. A total of 40 pregnancies resulted; a crude pregnancy rate was 40/106 (37.7%). There were no significant differences between either group in patients' age, type and duration of infertility; basal levels of FSH, LH and E2; number of gonadotropin ampoules used for ovulation induction; number of retrieved oocytes and number of transferred embryos. No cycle was canceled after initiation of gonadotropin stimulation. In our results, there were statistically significant lower mean uterine artery PI and RI in the pregnant group than in the non-pregnant group ($P < 0.05$). Arcuate artery PI value was lower in the pregnant group than in the non-pregnant group, but this did not reach statistical significance. Peak systolic velocity (Vs) values in both the mean uterine artery and arcuate artery were higher in the pregnant group than in the non-pregnant group; however, the difference was not statistically significant. **CONCLUSION:** Vascular impedance was calculated with PI, RI, and Vs values, among which PI was found to be the most important. Optimal uterine receptivity can be accomplished by reduced vascular resistance and increased blood flow, which will improve pregnancy success. We suggest the use of transvaginal color Doppler ultrasonography to measure the blood flow in uterine arteries and arcuate arteries before hCG in IVF cycles. PMID: 23234017

Ivanovski N. Chronic kidney disease in the developing countries! Are we really so different? Ann Afr Med. 2012 Apr-Jun;11(2):121.

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Comment on Ann Afr Med. 2012 Apr-Jun;11(2):119-20. PMID: 22500358

Ivić-Kolevska S, Miljković-Selimović B, Kocić B. Survival of Campylobacter jejuni in chicken meat at frozen storage temperatures. Acta Microbiol Immunol Hung. 2012 Jun;59(2):185-98.

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The aim of this study was to determine the survival of *Campylobacter jejuni* in chicken meat samples at frozen temperatures and given length of incubation and to determine the impact of aerobic bacteria on the survival of *C. jejuni*. The chicken meat samples were inoculated with *C. jejuni* NCTC 11351 suspensions and stored in bags at temperatures of -20°C and -70°C . The mean value of *C. jejuni* from meat samples decreased from 7.52 log₁₀ CFU/g after 30 minutes of incubation at ambient temperature, to 3.87 log₁₀ CFU/g on the eighth week of incubation at -20°C , and to 3.78 log₁₀ CFU/g at incubation at -70°C after the same incubation period. Both freezing temperatures, -20°C and -70°C , decreased the number of campylobacters. The presence of aerobic mesophilic bacteria did not influence the survival of *C. jejuni* in chicken meat samples. Keeping poultry meat at freezing temperatures is important for the reduction of *C. jejuni*, which has a strong influence on the prevention of occurrence of campylobacteriosis in humans. PMID: 22750779

Joksimovic N, Spasovski G, Joksimovic V, Andreevski V, Zuccari C, Omini CF. Efficacy and tolerability of hyaluronic acid, tea tree oil and methyl-sulfonyl-methane in a new gel medical device for treatment of haemorrhoids in a double-blind, placebo-controlled clinical trial. Updates Surg. 2012 Sep;64(3):195-201.

Clinic of Gastroenterohepatology, Medical Faculty Skopje, University of Skopje, Skopje, Macedonia.

Topical formulations are widely used in anti-haemorrhoidal treatment, but often lacking controlled clinical trials. Here, we report the results from a controlled clinical trial performed with a new gel medical device (Proctoial) containing hyaluronic acid with tea tree oil and methyl-sulfonyl-methane as major components. The total number of 36 haemorrhoidal patients (grade 1-3) was enrolled in a double-blind, placebo-controlled clinical trial and divided into 2 equal parallel groups. The anal pain, pain during

defecation, visible bleeding, pruritus and irritation/inflammation were recorded before and after 14-day treatment using a visual analogue scale both by the investigators and by the patients. Safety and tolerability of the treatments were also recorded. The new gel medical device statistically significantly reduced all the symptoms after the treatment compared to placebo. The results indicated also a very good tolerability and safety of the treatments. PMID: 22492249

Jordanova M, Rocha MJ, Rebok K, Rocha E. Changes in the amount of kidney pigmented macrophage aggregates throughout the breeding cycle of female Ohrid trout, *Salmo letnica* Kar. (Teleostei, Salmonidae). *Microsc Res Tech.* 2012 Feb;75(2):176-81.

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Changes in fish macrophages (Macs) are useful indicators of environmental pressures, but responses due to chemical and nonchemical stresses may be confounded by natural sources of variability. These may include sex and gonadal stage. In this study, we start addressing the following question: is the seasonally dependent ovary stage a factor to consider when using kidney Macs as biomarkers? To tackle this problem, the relative amount of pigmented Macs in kidney (head, trunk, and tail portions) was stereologically estimated in Ohrid trout, and related with the breeding status. The amount of Macs significantly increased from pre vitellogenesis to late vitellogenesis and showed a decreasing trend then after, with lower values noted after spawning in the head (1.9% versus 7.5% versus 2.0%), trunk (1.8% versus 7.5% versus 2.5%), and tail (2.5% versus 6.7% versus 2.9%) kidney. The decrease seen at spawning was significant in head and trunk kidney, and at post spawning it was significant for all kidney portions. The amounts of Macs were positively correlated with the ovary relative weights and plasma estradiol levels. We proved for the first time that fish kidney pigmented Macs can vary in amount during the breeding cycle. Our data, combined with literature, strongly support that the sex-steroid profile and kidney status-seasonal remodeling both influence the Macs pool; likely not only in female trout. So, while increases in Macs may warn of ecosystem problems, we show that using kidney Macs for biomonitoring should also take into account seasonally, particularly that related with ovary maturation. PMID: 21761499

Kenig N, Nikolovska J. Assessing the psychometric characteristics of the Macedonian version of the Oral Health Impact Profile questionnaire (OHIP-MAC49). *Oral Health Dent*

Manag. 2012 Mar;11(1):29-38.

University of Ss. Cyril and Methodius in Skopje, Republic of Macedonia.

AIM: The aim of this study was to adapt the Oral Health Impact Profile-49 (OHIP-49) for use by the Macedonian-speaking population and to assess its psychometric properties. **METHODS:** After piloting a back-translated version of the OHIP-49 questionnaire in Macedonian, the resulting Macedonian version of the Oral Health Impact Profile questionnaire (OHIP-MAC49) was administered to 247 patients who had been recruited in four groups: Group 1 was composed of 163 randomly chosen blood donors representing the general population; Group 2 was a convenience sample of 20 patients who attended a clinic for relief of dental pain; Group 3 was a sample of 29 prosthodontic patients; and Group 4 was composed of 35 students. In order to ensure that all questions were answered, data were gathered from participants in the four groups by trained and experienced interviewers. The internal reliability of the OHIP-MAC49 scale and its constituent seven subscales was calculated for Groups 1, 3, and 4 by using Cronbach's alpha coefficient and average inter-item correlations. The test-retest stability of the instrument was estimated by calculating the intra-class correlation coefficients and the limits of agreement of the scores obtained from the participants in Groups 3 and 4 in a repeat interview three to four weeks after the first interview. Convergent validity was evaluated by comparing OHIP-MAC49 scores-both total (0-4) and subscores (2-4) with self-reported health for Group 3 patients-using the Spearman coefficient of correlation. For the purpose of evaluating group validity, the OHIPMAC49 scores of Group 3 patients were compared by using Spearman's correlation coefficient. In addition, comparisons were made between patients with and without burning-mouth symptoms, temporomandibular pain, joint clicking, and oral habits (point-biserial correlation). The OHIP-MAC49 scores of subjects with and without dentures in Group 1 were compared by using point-biserial correlation. The responsiveness of the instrument was assessed by calculating the difference in OHIP-MAC49 means (total subscores) in Group 2 patients prior to and after treatment for relief of pain. **RESULTS:** The internal consistency of each subscale and the whole scale estimated was excellent. Cronbach's alpha coefficients for whole scale ranged from 0.92 to 0.95. The intra-class correlation coefficients ranged from 0.83 to 0.99, suggesting that the instrument had satisfactory reliability in terms of time stability. The questionnaire had acceptable responsiveness, confirmed by a significant differences ($P < 0.01$) between the mean OHIP-MAC49 score at baseline and follow-up, both for the total sum (0-4) and the sum scores (2-4). Convergent validity, evaluated by comparing OHIP-MAC49 scores with self-reported oral health in Group 1 and Group 3 patients, was confirmed, because all correlation coefficients were significant ($P < 0.01$). The results from testing the anticipated differences on the

basis of seven self-reported indicators of oral health in Group 3 patients, as well as the differences in OHIP-MAC49 scores between subjects in general population who wore and did not wear dentures, strongly suggest that the instrument has satisfactory group validity. **CONCLUSION:** The Macedonian version of the OHIP-49 demonstrated satisfactory validity, excellent reliability, and sufficient responsiveness and therefore can be used for assessing the impact of oral health on different aspects of quality of life in Macedonia. PMID: 22488030

Kirandjiski T, Mrenoski S, Celms I, Mitrov D, Dzadzovski I, Cvetkovikj I, Krstevski K, Picard-Meyer E, Viviani P, Malinovski D, Demerson JM, Cvetkovikj A, Davcheva K, Nakova E, Tomeska Mickova S, Cliquet F. First reported cases of rabies in the Republic of Macedonia. Vet Rec. 2012 Mar 24;170(12):312.

Animal Health and Welfare Sector, Treta Makedonska Brigada bb, Skopje 1000, Macedonia.

PMID: 22441980

Kocevski V, Pejov L. Anharmonic vibrational frequency shifts upon interaction of phenol+ with the open shell ligand O₂. The performance of DFT methods versus MP2. J Phys Chem A. 2012 Mar 1;116(8):1939-49.

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Anharmonic vibrational frequency shifts of the phenol(+) O-H stretching mode upon complex formation with the open-shell ligand O₂ were computed at several DFT and MP2 levels of theory, with various basis sets, up to 6-311++G(2df,2pd). It was found that all DFT levels of theory significantly outperform the MP2 method with this respect. The best agreement with the experimental frequency shift for the hydrogen-bonded minimum on the potential energy surfaces was obtained with the HCTH/407 functional (-93.7 cm⁻¹) theoretical vs -86 cm⁻¹) experimental), which is a significant improvement over other, more standard DFT functionals (such as, e.g., B3LYP, PBE1PBE), which predict too large downshifts (-139.9 and -147.7 cm⁻¹), respectively). Good agreement with the experiment was also obtained with the mPW1B95 functional proposed by Truhlar et al. (-109.2 cm⁻¹). We have attributed this trend due to the corrected long-range behavior of the HCTH/407 and mPW1B95 functionals, despite the fact that they have been designed primarily for other purposes. MP2 method, even with the largest basis set used, manages to reproduce only less than 50% of the experimentally detected frequency downshift for the hydrogen-bonded dimer. This was attributed to the

much more significant spin contamination of the reference HF wave function (compared to DFT Kohn-Sham wave functions), which was found to be strongly dependent on the O-H stretching vibrational coordinate. All DFT levels of theory outperform MP2 in the case of computed anharmonic OH stretching frequency shifts upon ionization of the neutral phenol molecule as well. Besides the hydrogen-bonded minimum, DFT levels of theory also predict existence of two other minima, corresponding to stacked arrangement of the phenol(+) and O₂ subunits. mPW1B95 and PBE1PBE functionals predict a very slight blue shift of the phenol(+) O-H stretching mode in the case of stacked dimer with the nearly perpendicular orientation of oxygen molecule with respect to the phenolic ring, which is entirely of electrostatic origin, in agreement with the experimental observations of an additional band in the IR photodissociation spectra of phenol(+)-O₂ dimer [Patzer, A.; Knorke, H.; Langer, J.; Dopfer, O. Chem. Phys. Lett. 2008, 457, 298]. The structural features of the minima on the studied PESs were discussed in details as well, on the basis of NBO and AIM analyses. PMID: 22276555

Krstevska V, Stojkovski I, Zafirova-Ivanovska B. Concurrent radiochemotherapy in locally-regionally advanced oropharyngeal squamous cell carcinoma: analysis of treatment results and prognostic factors. Radiat Oncol. 2012 May 28;7:78.

Department of Head and Neck Cancer, University Clinic of Radiotherapy and Oncology, Skopje, Macedonia.

BACKGROUND: Concurrent radiochemotherapy is a recommended treatment option for patients with locally advanced squamous cell head and neck carcinomas with recent data showing the most significant absolute overall and event-free survival benefit achieved in patients with oropharyngeal tumours. The aim of this study was to analyse the results of three-dimensional conformal radiotherapy given with concomitant weekly cisplatin in patients with advanced oropharyngeal carcinoma and to identify prognostic factors influencing outcomes of this patients category. **METHODS:** Sixty-five patients with stage III or IV squamous cell carcinoma of the oropharynx who underwent concurrent radiochemotherapy between January 2005 and December 2010 were retrospectively analyzed. All patients received radiotherapy to 70 Gy/35 fractions/2 Gy per fraction/5 fractions per week. Concurrent chemotherapy consisted of weekly cisplatin (30 mg/m²) started at the first day of radiotherapy. **RESULTS:** Median age was 57 years (range, 36 to 69 years) and 59 (90.8%) patients were male. Complete composite response was achieved in 47 patients (72.3%). Local and/or regional recurrence was the most frequent treatment failure present in 19 out of 25 patients (76.0%). At a median follow-up of 14 months

(range, 5 to 72 months), 2-year local relapse-free, regional relapse-free, locoregional relapse-free, disease-free, and overall survival rates were 48.8%, 57.8%, 41.7%, 33.2% and 49.7%, respectively. On multivariate analysis the only significant factor for inferior regional relapse-free survival was the advanced N stage ($p = 0.048$). Higher overall stage was independent prognostic factor for poorer local relapse-free survival, locoregional relapse-free survival and disease-free survival ($p = 0.022$, $p = 0.003$ and $p = 0.003$, respectively). Pre-treatment haemoglobin concentration was an independent prognostic factor for local relapse-free survival, regional relapse-free survival, locoregional relapse-free survival, disease-free survival, and overall survival ($p = 0.002$, $p = 0.021$, $p = 0.001$, $p = 0.002$ and $p = 0.002$, respectively). CONCLUSIONS: Poor treatments results of this study suggested that introduction of intensity-modulated radiotherapy, use of induction chemotherapy followed by concurrent radiochemotherapy, accelerated radiotherapy regimens, and molecular targeted therapies could positively influence treatment outcomes. The incorporation of reversal of anaemia should be also expected to provide further improvement in locoregional control and survival in patients with advanced squamous cell carcinoma of the oropharynx. PMID: 22640662. PMCID: PMC3404949. PMID: 22640662

Krstevska V. Early stage squamous cell carcinoma of the pyriform sinus: a review of treatment options. Indian J Cancer. 2012 Apr-Jun;49(2):236-44.

Department of Head and Neck Cancer, University Clinic of Radiotherapy and Oncology, Skopje, Republic of Macedonia.

The purpose of this review of the literature was to present treatment options for early stage pyriform sinus cancer. Squamous cell carcinoma of the pyriform sinus, as the most frequent cancer arising from the hypopharynx, is rarely diagnosed in its early stage. Based on evidence from retrospective studies, conservation surgery and definitive radiotherapy are considered the available treatment modalities for patients presenting with stage T1 and T2 pyriform sinus carcinomas without clinical evidence of neck lymph node metastases, offering similar results with respect to disease control and functional organ preservation. Also, the high risk of occult metastatic nodal disease even in the earliest stage of pyriform sinus cancer entails elective neck dissection or elective neck irradiation to be considered mandatory. However, for patients with early stage pyriform sinus cancer, no level 1 study exists in which conservation surgery is compared with radiotherapy alone for the evaluation of local control or survival. Randomized multicenter controlled trials evaluating efficacy of conservation surgery and definitive radiotherapy, and correctly interpreting functional outcome for each of the treatment procedures examined are necessary to

obtain sufficient evidence to influence the decision in the choice of the most effective treatment for early pyriform sinus cancer. PMID: 23107977

Lazarevik V, 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.

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

PMID: 23275476

Madjunkova S, Volk M, Peterlin B, Plaseska-Karanfilska D. Detection of thrombophilic mutations related to spontaneous abortions by a multiplex SNaPshot method. Genet Test Mol Biomarkers. 2012 Apr;16(4):259-64.

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

Spontaneous abortion is a significant clinical problem of different etiologies. Certain thrombophilia gene mutations have been associated with an increased risk of spontaneous abortion. Also, mutations in folate-related genes can lead to abnormal chromosomal segregation during meiosis which is the most common cause of spontaneous abortion. We have developed a multiplex single-base extension reaction assay that allows simultaneous analysis of 10 different mutations in thrombophilia- and folate-related genes (Factor V Leiden G1691A, Factor V H1299R, Factor II G20210A, Factor XIII V34L, PAI-I -675 4G/5G, FGB -455G/A, MTHFR C677T, MTHFR A1298C, MTR A2756G, and MTRR A66G). Using this method we have studied 232 women who had a spontaneous abortion and 209 of their male partners. Prevalence of Factor II G20210A and Factor V H1299R mutations was significantly higher in the women than in their male partners (2.4% and 0.7%, respectively [$p=0.0499$] for the Factor II mutation and 9.3% and 5.7%, respectively [$p=0.0485$] for the Factor V mutation). The prevalence of MTHFR C677T, MTHFR A1298C, MTR A2756G, and MTRR A66G mutations did not differ between the studied groups. In conclusion, we have developed a rapid, simple, reliable, and inexpensive multiplex SNaPshot method for determination of 10 thrombophilic mutations that may result in spontaneous abortions. PMID: 22023244. PMCID: PMC3326265. PMID: 22023244

Makraduli L, 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.

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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

Manuševa N, Novotni A, Bajraktarov S, Zafirova-Ivanovska B. Some QEEG parameters and gender differences in schizophrenia patients. *Psychiatr Danub.* 2012 Mar;24(1):51-6.

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BACKGROUND: Gender issues are extensively explored in schizophrenia. A mounting body of research evidence suggests that there are gender differences in the age at onset, duration of untreated psychosis and presented psychopathology. In recent years, in order to obtain neurophysiologic explanation for the disturbed behavior and thinking in schizophrenia, numerous studies have been performed focusing on the QEEG parameters. However, the results were inconclusive. The aim of this study was to investigate the gender differences in some clinical and QEEG parameters in schizophrenia patients. **SUBJECTS AND METHODS:** Thirty schizophrenia patients were enrolled in the study (M/F ratio 13/17; mean age 34 years). The QEEG parameters which were analyzed were amplitude, mean frequency and relative power of the main bands of the basic activity. Clinical assessment was performed using the PANSS, BPRS and CGI scales. **RESULTS:** QEEG parameters demonstrating statistically significant difference were amplitude and relative power in beta activity and lower mean theta frequency over left frontal, temporal and parietal regions in female patients who also had statistically significant differences in PANSS and BPRS scores. **CONCLUSION:** Differences in amplitude and relative power in the beta bands in female schizophrenic patients are associated with more severe actual psychopathology. Considering the relatively small sample, the current results must be replicated with a larger group of drug-free patients to confirm the

findings. PMID: 22447086

Matveeva N, Zivadinovik J, Zdravkovska M, Jovevska S, Bojadzieva B. Histological composition of lumbar disc herniations related to the type of herniation and to the age. *Bratisl Lek Listy.* 2012;113(12):712-7.

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OBJECTIVES: To compare the data for histologic composition of the herniated disc material between different types of disc herniations and between patients of different age. **BACKGROUND:** Lots of studies have investigated the histologic composition of disc herniations. Few studies have examined the presence of granulation tissue related to the type of herniations and age of the subjects. **METHODS:** 120 patients divided in to two age groups underwent MR imaging before microsurgical removal of the herniations. Disc herniations were divided in to two groups, non migrated and large migrated disc herniations. The histologic assessment of the herniated material is done by dividing the intercellular matrix into four types. The existence of areas of granulation tissue and hyaline cartilage is evaluated too. **RESULTS:** The tissue composition showed significant differences between patients of different age. Areas of granulation tissue and neovascularisation are found in 12% of 64 protrusions and contained extrusions, and in 29% of 56 large migrated disc extrusions ($p=0.029$). In elderly patients the tissue composition changed with a significant decrease of prevailing nucleus pulposus composition in 7% of 60 ($p=0.000$) and a significant increase of prevailing fibrous tissue composition in 40% of 60 patients ($p=0.000$). Areas of granulation tissue and neovascularisation were found in 27% of 60 patients aged ≤ 50 and in 13% of 60 patients aged >50 . **CONCLUSIONS:** The tissue composition of the herniated material showed more expressed differences between subjects of different age. Granulation tissue and neovascularisation were more frequent findings in large migrated disc herniations and in patients aged 35 to 50 years. PMID: 23173629

Mile B, Valerija K, Krsto G, Ivan V, Ilir D, Nikola L. Doxycycline-rifampin versus doxycycline-rifampin-gentamicin in treatment of human brucellosis. *Trop Doct.* 2012 Jan;42(1):13-7.

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This prospective, non-randomized trial, compared the efficacy and tolerance of a doxycycline-rifampin regimen, administered for 45 days, versus doxycycline-rifampin given for 45 days plus

gentamicin for the first 7-10 days, in the treatment of human brucellosis. Of 238 patients that were initially included in the study, 181 were finally evaluated. Ninety-four were treated with the doxycycline-rifampin and 87 with the doxycycline-rifampin-gentamicin regimens. In the doxycycline-rifampin group: relapses were noted in 13 (13.8%) patients; therapeutic failures in five (5.3%); and mild adverse effects in 28 (29.8%). In the doxycycline-rifampin-gentamicin group: four (4.6%) relapsed; and five (5.7%) therapeutic failures were registered. Mild adverse effects were registered in 29 (33.3%) patients. The doxycycline-rifampin-gentamicin regimen demonstrated a significantly lower relapse rate compared to the doxycycline-rifampin combination ($P = 0.034$). We conclude that adding gentamicin for the first 7-10 days to the standard oral doxycycline-rifampin regimen can decrease the rate of relapses. PMID: 22290107

Minov J, Karadžinska-Bislimovska J, Vasilevska K, Nelovska Z, Risteska-Kuc S, Stoleski S, Mijakoski D. Smoking among Macedonian workers five years after the anti-smoking campaign. Arh Hig Rada Toksikol. 2012 Jun 1;63(2):207-13.

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To assess the efficacy of nationwide anti-smoking campaign, we compared the findings of a study on worker smoking performed in 2005 with our latest cross-sectional study completed in 2010. It included 753 randomly selected workers, of whom 126 office, 108 construction, 93 agricultural, 97 petroleum refinery, 114 textile, 117 food processing workers, and 98 cleaners. Information was collected with a self-administered questionnaire. The prevalence of current smokers among all workers was 35.4 %, ranging from 30.2 % in office workers to 43.5 % in construction workers. It did not significantly differ from the prevalence recorded in 2005 (35.4 % vs. 36.8 %, respectively; $P=0.441$). Mean pack-years smoked among all smokers was 12.4 ± 2.3 , ranging from 10.9 in administrative workers to 13.7 in agricultural workers. We did not find any significant difference in the prevalence of current smokers between male and female workers and between workers aged less or more than 40 years, as well as between workers of higher and lower education. The prevalence of ex-smokers was 10.5 %, ranging from 8.4 % in construction workers to 12.1 % in administrative workers, whereas the prevalence of passive smokers was 29.1 %, ranging from 26.2 % in food processing workers to 32.9 % in agricultural workers. Our findings indicate that the prevalence of current and passive smokers has remained high regardless of the anti-smoking campaign and call for stricter implementation of anti-smoking regulations. PMID: 22728803

Mirceski V, Hocevar SB, Ogorevc B, Gulaboski R, Drangov I. Diagnostics of anodic stripping mechanisms under square-wave voltammetry conditions using bismuth film substrates. Anal Chem. 2012 May 15;84(10):4429-36.

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

A mechanistic study to provide diagnostics of anodic stripping electrode processes at bismuth-film electrodes is presented from both theoretical and experimental points of view. Theoretical models for three types of electrode mechanisms are developed under conditions of square-wave voltammetry, combining rigorous modeling based on integral equations and the step function method, resulting in derivation of a single numerical recurrent formula to predict the outcome of the voltammetric experiment. In the course of the deposition step, it has been assumed that a uniform film of the metal analyte is formed on the bismuth substrate, in situ deposited onto a glassy carbon electrode surface, without considering mass transfer within either the bismuth or the metal analyte film. Theoretical data are analyzed in terms of dimensionless critical parameters related with electrode kinetics, mass transfer, adsorption equilibria, and possible lateral interactions within the deposited metal particles. Theoretical analysis enables definition of simple criteria for differentiation and characterization of electrode processes. Comparing theoretical and experimental data, anodic stripping processes of zinc(II), cadmium(II), and lead(II) are successfully characterized, revealing significant differences in their reaction pathways. The proposed easy-to-perform diagnostic route is considered to be of a general use while the bismuth film exploited in this study served as a convenient nonmercury model substrate surface. PMID: 22462643

Mirceva G, Cingovska I, Dimov Z, Davcev D. Efficient approaches for retrieving protein tertiary structures. IEEE/ACM Trans Comput Biol Bioinform. 2012 Jul-Aug;9(4):1166-79.

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The 3D conformation of a protein in the space is the main factor which determines its function in living organisms. Due to the huge amount of newly discovered proteins, there is a need for fast and accurate computational methods for retrieving protein structures. Their purpose is to speed up the process of understanding the structure-to-function relationship which is crucial in the development of new drugs. There are many algorithms addressing the problem of

protein structure retrieval. In this paper, we present several novel approaches for retrieving protein tertiary structures. We present our voxel-based descriptor. Then we present our protein ray-based descriptors which are applied on the interpolated protein backbone. We introduce five novel wavelet descriptors which perform wavelet transforms on the protein distance matrix. We also propose an efficient algorithm for distance matrix alignment named Matrix Alignment by Sequence Alignment within Sliding Window (MASASW), which has shown as much faster than DALI, CE, and MatAlign. We compared our approaches between themselves and with several existing algorithms, and they generally prove to be fast and accurate. MASASW achieves the highest accuracy. The ray and wavelet-based descriptors as well as MASASW are more accurate than CE. PMID: 22025763

Palcevaska-Kocevska S, Aluloska N, Krstevska M, Shukarova-Angelovska E, Kojik L, Zisovska E, Kocevski D, Kocova M. Correlation of serum adiponectin and leptin concentrations with anthropometric parameters in newborns. Srp Arh Celok Lek. 2012 Sep-Oct;140(9-10):595-9.

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INTRODUCTION: It has been shown that some adipocytokines and their mutual relationship can be indicators of fetal and neonatal growth. Physiological role of leptin and adiponectin in fetal and neonatal growth is not well established. **OBJECTIVES:** The aim of this study was to assess the correlation of the anthropometrics parameters and serum concentration of leptin and adiponectin levels in healthy newborns. **METHODS:** A cohort of 110 neonates, born after uncomplicated singleton pregnancies at term, were classified as AGA ($n = 60$), SGA ($n = 30$) and LGA ($n = 20$) according to the Lubchenco curves. Anthropometric parameters of the neonates: birth weight (BW), birth length (BL), body weight/body length ratio (BW/ BL), Body Mass Index (BMI) and Ponderal Index (II) were recorded after birth. **RESULTS:** Mean serum leptin and adiponectin levels in both sexes were not significantly different (male: 1.8 ± 0.75 ; 29.5 ± 22.89 and female: 2.0 ± 0.99 ; 31.6 ± 23.51 ng/mL). There was a significant difference between leptin levels in AGA and LGA newborns (11.9 ± 0.84 vs. 3.1 ± 1.50 ng/mL) ($p < 0.05$), and in adiponectin levels between AGA and LGA compared to SGA newborns ($32. \pm 23.29$ and 43.4 ± 31.24 vs. 12.6 ± 2.43 ng/mL, respectively; $p < 0.05$; $p < 0.05$). Leptin and adiponectin levels were positively correlated with BW ($r = 0.63$ and $r = 0.41$), BL ($r = 0.63$, $r = 0.42$), BW/BL ($r = 0.61$, $r = 0.41$), BMI ($r = 0.54$, $r = 0.35$), and PI ($r = 0.47$, $r = 0.29$, ($p < 0.01$). **CONCLUSION:** Significantly higher adiponectin levels were found in AGA neonates compared to SGA neonates. Leptin and adiponectine levels were positively correlated with birth weight. These findings

suggest that these adipocytokines may be involved in fetal growth regulation. PMID: 23289275

Pereska Z, Bozinovska C, Dimitrovski C, Cakalarovski K, Chibishev A, Zdravkovska M, Babulovska A, Janicevic D. Heroin dependence duration influences the metabolic parameters: mechanisms and consequences of impaired insulin sensitivity in hepatitis C virus seronegative heroin dependents. J Addict Med. 2012 Dec;6(4):304-10.

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OBJECTIVE: Carbohydrate metabolism disorder in heroin dependence is an issue with long history and contradicting results. The aim of the study was to evaluate basal insulin sensitivity in hepatitis C virus seronegative heroin dependents with normal body mass index, taking into consideration the duration of heroin dependence. **METHOD:** 78 heroin dependents and 32 healthy controls were enrolled in the cross-sectional, prospective study. The dependents were observed in 2 groups: group 1 with dependence duration less than or equal to 3 years and group 2 with more than 3 years. Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) and β -cell function (HOMA-B%) were used to define basal glucose-insulin homeostasis. **RESULTS:** The group with longer dependence duration had HOMA-IR (2.23 ± 3.15) significantly higher compared with the control group (1.23 ± 0.53 , $P = 0.016$) but lower compared with the group with the shorter dependence duration (2.65 ± 2.66 , $P = 0.024$), after adjustment for HOMA-B%, waist circumference, and aspartate aminotransferase. The decrease in HOMA-IR during prolonged heroin addiction was significantly associated with the reduced β -cell function ($P < 0.001$) and waist circumference ($P = 0.004$). **CONCLUSIONS:** Heroin dependence is associated with increased insulin resistance in hepatitis C virus seronegative heroin dependents. Prolonged heroin use is associated with reduction of basal β -cell pancreatic function with decreased insulin resistance controlled for waist circumference, but still inducing significantly decreased basal insulin sensitivity. PMID: 23013781

Pesevska S, Nakova M, Gjorgoski I, Angelov N, Ivanovski K, Nares S, Andreana S. Effect of laser on TNF-alpha expression in inflamed human gingival tissue. Lasers Med Sci. 2012 Mar;27(2):377-81.

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This study sought to evaluate the effect of low-level laser treatment combined with scaling and root planing (SRP) on gingival tissue levels of TNF-alpha

in subjects with periodontal disease. Eighty gingival papilla biopsy samples were obtained from 60 patients diagnosed with chronic advanced periodontitis; randomly assigned to three treatment groups (n = 20), as well as 20 subjects with no periodontal disease (group A). Group B received SRP on a single quadrant/day for four consecutive days. On day 5, all quadrants were rescaled. Groups C and D received the same treatment as group B plus laser application with the low-level diode laser (630-670 nm, 1.875 J/cm(2)) for five and ten consecutive days, respectively. Papilla biopsies were obtained from subjects and evaluated by ELISA for levels of TNF-alpha. The values in the control group were 5.2 ± 3.21 pg/mg and baseline values for the examined groups were 46.01 ± 16.69 . Significantly decreased level of TNF-alpha for groups C and D was found after treatment, while group B demonstrated reduction of TNF-alpha of 31.34%. The results of this study show suppression of TNF-alpha in gingival tissue after low-level laser treatment as adjunct to SRP. Data may suggest beneficial anti-inflammatory effects of the laser treatment when used as adjunctive periodontal treatment. PMID: 21380536

Petanovski Z, Dimitrov G, Aydin B, Hadzi-Lega M, Sotirovska V, Susleski D, Saltirovski S, Matevski V, Stojkovska S, Petanovska E, Savic M, Balkanov T. Impact of active female smoking on controlled ovarian stimulation in intracytoplasmic sperm insemination cycles. Med Glas (Zenica). 2012 Aug;9(2):273-80.

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AIM: To examine the impact of smoking among females on controlled ovarian stimulation (COS), at intra-cytoplasmic sperm injection (ICSI) outcome. METHODS: A prospective analysis of outcomes of 876 women (fresh, non donor cycles) of which 559 (63.8%) were non-smokers, 317 (36.2%) were smokers, underwent standard COS/ICSI treatment. RESULTS: Among smokers, the average time of COS, expressed in days, was significantly longer compared with non-smokers (10.5 ± 2.10 vs. 10 ± 1.90 p less than 0, 05). There were no registered significant differences in the number of retrieved oocytes, (10.4 ± 6.8 vs 10.3 ± 6.9), mature oocytes (8.6 ± 5.8 vs. 8.4 ± 5.9), in the group of non-smokers versus smokers. However, smoking and age have a significant impact of the number of high-quality embryos, i.e. older smokers had a lower number of high-quality transferred embryos (non-smokers ≥ 35 years: smokers ≥ 35 years; 1.9 ± 1.1 vs. 1.6 ± 1). On multiple logistic regression analysis, factor that had a significantly negative impact of clinical pregnancy was maternal age. CONCLUSION: Smoking among patients entering the COS and ICSI fertilization process had insignificant negative impact on the final outcome of the process resulting in reduced

pregnancy rate. The chance for the pregnancy declines with age, but smoking did not significantly influence the outcome. PMID: 22926363

Petrovska BB. Historical review of medicinal plants' usage. Pharmacogn Rev. 2012 Jan;6(11):1-5.

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Healing with medicinal plants is as old as mankind itself. The connection between man and his search for drugs in nature dates from the far past, of which there is ample evidence from various sources: written documents, preserved monuments, and even original plant medicines. Awareness of medicinal plants usage is a result of the many years of struggles against illnesses due to which man learned to pursue drugs in barks, seeds, fruit bodies, and other parts of the plants. Contemporary science has acknowledged their active action, and it has included in modern pharmacotherapy a range of drugs of plant origin, known by ancient civilizations and used throughout the millennia. The knowledge of the development of ideas related to the usage of medicinal plants as well as the evolution of awareness has increased the ability of pharmacists and physicians to respond to the challenges that have emerged with the spreading of professional services in facilitation of man's life. PMID: 22654398

Petrovska S, Dejanova B, Jurisic V. Estrogens: mechanisms of neuroprotective effects. J Physiol Biochem. 2012 Sep;68(3):455-60.

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Within the last few years, there has been a growing interest in the neuroprotective effects of estrogen and the possible beneficial effects of estrogen in neurodegenerative diseases such as stroke, Alzheimer's disease, and Parkinson's disease. The concept of neuroprotective effects of estrogen in women remains controversial because these effects may vary with the timing of treatment. Research increasingly suggests that changes in estrogen levels during aging may increase risk for Alzheimer's disease, the most common type of dementia. This update reviews the newest information about estrogen and cognitive aging, including information regarding the role of bioavailable estrogen in older women and men. PMID: 22371015

Plaseski T, Noveski P, Popeska Z, Efremov GD, Plaseska-Karanfilska D. Association study of single-nucleotide polymorphisms in FASLG, JMJDIA, LOC203413, TEX15, BRDT, OR2W3, INSR,

and TAS2R38 genes with male infertility. J Androl. 2012 Jul-Aug;33(4):675-83.

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Infertility is a major health problem today, affecting about 15% of couples trying to conceive a child. Impaired fertility of the male factor is causative in 20% of infertile couples and contributory in up to another 30%-40%. Based on association studies, an increasing number of gene polymorphisms have been proposed to modulate the efficiency of spermatogenesis. Here, we have investigated the possible association of 9 single-nucleotide polymorphisms (SNP) in 8 different genes-FASLG, JMJDIA, LOC203413, TEX15, BRDT, OR2W3, INSR, and TAS2R38--with male infertility. We analyzed a total of 136 men with idiopathic infertility (60 azoospermic and 76 oligozoospermic) and 161 fertile controls. Our study group included individuals of different ethnic origin: 93 of the infertile men were Macedonians, 32 were Albanians, and 11 were of other origin. The control group was composed of 125 Macedonian and 36 Albanian men. The methodology included multiplex polymerase chain reaction/SNaPshot analyses, followed by capillary electrophoresis on an ABI3130 Genetic Analyzer. Of the 9 SNPs evaluated, 3 are significantly associated ($P < .05$) with male infertility: SNPs rs5911500 in LOC203413, rs3088232 in BRDT, and rs11204546 in OR2W3. SNP rs5911500 showed the strongest association with infertility among Albanians ($P = .0001$), whereas rs3088232 was most significantly associated with azoospermia among Macedonians ($P = .0082$). Moreover, the frequency of co-occurrence of LOC203413 minor T allele with either homozygosity or heterozygosity for the BRDT minor G allele was significantly higher among both azoospermic (6 of 60 [10%]; $P = .0057$; odds ratio [95% confidence interval], 8.83 [1.73-45.08]) and oligozoospermic (10 of 76 [13.2%]; $P = .0002$; odds ratio [95% confidence interval], 12.04 [2.57-56.47]) men in comparison with fertile controls (2 of 161 [1.2%]). PMID: 22016351

Pluncevic J. Influence of the physical activity on the cognitive functions with people depending on their age. Med Arh. 2012;66(4):271-5.

Faculty of Medicine, University of Skopje, Republic of Macedonia.

In comparison with the number of studies which have examined the physical activity influence on the cognitive capabilities with the adults (above 60 years of age), researches for children, adolescents and young adult population are rarely done. The examination of the potential connection, role or influence between Physical Activity and cognition during early age (the first third of the human life) is

very complex and subtle due to a large number of external factors which are present in the period during which the cognitive capabilities are still being developed. Regular physical activity improves the physiological and psychological aspect of human health. Due to the well known advantages and benefits from the physical activity, one would expect it to be more present in the life of contemporary man. But it is a fact that the level of physical activity with people decreases in the course of lifetime, especially in the period when young people move from secondary school to university. The decrease of the physical activity additionally increases the pressure over the young academic persons. There is not enough literature which examines the connection of the neuropsychological indicators and physical activity with young adults. It is obvious the need for further researches in this field which will create a solid base for the connection of the physical activity and cognition, the same one that is found for the adult population. Within the frame of positive role the physical activity has over the cognitive health, it is suggested as a means of reducing the risk of developing cognitive decrease connected with getting old. Future vast randomized researches and interventions would have to test the quantity and the type of physical activity which would be recommended in order to prevent or postpone the cognitive decrease. PMID: 22919885

Popovska-Jankovic K, Tasic V, Bogdanovic R, Miljkovic P, Golubovic E, Soylyu 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.

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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

Shirgoska B, Netkovski J. New techniques and devices for difficult airway management. Acta Clin Croat. 2012 Sep;51(3):457-61.

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The purpose of this review is to compare old conventional techniques and devices for difficult airway management and new sophisticated techniques and devices. Recent techniques and devices are defined as the American Society of Anesthesiology (ASA) practice guidelines for the management of difficult airway, published in 1992, reviewed in 1993 and updated in 2003. According to ASA, the techniques for difficult airway management are divided into techniques for difficult intubation and techniques for difficult ventilation. Awake fiberoptic intubation is the technique of choice for difficult airway management prescribed by the World Health Organization document for patient safety in the operating theater. Conventional techniques for intubation used direct visualization. The new generation of devices does not require direct visualization of the vocal cords for endotracheal tube placement. They allow better glottis view and successful endotracheal placement of the tube with indirect laryngoscopy. New intubation devices such as video laryngoscopes facilitate endotracheal intubation by indirect visualization of glottis structures without aligning the oral, pharyngeal and laryngeal axes in patients with cervical spine abnormality. Video laryngoscopes such as V-Mac and C-Mac, Glide scope, McGrath, Airway Scope, Airtraq, Bonfils and Bullard laryngoscope are widely available at the market. Airway gadgets are lighted stylets and endotracheal tube guides. The principal conclusion of this review is that utilization of these devices can be easily learned. The technique of indirect laryngoscopy is currently used for managing difficult airway in the operating room as well as for securing the airway in daily anesthesia routine. PMID: 23330414

Shishovska MA, Stefova MT. Fast and universal HPLC method for determination of permethrin in formulations using 1.8- μ m particle-packed column

and performance comparison with other column types. J Chromatogr Sci. 2012 Jan;50(1):43-50.

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An HPLC method has been developed for the fast separation and quantification of permethrin using C18 column packed with 1.8 μ m particles. The method is specific with good resolution to degradation products and to other present components. It has acceptable validation results. The run time is 4.5 min (or may be within 1.6 min in rapid resolution mode) with an organic solvent consumption of 3.6 mL per run. The method has been applied to samples of formulations for various uses: mattress cleaner, shampoo, and veterinary powder. The performance of the applied column is compared with other common column types. The relationships between linear velocity of the mobile phase (u) and resolution factor (R_s), back-pressure (ΔP), and efficiency (H) are presented. The experimental data shows the advantages of 1.8- μ m particle columns to be a significant reduction in solvent consumption (by factor of 4.4 and 1.5) and a reduction in run-time (by factor 4.7 and 1.5), and the weaknesses are a high back-pressure and lower efficiency. Finally, it has been shown that use of 1.8- μ m particle packed columns with conventional HPLC systems is possible, but with limitations in mobile phase flow-rate. PMID: 22291055

Smilkov D, Kocarev L. Influence of the network topology on epidemic spreading. Phys Rev E Stat Nonlin Soft Matter Phys. 2012 Jan;85(1 Pt 2):016114.

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The influence of the network's structure on the dynamics of spreading processes has been extensively studied in the last decade. Important results that partially answer this question show a weak connection between the macroscopic behavior of these processes and specific structural properties in the network, such as the largest eigenvalue of a topology related matrix. However, little is known about the direct influence of the network topology on the microscopic level, such as the influence of the (neighboring) network on the probability of a particular node's infection. To answer this question, we derive both an upper and a lower bound for the probability that a particular node is infective in a susceptible-infective-susceptible model for two cases of spreading processes: reactive and contact processes. The bounds are derived by considering the n -hop neighborhood of the node; the bounds are tighter as one uses a larger n -hop neighborhood to calculate them. Consequently, using local information for

different neighborhood sizes, we assess the extent to which the topology influences the spreading process, thus providing also a strong macroscopic connection between the former and the latter. Our findings are complemented by numerical results for a real-world email network. A very good estimate for the infection density ρ is obtained using only two-hop neighborhoods, which account for 0.4% of the entire network topology on average. PMID: 22400632

Spasovski G, Vanholder R. Kidney transplantation in emerging countries: do we know all issues? *Minerva Urol Nefrol.* 2012 Sep;64(3):183-9.

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Although it seems that end stage renal disease (ESRD) therapies gradually become more accessible in the developing world, yet, the vast majority of people living in those areas do not have access to dialysis and especially transplantation because of the economic and technological inequality as compared with the developed world. Despite the great advantage in survival and considerable socioeconomic advantages of transplantation vs. dialysis, there is a widespread recognition that the growing gap between organ supply and demand will continue into the foreseeable future. Several reasons might be considered in this regard as: insufficient data on the topic in the public domain, inadequate governmental financial resources, lack of public awareness, education and motivation for organ donation as well as the low number of organized teams of transplant surgeons and nephrologists, and lack of organizational infrastructure, i.e. coordinators. The defined priorities for the future in terms of improving living donor transplantation, composition of the official waiting lists and registries of transplant recipients and living donors and the role of transplant professionals have been discussed. In conclusion, whatever the governmental support is, as professionals, we should just reinforce our efforts to help our patients as best as we can in the current situation. PMID: 22971683

Spasovski G, Zdravkovska V, Zabzun M, Antarorov R, Ivanovski K, Janakievska P, Neskovski J, Karceva-Sarajlia E, Panova B, Petrovska T, Zulbeari L, Masin-Spasovska J, Taleska-Matovska N, Gelev S. Achievements in CKD-MBD guidelines targets: is there a progress in the implementation practice? *Int Urol Nephrol.* 2012 Dec;44(6):1791-8.

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BACKGROUND: Guidelines should help the practicing

nephrologists to reduce the variability in diagnostic and treatment strategies, and achieve the best possible patients' outcomes. The aim of our study was to look at the treatment strategies and the shortcomings in the implementation of the chronic kidney disease mineral and bone disorder (CKD-MBD) KDOQI guidelines in dialysis units across the Republic of Macedonia in 2009, and to analyze trends with regard to our previous analysis from 2005. METHODS: A questionnaire was sent in 2009 to all dialysis units in our country for data concerning CKD-MBD in dialysis patients. This study included 742 patients, comparable with the reply we got on the same our 2005 survey, with a total of 588 patients. We collected the last 6 months mean values of biochemical parameters [calcium (Ca), phosphate (P), and intact parathyroid hormone (iPTH)], as well as treatment data including dialysate Ca concentration, phosphate binding agents, and vitamin D doses. RESULTS: The majority of patients in both surveys had values within the target ranges for all parameters, except for iPTH, which was <150 pg/ml in most patients, in both reports. Compared to the 2005 study, in 2009 we found a significantly improved control of all four biochemical parameters, but a greater proportion of patients within guidelines targets was found only for serum Ca (79 vs. 67.4%, $P < 0.05$). Treatment with low Ca dialysate concentration of 1.25 mmol/L continued to be an underused option (3.7 vs. 6.1%), while the 1.75 mmol/L was still the standard dialysate in the majority of patients (57.7 vs. 64.2%). The dose of calcium carbonate was significantly reduced (2.77 ± 1.71 vs. 3.06 ± 1.54 , $P < 0.01$) in 2009 compared to 2005. The mean of the achieved targets increased significantly in 2009 (2.33 ± 1.05 vs. 2.13 ± 1.03 , $P < 0.01$). CONCLUSION: There was an improved control of all bone and mineral parameters in our dialysis units, following the publication of the CKD-MBD KDOQI guidelines. In order to improve the iPTH values, a more frequent use of low Ca dialysate (1.25 mmol/L) and of non-calcium-based phosphate binders in this small subset of patients should be implemented, as recommended by the guidelines. Individualization of the CKD-MBD management may be successful, even when newer treatment options are not available. Finally, the guidelines implementation process should be a continuous and self-monitored process, with the help of periodic surveys. PMID: 22173961

Spasovski G, Busic M, Piper P, Sarajlić L, Popović AS, Dzhaleva T, Codreanu I, Ratković MM, Popescu I, Lausević M, Avsec D, Raley L, Ekberg H, Ploeg R, Delmonico F. Current status of transplantation and organ donation in the Balkans--could it be improved through the South-eastern Europe Health Network (SEHN) initiative? *Nephrol Dial Transplant.* 2012 Apr;27(4):1319-23.

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Organ donation and transplantation activity in the majority of Balkan countries (Albania, Bosnia and Herzegovina, Croatia, Macedonia, Moldova, Montenegro, Serbia, Romania and Bulgaria) are lagging far behind international averages. Inadequate financial resources, unclear regional data and lack of government infrastructure are some of the issues which should be recognized to draw attention and lead to problem-solving decisions. The Regional Health Development Centre (RHDC) Croatia, a technical body of the South-eastern Europe Health Network (SEEHN), was created in 2011 after Croatia's great success in the field over the last 10 years. The aim of the RHDC is to network the region and provide individualized country support to increase donation and transplantation activity in collaboration with professional societies (European Society of Organ Transplantation, European Transplant Coordinators Organization, The Transplantation Society and International Society of Organ Donation and Procurement). Such an improvement would in turn likely prevent transplant tourism. The regional data from 2010 show large discrepancies in donation and transplantation activities within geographically neighbouring countries. Thus, proposed actions to improve regional donation and transplantation rates include advancing living and deceased donation through regular public education, creating current and accurate waiting lists and increasing the number of educated transplant nephrologists and hospital coordinators. In addition to the effort from the professionals, government support with allocated funds per deceased donation, updated legislation and an established national coordinating body is ultimately recognized as essential for the successful donation and transplantation programmes. By continuous RHDC communication and support asked from the health authorities and motivated professionals from the SEEHN initiative, an increased number of deceased as well as living donor kidney transplantations in the future should be more realistic. PMID: 22467749

Spiroski M, 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.

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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, 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.

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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

Stanoeva JP, Stefova M. Evaluation of the ion trap MS performance for quantification of flavonoids and comparison to UV detection. J Mass Spectrom. 2012 Nov;47(11):1395-406.

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The application of an ion trap mass spectrometer, usually employed for identification, has been here systematically evaluated for quantitative analysis of various conjugated forms of flavonoids and compared with UV quantification. Three MS methods were tested to assess the potential and limits of the ion trap for quantification of flavonoids: full-scan experiment MS(2), isolated ion experiment MS, and full-scan experiment MS. The test was performed using nine reference standards of flavonoids with six different aglycones: luteolin, apigenin, hypolaetin, 4'-O-methylhypolaetin, isoscutellarein and 4'-O-methylisoscutellarein in the form of 7-O-glucosides and diglucosides, mono or diacetylated, isolated from *Sideritis scardica*. The analytical characteristics of the tested MS methods were shown to be comparable to UV with regards to precision and accuracy, and superior for selectivity and sensitivity especially when using extracted ion chromatograms. Detection limits did not differ significantly between the MS methods but were significantly lower than those obtained with UV detection by one order of magnitude. Another issue addressed by these results was the choice of most suitable standard substances for quantification of flavonoids with various substituents attached when using MS. In UV detection, the nature of the aglycone is crucial for the absorbance properties, and various derivatives can be quantified with the available one with the same aglycone. Here, it was shown that in MS detection, one flavone derivative can be quantified using other available derivatives with similar substitution pattern with regards to attached and acetylated sugars, whereas the nature of the aglycone is not crucial. PMID: 23147814

Stavric K, Peova S, Trajkov D, Spiroski M. Gene polymorphisms of 22 cytokines in Macedonian children with atopic dermatitis. Iran J Allergy Asthma Immunol. 2012 Mar;11(1):37-50.

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Atopic dermatitis (AD) is a common chronically relapsing skin disease associated with abnormal cytokine production, and activation of T-helper 2 cells. The aim of this study was to determine whether cytokine gene polymorphisms might influence the development of AD. Single nucleotide polymorphisms in the genes for IL-1 α , IL-1 β , IL-1R, IL-2, IL-4, IL-6, IL-10, IL-12, TGF β , TNF and IFN γ were investigated by PCR and sequence specific primers in Macedonian patients with AD (67 children, age of 6 months to 5 years) and 301 normal unrelated individuals. Susceptible cytokine polymorphisms for AD for eleven genotypes (IL-4 -33/T:T IL-4 -1098/G:G, TGF β cdn25C:G, IL-4 -1098/T:T, IL-1 α -

889/C:T, IL-2 +166/T:T, IL-1 β -511/C:T, IL-12 -1188/C:T, IL-10 -1082/A:G, IL-1 β +3962/C:T, IFN γ +874/A:T), five diplotypes, six haplotypes, and for alleles were found. Protective cytokine polymorphisms for AD for seven cytokine genotypes (IL-4 -1098/G:T, TGF β cdn25/G:G, IL-4 -33/C:C, IL-1 α -889/C:C, IFN γ +874/A:A, IL-10 -1082/A:A, IL-1 β -511/C:C), one cytokine diplotypes, two cytokine haplotypes, and four cytokine alleles were also found. We concluded that several cytokine polymorphisms are protective, or susceptible associated with AD in population of Macedonians. PMID: 22427475

Stefanovski D, Walfisch A, Kedev S, Tager S. Isolated right coronary lesion and anterolateral papillary muscle rupture--case report and review of the literature. J Cardiothorac Surg. 2012 Aug 16;7:75.

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Ischemic rupture of the anterolateral papillary muscle is uncommon due to its dual blood supply. It usually follows an ischemic event involving branches of the left circumflex or left anterior descending arteries. We present a case of a patient admitted with an acute inferior wall myocardial infarction and an isolated distal right coronary artery occlusion. Acute mitral regurgitation with rupture of the anterolateral papillary muscle was diagnosed on the fifth post-infarction day. The patient underwent mitral valve replacement and coronary artery bypass grafting to the posterior descending artery. We conclude that anterolateral papillary muscle rupture may also result from an isolated right coronary lesion. PMID: 22898299

Sterjev Z, Trencavska GK, Cvetkovska E, Petrov I, Kuzmanovski I, Ribarska JT, Nestorovska AK, Matevska N, Naumovska Z, Jolevska-Trajkovic S, Dimovski A, Suturkova L. The association of C3435T single-nucleotide polymorphism, Pgp-glycoprotein gene expression levels and carbamazepine maintenance dose in patients with epilepsy. Neuropsychiatr Dis Treat. 2012;8:191-6.

Institute of Pharmaceutical Chemistry, Faculty of Pharmacy Skopje, Republic of Macedonia.

The ABCB1 gene encodes the P-glycoprotein (Pgp) protein, which is thought to transport various antiepileptic drugs. The single nucleotide polymorphism (SNP) (C3435T) in exon 26 of this gene correlates with the altered expression levels of P-glycoprotein, range of drug response and clinical conditions. In order to investigate the influence of this polymorphism on the susceptibility to and efficacy of carbamazepine therapy, we evaluated the allelic frequency and genotype distribution of this variant in

162 epilepsy patients from the Republic of Macedonia. Statistically significant differences were detected neither in the allelic frequency and genotype distribution between carbamazepine-resistant and carbamazepine-responsive epilepsy patients nor between the subgroups of carbamazepine (CBZ)-responsive patients treated with different CBZ doses. However, the T-allele was enriched in CBZ-responsive patients who required higher maintenance CBZ doses. This observation was substantiated by the findings that the median total plasma levels were the lowest in patients with CC (20 $\mu\text{mol/L}$) followed by CT (23 $\mu\text{mol/L}$) and TT (29 $\mu\text{mol/L}$) genotypes. Patients with a CC genotype also had a higher likelihood of response compared to patients with CT or TT genotypes over a wide range (400-1000 mg/day) of initial doses of CBZ. The T allele showed a reduced expression of ~5% compared to the C allele in peripheral blood mononuclear cells in heterozygotes for the variant. This difference might be translated into ~10% difference in homozygotes for the variant, which would explain the trend towards a dose-dependent efficacy of the CBZ treatment in patients with different genotypes. A larger prospective study is warranted to clarify the clinical utility of a genotypespecific individualized CBZ therapy. PMID: PMC3346059. PMID: 22570551

Stojanovska Z, Januseski J, Boev B, Ristova M. Indoor exposure of population to radon in the FYR of Macedonia. Radiat Prot Dosimetry. 2012 Jan;148(2):162-7.

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The authors present the results of a year-long survey of the indoor radon concentration levels in the FYR of Macedonia. A total number of 437 dwellings in eight statistical regions were subject to radon concentration measurements by using CR-39 track detectors. The annual mean indoor radon concentration in each measuring site was estimated from the four individual measurements with 3 months duration. The measuring period was from December 2008 to December 2009. The distribution of the results was nearly log-normal. The arithmetic and geometric mean values of the annual mean value of radon concentration were estimated to be 105 ± 84 and $84^{*}/1.9$ Bq m^{-3} , respectively. The annual effective dose due to indoor exposure to radon in the dwellings was estimated to be $2.1^{*}/1.9$ mSv y^{-1} . PMID: 21406429

Taseska M, Jaćimović R, Stibilj V, Stafilov T, Makreski P, Jovanovski G. Determination of trace elements in some copper minerals by k₀-neutron activation analysis. doi: 10.1016/j.apradiso.2011.07.009.

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Trace element contents in two copper minerals [brochantite $[\text{Cu}(4)\text{SO}(4)(\text{OH})(6)]$ and native Cu] using $k(0)$ -NAA were determined before and after quantitative removal of copper. The distribution of 44 elements in the studied minerals was investigated. An important advantage of the proposed method is the possibility to determine the content of several elements (Al, Dy, Mg, Mn and V) via their short-lived nuclides after the electrolytic removal of Cu due to the elimination of matrix interferences. PMID: 21816618

Teovska Mitrevska N, Eleftheriadou V, Guarneri F. Quality of life in vitiligo patients. Dermatol Ther. 2012 Nov-Dec;25 Suppl 1:S28-31.

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Quality of life is defined by the World Health Organization as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns." Often overlooked in the past, it is nowadays considered, in a more holistic view of medicine, a decisive factor to understand the impact of diseases and improve the quality of medical care. Such evaluation is particularly relevant for dermatological diseases, because visibility of the lesions can significantly affect self-esteem and social relationships. Vitiligo represents an emblematic case: often disfiguring and located in visible areas, confused in the past (and, in many world regions, even in the present) with leprosy, often perceived by physicians as a harmless, purely cosmetic problem, it significantly decreases the quality of life of affected persons. After a brief overview on definition, usefulness and methods for the assessment of quality of life, the authors examine the peculiarities of its relationship with skin diseases, particularly vitiligo. The state of the art of knowledge and research in this field is presented, together with data showing usefulness and positive results of a multidisciplinary approach, which adequately keeps into account perceived quality of life, on patient's satisfaction, adherence to treatment protocols and, ultimately, better outcome of treatments. In this context, an important role can be played by support communities, groups of patients and dedicated associations and societies, connected through modern communication networks like the Internet. PMID: 23237035

Tonic-Ribarska J, Haxhiu A, Sterjev Z, Kiteva G, Suturkova L, Trajkovic-Jolevska S. Development and validation of a bioanalytical LC-UV method with solid-phase extraction for determination of valproic acid in saliva. Acta Pharm. 2012

Jun;62(2):211-20.

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A bioanalytical HPLC method with UV detection for the determination of the antiepileptic drug valproic acid in human saliva has been developed and validated. Saliva represents an alternative matrix for therapeutic monitoring of antiepileptic drugs due to the increasing interest in free drug concentration. The proposed method involved solid-phase extraction for sample preparation and yielded very good mean recoveries of 99.4 % and 97.9 % for valproic acid and IS, respectively. The calibration function for valproic acid was linear over the concentration range of 1.0-50.0 µg mL⁻¹ (R² = 0.9989). Within-run and between-run precision and accuracy were studied at four concentrations and RSDs were less than 7.3 and 2.2 %, while accuracy values were higher than 96.8 and 97.5 %, respectively. The described method provides sensitivity, linearity, precision, accuracy and is suitable for analyses of valproic acid in saliva samples. PMID: 22750819

Trajkov D, Petlichkovski A, Efinska-Mladenovska O, Hristomanova S, Djulejic E, Kirijas M, Senev A, Spiroski M. Distribution of 22 cytokine gene polymorphisms in Roma from the Republic of Macedonia. Iran J Allergy Asthma Immunol. 2012 Dec;11(4):282-93.

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The aim of this study was to analyze 22 cytokine polymorphisms in the Roma population from the Republic of Macedonia. The Roma population consists of 77 healthy unrelated individuals, residents of different geographical regions of the Republic of Macedonia (Skopje, Gostivar, and Kochani). Blood samples were collected after obtaining written consent. DNA was isolated from peripheral blood and 22 polymorphisms were typed: IL1A -889, IL1B -511, IL1B +3962, IL1R pst1 1970, IL1RN mspa11100, IL4RA +1902, IL12 -1188, IFNG utr5644, TGF-β1 cdn10, TGF-β1 cdn25, TNF-α -308, TNF-α -238, IL-2 -330, IL-2 +166, IL-4 -1098, IL-4 -590, IL-4 -33, IL-6 -174, IL-6 565, IL-10 -1082, IL-10 -819, and IL-10 -592. Cytokine genotyping was performed by PCR-SSP. The population genetics analysis package, PyPop, was used for analysis of the cytokine data. Fnd was negative and significantly different from 0 for IL-4 -590 (p of F=0.006), IL-10 -1082 (p of 1 cdn25βF=0.010), IFN utr5644 (p of F=0.024), IL-4 -1098 (p of F=0.026) and TGF- (p of F=0.001) alleles, as well as for IL-2 haplotypes (p=0.025). Several SNPs (IL-12B -1188, IL-2 -330, IL-4 -1098, IL-4 -590, and IL-10 -1082) were not in HWP (p<0.05). A few SNPs (IL-12B -1188, IL-2

-330, IL-4 -1098, IL-4 -590, and IL-10 -1082) and several observed frequencies of cytokine diplotypes (IL-2/GG: TG, IL-2/TG: TG, IL-4/GCC: GCC, IL-4/TTC: TTC, IL-4/TTT: TTC, IL-10/GCC: GCC, IL-10/ATA: GCC, IL-10/ACC: GCC, and IL-10/ACC: ATA) were not in HWP and were significantly different from the expectations. Hardy Weinberg proportion could not be calculated for TNF and diplotypes belong to GG genotype or GG:GG diplotype. The results of cytokine polymorphisms in Roma population can be used for characterization of the current genetic profile of the Gypsies, anthropological comparisons, as well as for the association studies with different diseases. PMID: 23264404

Trojik T, Shosholcheva M, Radulovska-Chabukovska J, Lovach-Chepujnoska M. Evaluation of effects of repetitive recruitment maneuvers. Acta Inform Med. 2012 Jun;20(2):85-9.

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INTRODUCTION: acute respiratory failure is manifested clinically as patient with variable degrees of respiratory distress, but characteristically an abnormal arterial blood partial pressure of oxygen or carbon dioxide. The application of mechanical ventilation in this setting can be life saving. **GOALS:** The aim of this study is to evaluate the effects of two recruitment maneuvers not only on oxygenation, but on aeration of the lung as well. For that purpose chest x ray and thoracic computed tomography scan (CT) of the lung were used as safe and objective methods for evaluation the impact of recruitment maneuvers on aeration of the lung. CT scan and chest x ray were performed before recruitment maneuvers as confirmation of diagnose and one day after the last recruitment maneuvers. **MATERIAL AND METHODS:** Sixty patients who met ar DS criteria of the american european consensus conference were included in this study. This study was conducted in iCU in our hospital between november 2009 and December 2011. Patients were orally intubated, sedated with 0.2-0.4 µg/kg /min and midazolam 4 mg/h, and ventilated with evita 2 Dura ventilator (Dragger germany). According to the recom-mendation of the Consensus Conference of the american College of Chest physician all patients had an arterial catheter and cen-tral venous catheter. Hemodynamic data were collected from Data Ohmeda monitors. Gas analyses were mesured from blood samples taken from arteria radialis. Partial pressure of oxygen of mixed blood was measured from blood sample taken from v jugularis interior. We used arterial blood colection syringe Bd preset, and blood samples were analyzed with aVI 995HB blood gas analiser. **RESULTS: HEMODYNAMIC CHANGES:**

there wasn't any differences in heart rate, and mean arterial blood pressure before the recruitment five minutes and sixty minutes after the recruitment in both groups. respiratory mechanics: Highest values of the compliance are achieved during the recruitment maneuver in both groups. There was better improvement in compliance during the e sigh recruitment maneuver, then in Cpap recruitment maneuver. There was improvement in chest X ray in both groups. 93.4% of patients in the Cpap group and 96.7% in e sigh group. CT scan: in Cpap group there were 8 patients with focal changes and 22 patients with diffuse changes. in e sigh group 29 patients had diffuse changes of the lung and one patient had focal changes. We noticed that there was better improvement in aeration in patients with diffuse changes of the lung 96.7% in e sigh group and 73.3% in Cpapgroup. In patient with focal changes there was improvement in 26.7% in e sigh group and 3.3% in Cpap group. We noticed that there was better improvement in aeration in patients with diffuse changes than in patients with focal changes. E sigh maneuver had better impact on aeration of the lung then Cpap recruitment maneuver. CONCLUSION: In our study we proved that e sigh recruitment maneuvers better improved oxygenation in arterial blood than Cpap recruitment maneuver. Repetative e sigh maneuvers proved to be essential for arDS patients. They reopened collapsed alveoli and improved aeration of the lung which was confirmed by X ray and CT scan as an objective methods for verification of lung condition. PMID: 23322958