

Macedonian International Medical Publications Indexed in PubMed in 2009

Macedonian Journal of Medical Sciences

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Abstract

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We present abstracts of published papers in international journals deposited in PubMed between 2009-01-01 and 2009-12-31 from the scientists affiliated in institutions from the Republic of Macedonia [(Macedonia[Affiliation]) NOT (Prilozi[Journal])] (searched October 09, 2010). English summaries are published as they are deposited by PubMed.

A total number of 59 papers were indexed in PubMed during 2009 year [1 paper in 2008, 51 papers in 2009, and 7 papers in 2010 (ahead of print)].

Two papers were indexed with the first instead of the second name (Antonela L, Vladimir T and Nada PJ). One paper (Crcarevska MS, Dodov MG, Petrusevska G, Gjorgoski I, Goracinova K. Bioefficacy of budesonide loaded crosslinked polyelectrolyte microparticles in rat model of induced colitis. J Drug Target. 2009;17(10):788-802.) was cited twice with the identical content (PMID: 19938950 and PMID: 19650758). Editorial Boards (Acta Ophthalmol, J Drug Target, and Med Arh), authors, or responsible person from the Central Medical Library are obliged to correct these mistakes in PubMed.

Three papers (Mitreva Z, Veljanovska L, Hristov N. Images in cardiothoracic surgery. Aorto-bilateral-femoral-bilateral-popliteal bypass for Leriche syndrome with occlusion of both superficial femoral arteries. Ann Thorac Surg. 2009;88(2):683; Mitrev Z, Belostotski V, Veljanovska L, Hristov N. Images in cardio-thoracic surgery: DeBekay repair for type III thoracoabdominal aortic aneurysm. Eur J Cardiothorac Surg. 2009;35(5):905; and Sukarova Stefanovska E, Dejanova V, Tchakarova P, Petkov G, Efremov GD. Genetic inversions among hemophilia A patients from Macedonia and Bulgaria. Acta Haematol. 2008;120(3):192-4) are without abstract.

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

Antonela L, Vladimir T. Refractive errors in children and young adults with Down's syndrome. Acta Ophthalmol. 2009 Oct 16. [Epub ahead of print].

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Purpose: Down's syndrome (DS) is the most common chromosomal anomaly. Numerous ophthalmic features have been reported. The aim of our study was to inves-

tigate the incidence of refractive errors in children and young adults with DS in Macedonia. Methods: Fifty-six children and young adults with DS, aged 2-28 years, from Macedonia, underwent slit-lamp examination, ocular motility and refraction. Results: The overall incidence of refractive errors in the Macedonian children and young adults with DS was 96.4%. A total of 17.8% of the subjects had myopia, 23.2% had hypermetropia and 55.3% had astigmatism. Strabismus was seen in 13

(23.2%) of the subjects (nine had esotropia, three had exotropia, one had hypertropia). Conclusions: The incidence of refractive errors in Macedonian children and young adults with DS was similar to that in Asian children. Compared with White (Caucasian) and Asian children with DS, Macedonian children and young adults exhibited lower incidences of hypermetropia and myopia, and a higher incidence of astigmatism, in which oblique astigmatism represented the predominant type. PMID: 19843014 [PubMed - as supplied by publisher]

Arsova-Sarafinovska Z, Eken A, Matevska N, Erdem O, Sayal A, Savaser A, Banev S, Petrovski D, Dzikova S, Georgiev V, Sikole A, Ozgök Y, Suturkova L, Dimovski AJ, Aydin A. Increased oxidative/nitrosative stress and decreased antioxidant enzyme activities in prostate cancer. Clin Biochem. 2009;42(12):1228-35. Epub 2009 May 22.

Republic Institute for Health Protection, Department of Drug Quality Control, Skopje, Republic of Macedonia.

OBJECTIVES: The study was aimed to evaluate the oxidative/nitrosative stress status in prostate cancer (CaP) and benign prostatic hyperplasia (BPH). **DESIGN AND METHODS:** 312 men from two different populations were included: 163 men from Macedonia (73 CaP patients, 67 BPH patients and 23 control subjects) and 149 men from Turkey (34 prostate cancer patients, 100 BPH patients and 15 control subjects). We measured erythrocyte malondialdehyde (MDA) levels, erythrocyte activities of superoxide dismutase (CuZn-SOD), glutathione peroxidase (GPX) and catalase (CAT); plasma nitrite/nitrate (NO(2)(-)/NO(3)(-)), cGMP and 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels. **RESULTS:** A similar pattern of alteration in the oxidative/nitrosative stress-related parameters was found in both, Macedonian and Turkish studied samples: higher MDA concentrations with lower GPX and CuZn-SOD activities in CaP patients versus controls and BPH groups. The CAT activity was decreased in the CaP patients versus controls in the Turkish studied sample. Furthermore, CaP patients had increased plasma NO(2)(-)/NO(3)(-) and cGMP levels versus controls and BPH groups in both studied samples. **CONCLUSIONS:** This study has confirmed an imbalance in the oxidative stress/antioxidant status and revealed an altered nitrosative status in prostate cancer patients. PMID: 19465015 [PubMed - indexed for MEDLINE]

Arsova-Sarafinovska Z, Matevska N, Eken A, Petrovski D, Banev S, Dzikova S, Georgiev V, Sikole A, Erdem O, Sayal A, Aydin A, Dimovski AJ. Glutathione peroxidase 1 (GPX1) genetic polymorphism, erythrocyte GPX activity, and prostate cancer risk. Int Urol Nephrol. 2009;41(1):63-70. Epub 2008 Jun 19.

Department of Drug Quality Control, Republic Institute for Health Protection, Skopje, Republic of Macedonia.

Glutathione peroxidase 1 (GPX1) is a ubiquitously expressed selenium-dependent enzyme that protects cells against oxidative damage by reducing hydrogen peroxide and a wide range of organic peroxides. Some epidemiological studies have correlated low GPX activity or particular GPX1 polymorphisms with enhanced risk of cancer, although these correlations have not been consistently observed in all populations. Therefore, we conducted the present study to evaluate the possible association of GPX1 Pro198Leu polymorphism and erythrocyte GPX activity with the risk of developing prostate cancer and to clarify whether erythrocyte GPX activity levels were correlated with the GPX1 Pro198Leu genotype in the Macedonian population. The GPX1 Pro198Leu genotype was determined in 82 prostate cancer cases and 123 control individuals. We found an overall protective effect of the variant Leu allele of the GPX1 polymorphism on the prostate cancer risk. Heterozygous carriers of the variant Leu allele had a significantly lower risk of prostate cancer compared with homozygous wild-type individuals (OR, 0.38; 95% CI, 0.20-0.75; P = 0.004). Erythrocyte GPX activity was analyzed in 73 cases and 91 controls. The erythrocyte GPX activity in the cancer group was lower than in the healthy controls. Additionally, we compared the erythrocyte GPX activity in the control group of 90 subjects and found no significant differences by genotype. These findings suggest that individual susceptibility of prostate cancer may be modulated by GPX1 polymorphism and that the combination of genetic factors involved in oxidative response with environmental carcinogens may play an important role in prostate carcinogenesis. PMID: 18563616 [PubMed - indexed for MEDLINE]

Bosevski M, Borozanov V, Tosev S, Peovska I, Meskovska-Bongard S, Georgievska-Ismail L. Predictors for peripheral and carotid revascularization in a population-based cohort with type 2 diabetes. Angiology. 2009;60(1):46-9. Epub 2008 May 28.

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The study was aimed to define the predictors for peripheral and carotid revascularization in type 2 diabetic population. In all, 279 patients with type 2 diabetes and peripheral arterial disease were enrolled in a cohort longitudinal study. Study population was followed up for 24 months for the need and performance of peripheral or carotid revascularization. Logistic regression analysis was conducted to identify variables predictive of revascularization, when lipid plasma levels, glycemia, arterial hypertension, blood pressures, ankle-brachial index, intima-media thickness, body mass index, waist circumference, and hip distances were put in a model. Total cholesterol and maximal value of carotid intima-media thickness were presented as factors that independently influenced the performed peripheral revascularization. Waist circumference is defined as independent factor associated with carotid endarterectomy. Measurement of carotid intima-media thickness, waist circumference, and plasma lipid levels in type 2 diabetes with manifested peripheral and carotid arterial disease should be recommended in a manner of proper risk stratification of this population. PMID: 18508848 [PubMed - indexed for MEDLINE]

Bosilkovski M, Katerina S, Zaklina S, Ivan V. The role of Brucellacapt test for follow-up patients with brucellosis. Comp Immunol Microbiol Infect Dis. 2010;33(5):435-42. Epub 2009 Jul 21.

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The dynamic of Brucellacapt titers was evaluated in 104 patients with brucellosis with favorable outcome and in 28 patients with persistent illness duration, during the follow-up period of 15 months. In patients with favorable outcome, a permanently decreasing tendency of Brucellacapt titers was evident. Titers \leq 1/320 were noted in 27% and 90% of the patients, at the end of the 4th and 15th month, respectively. In patients with persistent disease, persistence or slow titre regression during the entire follow-up period was evident. Four and 15 months of the treatment, titers of 1/320 were registered in 4%, and 14%, respectively, and in no one less than 1/320. The evaluation of Brucellacapt titres between recovered and patients with persistent illness showed significant difference at the 3rd month after beginning of treatment. The evolution of Brucellacapt

titers over time proves to be a handy indicator of brucellosis activity when combined with clinical parameters. PMID: 19625085 [PubMed - in process]

Bosilkovski M, Dimzova M, Grozdanovski K. Natural history of brucellosis in an endemic region in different time periods. Acta Clin Croat. 2009;48(1):41-6.

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The aim of the study was to determine the evolution and outcome of human brucellosis in an endemic region in relation to time interval. Retrospective analysis was employed to compare demographic, epidemiological, clinical, laboratory features and the outcome of patients with brucellosis, treated at University Department of Infectious Diseases in Skopje during two different periods of time. A series of 159 patients were studied in the first (1990-1991) and 138 in the second (2003-2005) study period. Patients treated in the second period were older (34.6 \pm 20.9 vs. 30.0 \pm 17.7 years; P=0.041) and acquired brucellosis less frequently on ingestion of incriminated food (34.8% vs. 47.2%; P=0.031). Focal forms were more evident in the second period (66.7% vs. 50.3%; P=0.004), mainly due to osteoarticular localization. Post-treatment follow up was more efficient in the second group (76.1% vs. 61%; P=0.005). There was no difference according to disease outcome in spite of different therapeutic trials during the two study periods. In conclusion, the established differences showed an improvement in the understanding of the disease by the general population as well as upgrading of some aspects considering medical activities. Nevertheless, this endemic region still lacks the most important measure, i.e. development and implementation of an appropriate national program for efficient control of the disease. PMID: 19623871 [PubMed - indexed for MEDLINE]

Crcarevska MS, Dodov MG, Petrusevska G, Gjorgoski I, Goracinova K. Bioefficacy of budesonide loaded crosslinked polyelectrolyte microparticles in rat model of induced colitis. J Drug Target. 2009;17(10):788-802.

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A targeted delivery system for inflammatory bowel dis-

eases, chitosan-Ca-alginate microparticles efficiently loaded with budesonide (BDS), were designed using one-step spray-drying process. They were eudragit-coated and examined for in vivo efficacy. Experimental colitis was induced by rectal instillation of 2,4,6-trinitrobenzene sulphonic acid (TNBS) into male Wistar rats. Drugs were administered by oral gavage daily for 5 days. Colon/body weight ratio, gross morphological and histological evaluation, and clinical activity score were determined as inflammatory indices. Individual clinical and histological evaluation showed that colitis severity was suppressed the most greatly in order BDS < BDS/C-Ca-A < E-BDS/C-Ca-A. Clinical activity score decreased in the same order. Statistical analyses of total score points indicate that the incorporation of BDS in microparticles had significant differences in favor of efficacy of designed delivery system with mucoadhesive and controlled release properties (one-way ANOVA, $P < 0.05$). The results established the prediction by previous in vitro studies. PMID: 19938950 [PubMed - indexed for MEDLINE]

Crcarevska MS, Dodov MG, Petrussevska G, Gjorgoski I, Goracinova K. Bioefficacy of budesonide loaded crosslinked polyelectrolyte microparticles in rat model of induced colitis. J Drug Target. 2009 Aug 4. [Epub ahead of print]

Institute of Pharmaceutical Technology, Faculty of Pharmacy, Ss. Cyril and Methodius University, Skopje, Macedonia.

A targeted delivery system for inflammatory bowel diseases, chitosan-Ca-alginate microparticles efficiently loaded with budesonide (BDS), were designed using one-step spray-drying process. They were eudragit-coated and examined for in vivo efficacy. Experimental colitis was induced by rectal instillation of 2,4,6-trinitrobenzene sulphonic acid (TNBS) into male Wistar rats. Drugs were administered by oral gavage daily for 5 days. Colon/body weight ratio, gross morphological and histological evaluation, and clinical activity score were determined as inflammatory indices. Individual clinical and histological evaluation showed that colitis severity was suppressed the most greatly in order BDS < BDS/C-Ca-A < E-BDS/C-Ca-A. Clinical activity score decreased in the same order. Statistical analyses of total score points indicate that the incorporation of BDS in microparticles had significant differences in favor of efficacy of designed delivery system with mucoadhesive and controlled release properties (one-way ANOVA, $P <$

0.05). The results established the prediction by previous in vitro studies. PMID: 19650758 [PubMed - as supplied by publisher]

Dimitrova G, Kato S, Fukushima H, Yamashita H. Circulatory parameters in the retrobulbar central retinal artery and vein of patients with diabetes and medically treated systemic hypertension. Graefes Arch Clin Exp Ophthalmol. 2009;247(1):53-8. Epub 2008 Sep 3.

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BACKGROUND: We aim to study the circulatory parameters in the retrobulbar central retinal artery and vein in diabetic patients with and without medically treated systemic hypertension. **METHODS:** The study included 108 patients with diabetes that were allocated in four different groups according to the presence of diabetic retinopathy (DR) and hypertension: group 1-patients without DR and without hypertension ($n = 23$), group 2-patients without DR and with hypertension ($n = 21$), group 3-patients with nonproliferative DR and without hypertension ($n = 36$), group 4-patients with nonproliferative DR and with hypertension ($n = 28$). The circulatory parameters that were evaluated were: peak systolic blood velocity (PSV), end-diastolic blood velocity (EDV), maximum venous velocity (V_{max}), minimum venous velocity (V_{min}) and the Pourcelot index which were measured using color Doppler imaging. Non-parametric tests were used to test inter-group differences. Spearman's coefficient of correlation was tested between ocular perfusion pressure and the circulatory parameters in each of the patient groups. Contingency table was performed to test the relation of diabetic retinopathy and hypertension to the PSV in the central retinal artery. **RESULTS:** The PSV and EDV in the central retinal artery was significantly higher in group 1 ($p = 0.02$, $p = 0.04$) and group 2 ($p = 0.02$, $p = 0.02$) than in group 3. The Pourcelot index in the central retinal vein was significantly lower in group 1 than in group 4 ($p = 0.02$), and in group 2 than in groups 3 and 4 ($p = 0.02$, $p < 0.01$). A significant relationship was detected between the presence of hypertension, the stage of diabetic retinopathy and the PSV in the central retinal artery of our patients ($\chi^2 = 8.29$; $p = 0.04$). **CONCLUSION:** Medically treated hypertension affects the retrobulbar circulatory parameters in the central retinal artery and vein in diabetes. PMID: 18766369 [PubMed - indexed for MEDLINE]

Dimovska S, Stafilov T, Sajn R, Frontasyeva M. Distribution of some natural and man-made radionuclides in soil from the city of Veles (Republic of Macedonia) and its environs. Radiat Prot Dosimetry. 2010;138(2):144-57. Epub 2009 Oct 28.

Republic Institute for Health Protection, Skopje, Macedonia.

A systematic study of soil radioactivity in the metallurgical centre of the Republic of Macedonia, the city of Veles and its environs, was carried out. The measurement of the radioactivity was performed in 55 samples from evenly distributed sampling sites. The gross alpha and gross beta radioactivity measurements were made as a screening, using a low background gas-flow proportional counter. For the analysis of (40)K, (238)U, (232)Th and (137)Cs, a P-type coaxial high purity germanium detector was used. The values for the activity concentrations of the natural radionuclides fall well within the worldwide range as reported in the literature. It is shown that the activity of man-made radionuclides, except for (137)Cs, is below the detection limit. (137)Cs originated from the atmospheric deposition and present in soil in the activity concentration range of 2-358 Bq kg(-1) is irregularly distributed over the sampled territory owing to the complicated orography of the land. The results of gamma spectrometry are compared to the K, U, and Th concentrations previously obtained by the reactor neutron activation analysis in the same soil samples. PMID: 19864326 [PubMed - indexed for MEDLINE]

Djulejic E, Petlichkovski A, Trajkov D, Hristomanova S, Middleton D, Spiroski M. Distribution of killer cell immunoglobulinlike receptors in the Macedonian population. Hum Immunol. 2010;71(3):281-8. Epub 2009 Dec 22.

Faculty of Medicine, Institute of Immunobiology and Human Genetics, University Ss. Kiril and Metodij, Skopje, Republic of Macedonia.

The aim of this study was to analyze killer immunoglobulinlike receptor (KIR) gene polymorphism in the Macedonian population. The study sample consists of 214 healthy unrelated individuals, aged 20-35 years. All individuals are of Macedonian origin and nationality, and residents of different geographic regions. The population genetics analysis package, Arlequin, was used for analysis of the data. We found that all 16 KIR genes were observed in the Macedonian population and framework genes KIR3DL3, KIR2DL4,

and KIR3DL2 were present in all individuals. A total of 56 different KIR genotypes were found in the Macedonian population, based on the presence of 16 KIR genes. Neighbor-joining phylogenetic tree, constructed on the basis of standard genetic distances of KIR genes, shows that Macedonian population is in the same cluster with England West Midlands Indian Asian, Brazil SouthEast Caucasian, Romania Caucasians, Spain Basque, England West Midlands Caucasian, France Reunion, and Spain Granada populations. The frequency of KIR loci in Macedonian population shares several general features with other Caucasoid populations studied before. PMID: 20004695 [PubMed - indexed for MEDLINE]

Dzekova P, Asani A, Selim G, Gelev S, Trajceska L, Amitov V, Selja N, Zabzun M, Mena S, Gaseva M, Sikole A. Long-term follow up of sustained viral response after treatment of hepatitis C with pegylated interferon alpha-2a in hemodialysis patients. Int J Artif Organs. 2009;32(3):180-4.

University Clinic of Nephrology, Skopje - Macedonia.

PURPOSE: The aim of this study was to evaluate the persistence of sustained viral response after treatment of hepatitis C with pegylated interferon alpha-2a in hemodialysis patients. **METHODS:** 14 hemodialysis patients with chronic hepatitis C were treated with pegylated interferon alpha-2a for a period of 48 weeks. Achieved sustained viral response rate was 35.7% (5/14 patients) at week 72, i.e. 24 weeks after the treatment ended. All treated patients were then prospectively followed until week 144. Follow-up viral data, such as HCV antibodies, serum HCV RNA, and HCV RNA genotype, were determined at week 96 and week 144. HCV antibodies were determined by a 3rd-generation ELISA assay. The presence of HCV RNA was determined using reverse transcriptase polymerase chain reaction (AMPLICOR Hepatitis C Virus Test). HCV genotype was analyzed by reverse transcriptase polymerase chain reaction followed by hybridization of amplified products. The biochemical data were recorded every 24 weeks during the follow-up period. **RESULTS:** The 5 patients (35.7%), who achieved sustained viral response (SVR), remained HCV RNA negative at week 96. At week 144, 4 hemodialysis patients (28.6%) remained HCV RNA negative. There was a relapse of HCV infection in 1 patient after week 96 of the study. The patients who remained HCV RNA negative also maintained the achieved biochemical response throughout the follow-up period. **CONCLUSION:** Long-term follow-up of treated hemodialysis patients with pegylated interferon alpha-

2a showed persistence of the sustained viral and biochemical response. PMID: 19440994 [PubMed - indexed for MEDLINE]

Filipovski V, Banev S, Janevska V, Dukova B. Granular cell tumor of the breast: a case report and review of literature. Cases J. 2009;2:8551.

Institute of Pathology, Medical Faculty, University of "St Cyril and Methodius" Street Vodnjanska bb, Skopje, 1000 Republic of Macedonia.

A 22-year-old female patient presented with a breast mass lesion with a clinical suspicion of a fibroadenoma. Histological evaluation revealed a rare benign neoplasm - granular cell tumor. Granular cell tumor is rare neoplasm that may arise in virtually any body site, and in 5% it occurs in the breast. The histogenesis of this tumor is still rather controversial and currently the most acceptable theory is a Schwann cell origin. The main histological feature is granular cytoplasm of the tumor cells. From a clinical point of view there is a similarity between granular cell tumor and mammary carcinoma on mammography and ultrasound. Pathohistologically, sometimes, differential diagnostic difficulties exist concerning apocrine carcinoma, histiocytic lesions and metastatic neoplasms. PMCID: PMC2769456; PMID: 19918386 [PubMed - in process]

Fustik S, Jacovska T, Spirevska L, Koceva S. Protein-energy malnutrition as the first manifestation of cystic fibrosis in infancy. Pediatr Int. 2009;51(5):678-83. Epub 2009 Mar 20.

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BACKGROUND: The protein-energy malnutrition (PEM) that is characterized by hypoproteinemia, edema, and anemia has been reported in 5-13% of infants with cystic fibrosis (CF). Due to the surprising higher incidence of PEM as the first presenting manifestation of CF in Macedonia, the aim of the present study was to evaluate the possible risk factors in its development. **METHODS:** Clinical and laboratory profiles (hemoglobin, red blood cell count, total serum protein, serum albumin and liver enzyme levels) and genotype data were analyzed in 115 newly diagnosed infants with CF, during the period 1990-2006. **RESULTS:** PEM manifested in 39 CF infants (33%), usually within the first 5 months of life and in breast-fed infants. Mean hemoglobin, red blood cell

count, total serum protein and serum albumin values in the PEM subgroup were, respectively, 76.0 g/L, 2.4 x 10¹²/L, 38.0 g/L and 16.6 g/L. Clinically significant liver involvement was found in 22 patients (56.4%) with PEM. Concerning the molecular basis of CF in these patients, PEM was always associated with triangle upF508, G542X, N1303K and other severe mutations. **CONCLUSION:** PEM is a common manifestation of CF in infancy. Early infant age, breast-feeding, impaired liver function and the presence of severe cystic fibrosis transmembrane conductance regulator mutations are predisposing factors for the development of PEM. PMID: 19419506 [PubMed - indexed for MEDLINE]

Glavas Dodov M, Calis S, Crcarevska MS, Geskovski N, Petrovska V, Goracinova K. Wheat germ agglutinin-conjugated chitosan-Ca-alginate microparticles for local colon delivery of 5-FU: development and in vitro characterization. Int J Pharm. 2009;381(2):166-75. Epub 2009 Jul 4.

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The aim of this work was to prepare lectin-conjugated chitosan-Ca-alginate microparticles (MPs) loaded with acid-resistant particles of 5-fluorouracil (5-FU) for efficient local treatment of colon cancer. MPs were prepared by a novel one-step spray-drying technique and after wheat germ agglutinin (WGA) conjugation, they were characterized for size, swelling behavior, surface charge, entrapment efficiency and in vitro drug release. Prepared particles were spherical, with 6.73 microg/mg of WGA conjugated onto their surface. The size and zeta potential increased after conjugation, from 6.6 to 14.7 microm and from 9.6 to 15.3 mV, while drug encapsulation was 75.6 and 72.8%, respectively after conjugation. The swelling behavior of beads was mainly determined by properties of the cross-linked chitosan-alginate network. In vitro drug release studies carried out in simulated in vivo conditions with respect to pH, confirmed the potential of the particles to release the drug in a controlled manner. Also, the drug release was not significantly affected by WGA conjugation. The retention of biorecognitive activity of WGA after covalent coupling to MPs was confirmed by haemagglutination test. Functionalized MPs showed excessive mucoadhesiveness in vitro, due to the positive surface charge, pH-dependent swelling of the matrix and lectin-

sugar recognition. PMID: 19580856 [PubMed - indexed for MEDLINE]

Gucev Z, Tasic V, Jancevska A, Popjordanova N, Koceva S, Kuturec M, Sabolic V. Friedreich ataxia (FA) associated with diabetes mellitus type 1 and hypertrophic cardiomyopathy. Bosn J Basic Med Sci. 2009;9(2):107-10.

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Progressive signs of ataxia in a eight years old girl prompted neurological investigation. The girl had unstable gait with incoordination of limb movements, impairment of position and vibratory senses, dysarthria, pes cavus, positive Babinski sign and scoliosis. At the age of fourteen the girl was referred in a comatose condition, in a severe diabetic ketoacidosis. Ataxia and hypoactive knee and ankle jerks prompted the analysis of the frataxin gene (FXN; 606829). The most common molecular abnormality: GAA trinucleotide repeat expansion in intron 1 was found with + 300 GAA repeats (1490bp) (normal individuals have 5 to 30 GAA repeat expansions, whereas affected individuals have from 70 to more than 1,000 GAA triplets). Electrocardiogram showed diffuse T wave inversion with sinus bradycardia, while ultrasound revealed concentric, symmetric hypertrophy of left ventricle leading to the diagnosis of hypertrophic cardiomyopathy. At the age of 14 years, the patient was bound to the wheel-chair, unable to walk. Her brother started to show ataxia at the age of 8 years, and subsequent analysis showed hypertrophic cardiomyopathy, too. His mutational analysis revealed the same frataxin abnormality, with + 300 GAA repeats. So far, no signs of diabetes occurred. The parents are heterozygous with FXN of 9 -10 GAA (490 bp). Both children received a beta blocker, while the girl's diabetes mellitus was treated by insulin preparations. This is a report of two siblings with Friedreich ataxia and hypertrophic cardiomyopathy. In addition, the girl developed type 1 diabetes mellitus. PMID: 19485941 [PubMed - indexed for MEDLINE]

Gucev Z, Tasic V, Jancevska A, Jordanova NP, Koceva S, Kuturec M, Sabolic V. Friedreich's ataxia (FA) associated with diabetes mellitus type 1 and hypertrophic cardiomyopathy: analysis of a FA family. Med Arh. 2009;63(2):110-1.

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Progressive signs of ataxia in a eight year old girl with hypo-active knee and ankle jerks, prompted the analysis of the frataxin gene (FXN; 606829). The most common molecular abnormality—GAA trinucleotide repeat expansion in intron 1—was found with +300 GAA repeats (1490 bp) (normal individuals have 5 to 30 GAA repeats expansions, whereas affected individuals have from 70 to more than 1000 GAA triplets). Additionally she had unstable gait with incoordination of limb movements, impairment of position and vibratory senses, dysarthria, pes cavus, positive Babinski sign and scoliosis. At the age of fourteen the girl was referred in a comatose condition, in severe diabetic ketoacidosis. Insulin dependent diabetes mellitus was since treated with insulin preparations. Electrocardiogram showed diffuse T wave inversion with sinus bradycardia, while ultrasound revealed concentric, symmetric hypertrophy of the left ventricle leading to the diagnosis of hypertrophic cardiomyopathy. At the age of 14, she is bound to the wheelchair, unable to walk. Her brother started to show ataxia at the age of 8 years and subsequent analysis also showed hypertrophic cardiomyopathy. His mutational analysis revealed the same frataxin abnormality with +300 GAA repeats. So far, no signs of diabetes occurred. The parental DNA was not available for analysis. PMID: 19537671 [PubMed - indexed for MEDLINE]

Gucev ZS, Pop-Jordanova N, Dumalovska G, Stomnaroska O, Zafirovski G, Tasic VB. Arthrogryposis multiplex congenital (AMC) in a three year old boy: differential diagnosis with distal arthrogryposis: a case report. Cases J. 2009;2:9403.

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INTRODUCTION: Arthrogryposis multiplex congenital (AMC) is characterized by contractions of multiple joints present at birth. The involved muscles are partially or totally replaced by fat or fibrous tissue. Talipes equinovarus and scoliosis are also frequently reported. **CASE PRESENTATION:** This 2 year was born after uneventful pregnancy, with normal birth weight and length. The parents are unrelated, young and healthy. No malformations or mental retardation have been reported in the family. Since his birth a specific posture was noted: internal rotation at the shoulders, extension at the elbows, and flexion at the wrists. In addition, the child has a severe equinovarus deformity of the feet. Syndactily

between II and III finger was also noted. His face is round with a frontal midline capillary hemangioma, while his jaw appears to be small. Mental development is normal. The karyotype is: 46, XY. CONCLUSIONS: About 150 syndromes have arthrogryphosis as a presenting sign. AMC is a distinct entity and distinction with the distal forms of arthrogryphosis can be difficult, since there is a considerable clinical and genetic heterogeneity. A comprehensive musculoskeletal evaluation and genetic consultation is necessary. PMID: PMC2809076; PMID: 20090872 [PubMed - in process]

Gucev ZS, Tasic V, Jancevska A, Kirovski I. A case of Silver-Russell syndrome (SRS): multiple pituitary hormone deficiency, lack of H19 hypomethylation and favourable growth hormone (GH) treatment response. J Genet. 2009;88(2):239-43.

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Hypomethylation of the imprinting control region 1 (ICR1) at the IGF2/H19 locus on 11p15 is linked to Silver-Russell syndrome (SRS) and/or hemihypertrophy. This SRS patient was born in term with weight of 3500 g (50 percentile) and length 48 cm (1 SD below the mean). He was first noticed at the age of 10 years for short stature (114.5 cm, -3.85 SD), relatively normal head circumference, a classic facial phenotype, hemihypertrophy (2.5 cm thinner left arm and leg in comparison to the right, asymmetric face), moderate clinodactyly and striking thinness (BMI of 15.3). At the age of 30, the body asymmetry ameliorated (1 cm thinner left arm and leg than the right), and BMI normalized (20.5 cm). Methylation analysis was performed by bisulphate treatment of DNA samples, radiolabelled PCR amplification, and digestion of the PCR products using restriction enzymes. The patient had normomethylation, and in addition hypopituitarism, with low levels of growth hormone (GH) (provocative testing before the start and after termination of GH treatment), thyroxin, TSH, FSH, LH and testosterone. The GH was given for six years, growth response was satisfactory and he reached an adult height of 166 cm. This is a first report of hypopituitarism in a patient with SRS without H19 hypomethylation. It seems that the lack of hypomethylation in this hypopituitary SRS patient is responsible, at least partly, for the favourable final adult height under GH treatment. PMID: 19700863 [PubMed - indexed for MEDLINE]

Gucev ZS, Kirovski I, Jancevska A, Popjordanova N, Tasic V. Papillorenal syndrome after Beta-interferon treatment in pregnancy. Ren Fail. 2009;31(7):602-5.

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Papillo-Renal Syndrome (PRS, or Renal-Coloboma Syndrome) is an autosomal dominant disorder, characterized by colobomatous eye defects, abnormal vascular pattern of the optic disk, renal hypoplasia, vesicoureteral reflux, high-frequency hearing loss, and sometimes central nervous system (CNS) abnormalities. The syndrome is associated with mutations in the PAX2 gene. This 11-year-old girl's mother was treated with beta-interferon (IFNbeta-1a) for multiple sclerosis (MS) during the pregnancy. The child failed to thrive in infancy and early childhood. The multicystic renal dystrophy, hypoplastic right kidney, and vesico-ureteral reflux (II-III grade) were diagnosed by ultrasound and radionuclide renal scan. Subsequently, a morning glory anomaly and coloboma of the optic disc was discovered. Renal failure progressively followed. MRI of the head revealed a cyst of the right optic nerve. Genetic analysis revealed a mutation of the PAX2 gene (619 insG). The multicystic renal dystrophy and a cyst of the optic nerve in association with PRS syndrome have only rarely been described. The fact that this PRS patient stemmed from a pregnancy under beta-interferon treatment raises the question whether IFNbeta-1a treatment during pregnancy has influenced the manifestation or the severity of the PAX2 mutant phenotype in this child. PMID: 19839859 [PubMed - indexed for MEDLINE]

Ignjatova L, Raleva M. Gender difference in the treatment outcome of patients served in the mixed-gender program. Bratisl Lek Listy. 2009;110(5):285-9.

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The aim of the study was to determine whether the treatment outcome differs for males and females in the mixed-gender methadone maintenance program. A prospective non-randomized study was performed to evaluate the efficiency of the treatment over a period of 6 months. In this study, 91 patients (60 male and 31 female) were included and the groups were compared by the variables such as relapses, frequency of re-

lapses, type of substance used and the manner of drug use. The results showed that 16 (51.6%) female addicts had 147 relapses and 23 (38.3%) male addicts had 118 relapses, but these differences were statistically not significant. Women made a significant relapse 43.7% more than men 21.7%, with heroine alone. The injectable drug abuse dominates in both genders, i.e. 56.2% of female examinees and 69.6% of male examinees injected the drugs, but this difference was not statistically proven. CONCLUSION: Gender has an influence on the response to the treatment. The outcome of the treatment measured through the drug use differs in the substance used. Women use more heroine than men, who in turn use more combinations of different drugs and legal psychoactive substances during the treatment (Tab. 7, Ref. 31). Full Text (Free, PDF) www.bmj.sk. PMID: 19507662 [PubMed - indexed for MEDLINE]

Ivic Kolevska S, Kocic B. Food contamination with salmonella species in the Republic of Macedonia. Foodborne Pathog Dis. 2009;6(5):627-30.

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OBJECTIVES: To evaluate contamination with *Salmonella* of food products from food markets in the Republic of Macedonia by assessment of the most frequently contaminated food products and the most frequently isolated serotypes of *Salmonella*. **METHODS:** This is a retrospective study analyzing data from the national database for microbiological safety of food products for the period from 2003 to 2005 as well as a prospective study for 2006 and 2007. Isolation and identification of *Salmonella* spp. were performed in the Laboratory for Sanitary Microbiology of the Republic Institute for Health Protection in Skopje, Macedonia. All samples were tested using the horizontal method for detection of *Salmonella* spp., according to ISO 6579:2002. Two immunological methods were used: Singlepath and VIDAS *Salmonella* spp. in food. **RESULTS:** Presence of *Salmonella* spp. was 0.04-0.06% during 2003-2005, 0.63% in 2006, and 0.39% in 2007. During the period 2003 to 2005, *Salmonella* spp. were most frequently isolated from meat and meat products (75%), followed by milk and dairy products. In 2006 and 2007, the most frequently contaminated food products were mechanically separated chicken meat (71% in 2006 and 75% in 2007). The most frequent serogroups of *Salmonella*

spp. in 2006 were C(1) (47%), followed by B and D (17.6%), and F (11.7%). In 2007, the most frequent serogroups of *Salmonella* spp. were C(1) (50%), followed by D (20%), E(3) (15%), and B (10%). **CONCLUSIONS:** We found an increasing trend in the contamination level of food products with *Salmonella* spp., especially in 2006 and 2007, in which the most frequently contaminated food products were mechanically separated chicken meat, milk, dairy products, and sweets, and the most frequently isolated serogroup was C(1). PMID: 19534594 [PubMed - indexed for MEDLINE]

Jordanova M, Miteva N, Santos N, Malhão F, Rocha E. Crystalline inclusions in hepatocytes and associated interhepatocytic macrophages from female Ohrid trout (*Salmo letnica* Kar.). Tissue Cell. 2009;41(4):281-5. Epub 2009 Feb 12.

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When characterizing the liver ultrastructure in Ohrid trout, we noticed that cells often displayed unusual cytoplasmic crystalline inclusions. Their morphology varied much, concerning the size, shape and electron density, showing aspects never reported in fish liver. In hepatocytes, the inclusions existed in close topographical relationship with dense bodies (often within them). Such "crystals" inclusions also existed in macrophages and in biliary passages lumina. Data revealed seasonal/breeding-related changes of the dense bodies and crystalline inclusions within hepatocytes; decreasing from the earliest to the more advanced ovary maturation stages. Additionally, based on the negative correlations between the amounts of dense bodies and of "crystals" and the ovary somatic ratio, we suggested there might be connections between the sex steroids status and the inclusions formation. A positive correlation between the quantities of "crystals" and of dense bodies further suggested that the inclusions might derive from normal processes, e.g., the females' cyclic liver changes, that involves dense bodies' turnover. However, a toxicological aetiology cannot be excluded. Additionally, multiple mechanisms can contribute to the "crystals" genesis. Facing literature reports and because the inclusions content seemed washed out during tissue processing, they are likely lipid in nature, but their exact composition and genesis require further analyses. PMID: 19217133 [PubMed - indexed for MEDLINE]

Kormusoska NB, Cundeva K, Stafilov T. Electrothermal atomic absorption spectrometric determination of cadmium and lead in traces in aquatic systems following flotation by two chromium(III) collectors. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2009;44(12):1274-81.

Krafting Grup, Skopje, Macedonia.

A fast flotation method for determination of cadmium and lead in aquatic systems by two chromium(III) collectors is described. The first collector is a colloid precipitate of hydrated chromium(III) oxide, $\text{Cr}_2\text{O}_3 \cdot x\text{H}_2\text{O}$, while the second is a bulk chromium(III) pentamethylenedithiocarbamate, $\text{Cr}(\text{PMDTC})_3$. Cadmium and lead present in water are incorporated into the collector mass at pH 7.5 by addition of 20 mg of Cr(III) and 0.4 mmol of pentamethylenammonium pentamethylenedithiocarbamate, PMA-PMDTC, to 0.5 L water sample. A solid precipitate was separated from the processed water system by air bubbles. After dissolving with strong acid, the solution is tested by electrothermal atomic absorption spectrometry (ETAAS). The limit of detection for Cd by flotation/ETAAS method is 0.002 $\mu\text{g L}^{-1}$, while for Pb is 0.04 $\mu\text{g L}^{-1}$. The precision of the method is expressed as relative standard deviations ranging of 5.0% for Cd (concentration range from 0.1 to 0.5 $\mu\text{g L}^{-1}$) and 4.25% for Pb (concentration range from 0.5 to 5 $\mu\text{g L}^{-1}$). The characteristic mass (mass that gives an integrated absorbance of 0.0044 s) of 1.06 pg for Cd and 16.7 pg for Pb were obtained. The method was validated by the standard additions and by its application to the reference materials (Surface water-SPS-SW-1, River Thames Water-LGC-6019). PMID: 19847715 [PubMed - indexed for MEDLINE]

Krstevska-Konstantinova M, Jancevska A, Kicova M, Gucev Z. Weight, height and puberty in a cohort of Macedonian girls. Med Arh. 2009;63(2):80-1.

Department of Endocrinology and Genetics, Pediatric Clinic, University Cyril and Methodius, Skopje, Macedonia.

Obesity is becoming a growing problem in developed and developing countries. Many studies report an increasing incidence of obesity in the last decade. The aim of our transversal epidemiological study was to evaluate the prevalence of overweight children, auxological characteristics and pubertal stage in healthy girls from first (200 girls), third (209), fifth (290) and seventh (223) grade of school. In this study 928 girls were evaluated

through systematic school examinations in the ambulance of municipality of Karposh, Skopje. The Rome and Turkish nationality, as well as Serbian were present in a small percentage, while detailed analysis was performed in the Macedonian and Albanian population of girls. The initiation of puberty (stage M2 or P2 by Tanner) was present in Macedonian girls: 4.3% of children in first grade, 23% in third grade, and 51.7% in fifth grade. In Albanians, in first grade M2 is present in 2.7%, in third grade 5.2%, and in fifth grade 46.9%. Body mass index (BMI SDS) was $+3.5 \pm 1.5$ in 35% of Macedonian girls and only 5% of Albanian girls. The Macedonian girls were also significantly higher ($p < 0.01$) and more obese than the Albanian girls. The pubertal stage was also more advanced in Macedonian girls. Most of the obese children who were included in the study reported increased consumption of fast food. Although in the past years obesity was not a problem in our country, it is becoming more severe with every year. PMID: 19537661 [PubMed - indexed for MEDLINE]

Kuzmanovski I, Novic M, Trpkovska M. Automatic adjustment of the relative importance of different input variables for optimization of counter-propagation artificial neural networks. Anal Chim Acta. 2009;642(1-2):142-7. Epub 2009 Jan 25.

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In this work we present a quantitative structure-activity relationship study with 49 peptidic molecules, inhibitors of the HIV-1 protease. The modelling was performed using counter-propagation artificial neural networks (CPANN), an algorithm which has been proven as a valuable tool for data analysis. The initial pre-processing of the data involved auto-scaling, which gives equal importance to all the variables considered in the model. In order to enhance the influence of some of the variables that carry valuable information for improvement of the model, we introduce a novel approach for adjustment of the relative importance of different input variables. Having involved a genetic algorithm, the relative importance was adjusted during the training of the CPANN. The proposed approach is capable of finding simpler efficient models, when compared to the approach with the original, i.e. equally important input variables. A simpler model also means more robust and less subjected to the overfitting model, therefore we consider the proposed procedure as a valuable im-

provement of the CPANN algorithm. PMID: 19427469 [PubMed - indexed for MEDLINE]

Makreski P, Jovanovski G. Minerals from Macedonia XXIII. Spectroscopic and structural characterization of schorl and beryl cyclosilicates. Spectrochim Acta A Mol Biomol Spectrosc. 2009;73(3):460-7. Epub 2008 Jul 17.

Institute of Chemistry, Faculty of Science, SS. Cyril and Methodius University, Arhimedova 5, 1000 Skopje, Republic of Macedonia. petremak@iunona.pmf.ukim.edu.mk

IR and Raman spectroscopy study on two collected cyclosilicate species: schorl (from tourmaline group), $\text{Na}(\text{Fe},\text{Mg})(3)\text{Al}(6)(\text{BO}(3))(3)\text{Si}(6)\text{O}(18)(\text{OH},\text{F})(4)$ and beryl $(\text{Be},\text{Mg},\text{Fe})(3)\text{Al}(2)\text{Si}(6)\text{O}(18)$ were carried out. Although beryl is nominally anhydrous mineral, vibrational results strongly indicate that $\text{H}(2)\text{O}$ molecules exist in the structural channels. The number of vibrational bands and their frequencies revealed the presence of $\text{H}(2)\text{O}$ type II, in which $\text{C}(2)$ symmetry axis of the water molecule is parallel to the structural channel (and to the c -axis of beryl). On the other hand, it was found that observed bands in the IR and Raman OH stretching region of the other tourmaline varieties appear as a result of the cation combinations involving dominant presence of Mg and Fe cations in the Y structural sites. The strong indication derived from the vibrational spectroscopic results that the studied mineral represents a schorl variety, coincide very well with the results obtained by powder X-ray diffraction and X-ray microprobe analysis. Both minerals show IR spectral similarities in the region below 1500 cm^{-1} , whereas the resemblance between the Raman spectra ($1500\text{-}100\text{ cm}^{-1}$) is less expressed confirming that these spectra are more sensitive to compositional changes and to structural disorder. The identification of both minerals was additionally supported by studying the powder X-ray diffraction diagrams. PMID: 18722809 [PubMed - indexed for MEDLINE]

Minov J, Karadzinska-Bislimovska J, Vasilevska K, Risteska-Kuc S, Stoleski S. Effects of passive smoking at work on respiratory symptoms, lung function, and bronchial responsiveness in never-smoking office cleaning women. Arh Hig Rada Toksikol. 2009;60(3):327-34.

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This cross-sectional study compares respiratory symptoms, lung function, and bronchial responsiveness between 27 office cleaning women exposed to environmental tobacco smoke at work and 57 unexposed controls. The age range of both groups was 24 to 56 years, and none of the women had ever smoked. Information on respiratory symptoms, cleaning work history, and passive smoking in the workplace were obtained with a questionnaire. The subjects also took a skin prick test to common inhalant allergens, a lung function test, and a histamine challenge. Despite smoking restriction in indoor environments, we found a high prevalence of passive smokers in the workplace (32.1 %). In these subjects we found a significantly higher prevalence of wheezing with breathlessness (25.9 % vs. 8.8 %; $P=0.036$), wheezing without cold (25.9 % vs. 7.0 %; $P=0.016$), and breathlessness after effort (29.6 % vs. 8.8 %; $P=0.014$) than in control subjects. Objective measurements showed a significantly lower MEF₂₅ (53.6 % vs. 63.7 %; $P=0.001$) and a significantly higher prevalence of borderline bronchial hyperresponsiveness (22.2 % vs. 7.0 %; $P=0.044$) in the passive smokers in the workplace. This study provides evidence of adverse respiratory effects in office cleaning women associated with passive smoking in the workplace. Our findings support a stricter implementation of the current national law to protect respiratory health of all workers. PMID: 19789162 [PubMed - indexed for MEDLINE]

Mirceski V, Dzimbova T, Sefer B, Krakutovski G. Electrochemistry of coupled electron-ion transfer of a heme-like complex in an artificial organic membrane. Bioelectrochemistry. 2010;78(2):147-54. Epub 2009 Sep 21.

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The electrochemistry of a heme-like complex 5,10,15,20-tetraphenylporphyriniron(III) chloride (Fe(III)-TPP-Cl) embedded in a lipophilic artificial membrane is studied by means of voltammetric techniques. The experimental system used comprises of a thin organic membrane hosting the redox probe, sandwiched between edge plane pyrolytic graphite electrode and an aqueous electrolyte solution. In the course of the voltammetric experi-

ment the redox transformation of Fe(III)-TPP-Cl at the electrode|membrane interface is accompanied by concomitant ion transfer reactions across the membrane|water interface. The overall electrochemical process proceeds as a coupled electron-ion transfer reaction providing insight into energetic and kinetic aspects of the complex membrane charge-transfer reactions. The membrane electrochemistry of Fe(III)-TPP-Cl involves two quasireversible redox transformations typical for the Fe(III)/Fe(II) couple. Both redox processes are coupled with a chemical reactions proceeding inside the membrane as well as by complex ion transfer reactions across the membrane|water interface comprising chloride expulsion from the membrane and cation ingress from the aqueous phase. PMID: 19833562 [PubMed - indexed for MEDLINE]

Mirceski V, Tomovski Z. Voltammetry based on fractional diffusion. J Phys Chem B. 2009;113(9):2794-9.

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A cyclic voltammetric experiment governed by anomalous diffusion of an electroactive species is theoretically analyzed by means of fractional calculus. The diffusion mass transfer under semi-infinite conditions at a planar electrode is ascribed by a Fick's second law-like differential equation in which the time derivative of the concentration function is of a fractional order α , ranging from 0 to 1. Rigorous solutions relating the concentrations of electroactive species with the electric current are derived by means of the Wright function for the case of a simple reversible electrode reaction of two chemically stable redox-active species having identical diffusion coefficients. A general mathematical solution for a voltammetric experiment, relating the surface concentrations with the current and electrode potential, is presented in the form of an integral equation. On the basis of the latter solution, the cyclic voltammetric experiment is simulated under variety of conditions, in order to inspect the influence of the fractional parameter α and to reveal its physical significance. Aiming to explain peculiar features of cyclic voltammograms, concentration profiles of electroactive species, together with the Cottrell-like equation, are analyzed for various α values. It has been established that the shape of a cyclic voltammogram depends strongly on α , varying from a steady-state sigmoid shape when $\alpha \rightarrow 0$ to a

conventional peak-like shape for $\alpha \rightarrow 1$. Whereas the midpeak potential is independent of α , the peak currents are proportional to $\sqrt{\alpha}$, where α is the sweep rate. PMID: 19243202 [PubMed]

Mitrev Z, Veljanovska L, Hristov N. Images in cardiothoracic surgery. Aorto-bilateral-femoral-bilateral-popliteal bypass for Leriche syndrome with occlusion of both superficial femoral arteries. Ann Thorac Surg. 2009;88(2):683.

Special Hospital for Surgery Filip Vtori, Skopje, Macedonia.

No abstract available.

PMID: 19632449 [PubMed - indexed for MEDLINE]

Mitrev Z, Belostotski V, Veljanovska L, Hristov N. Images in cardio-thoracic surgery: DeBekay repair for type III thoracoabdominal aortic aneurysm. Eur J Cardiothorac Surg. 2009;35(5):905. Epub 2009 Mar 9.

Special Hospital for Surgery Filip Vtori, Skopje, Macedonia.

No abstract available.

PMID: 19269842 [PubMed - indexed for MEDLINE]

Mitrovska S, Jovanova S. Low-molecular weight heparin enoxaparin in the treatment of acute coronary syndromes without ST segment elevation. Bratisl Lek Listy. 2009;110(1):45-8.

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OBJECTIVES: We compared the incidence of adverse cardiac outcomes of enoxaparin vs unfractionated heparin in the management of ACS-NSTE. **BACKGROUND:** Low-molecular-weight heparins are the potential new standard in the treatment of acute coronary syndromes without ST-segment elevation (ACS-NSTE). The benefit is addressed to significant diminution of the adverse clinical events—recurrent angina (RA), myocardial infarction (MI), heart failure (HF), cerebrovascular insult (ICV), coronary artery by-pass graft (CABG), percutaneous coronary intervention (PCI) and death. **METHODS:** Sixty patients with ACS-NSTE were

randomised to receive Enoxaparin 1 mg/kg body weight s.c twice daily (n=30) and unfractionated heparin (Heparin - "Biochemie" 25.000 IU/5 ml), according to Rashke nomogram (n=30). The end point were RA, MI, HF, ICV, CABG, PCI and death at day 180. The Kaplan-Meier estimation technique was used to compared the time to events for two treatments. A $p < 0.05$ was considered to indicate significance. RESULTS: For 180 days, RA, MI, HF, ICV and death were lower in the Enoxaparin vs UFH group (36.6% vs 73.3%, $p=0.001$), (30% vs 53.3%, $p=0.05$), (13.3% vs 23.3%, $p=0.31$), (3.3% vs 10%, $p=0.29$), (3.3% vs 10%, $p=0.31$), respectively. CABG were similar 13.3% ($p=0.96$). PCI were performing in 33.3% in UFH vs 90% in LMWH ($p=0.0001$). CONCLUSION: The use of Enoxaparin in ACS-NSTE schows impressive decrease of incidence of ischemic events (Fig. 7, Ref. 8). Full Text (Free, PDF) www.bmj.sk. PMID: 19408831 [PubMed - indexed for MEDLINE]

Nada P.J. Heart rate variability in the assessment and biofeedback training of common mental health problems in children. Med Arh. 2009;63(5):244-8.

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Heart rate variability (HRV) is a measure of the beat-to-beat variations in heart rate related to the work of autonomic nervous system. It may serve as a psychophysiological indicator for arousal, emotional state and stress level. We used this parameter in both the assessment and biofeedback training, for dealing with five groups of common mental health problem in school children (anxious-phobic, somatoform, obsessive-compulsive, attention deficit hyperactivity and conduct disorders). The obtained results were compared with healthy children at the same age. In order to define the four main characteristics of personality (extroversion/introversion, neuroticism/stability, psychopathological traits and honesty) Eysenck Personality Questionnaire was applied. Results showed significantly higher psychopathological traits in ADHD and somatoform group, lower extroversion in somatoform, higher neuroticism in OCD and lower lie scores in ADHD and OCD groups. As HRV instrument we used Heart Math Freeze-Framer System. After 15 sessions of training, children from nearby all groups showed improved high and medium HRV which corresponded to the improved clinical outcome. Hereby, the best results were obtained for conduct and anxiety disorder, and the worst for ADHD. PMID: 20380120

[PubMed - indexed for MEDLINE]

Pavlovska I, Orovchanec N, Stefanovski T, Zafirova-Ivanovska B. Tobacco use and the risk of lung cancer in Macedonia. Bratisl Lek Listy. 2009;110(5):319-23.

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INTRODUCTION: Lung cancer (LC) is one of the most common diseases in the world. Smoking is the most important "lifestyle" risk-factor attributed to the development of LC. OBJECTIVE: The aim of the study was to determine the existence of a causal association between cigarette smoking and the development and distribution of LC. MATERIAL AND METHODS: The case-control study was conducted in 91 patients with LC (investigated group-IG) and the same number of persons without malignant disease (control group-CG). Both groups were interviewed between 14 July 2005 and 14 July 2006. Risk analyses were done using unconditional logistic regression, which provided results in the form of crude odds ratio. The odds ratios and their 95% confidence intervals (CI) were computed. RESULTS: Cigarette smoking is wide spread among men with LC (68%), while in CG this percent is 40.3%. In IG, among females, current smokers and nonsmokers are represented equally. More than a half of the LC patients smoke between 21-40 c/d (56.8%). Smokers and ex-smokers have 4.05 (95% CI 1.78 < OR < 9.19) times significantly higher risk to become ill compared to the non-smokers. The risk for becoming ill is 9.33 (95% CI 3.56 < OR < 24.48) times higher in smokers who smoke >20 c/d ($p < 0.01$) compared to nonsmokers. The risk for developing LC is 4.55 (95% CI 1.86 < OR < 11.12) times higher in persons smoking >15 years >20 c/g, compared to those who smoke <15 years <20 c/d. CONCLUSION: Our study supports the statement that cigarette smoking is by far the most important risk factor for LC. Concerted control of smoking appears to be an important priority in LC prevention, including efforts to prevent adolescents from starting to smoke at an early age (Tab. 2, Fig. 2, Ref. 22). Full Text (Free, PDF) www.bmj.sk. PMID: 19507672 [PubMed - indexed for MEDLINE]

Pesevska S, Nakova M, Ivanovski K, Angelov N, Kesic L, Obradovic R, Mindova S, Nares S. Dental hypersensitivity following scaling and root planing:

comparison of low-level laser and topical fluoride treatment. *Lasers Med Sci.* 2010;25(5):647-50. Epub 2009 Jun 1.

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The aim of this study is to compare the effectiveness of low-level laser irradiation to traditional topical fluoride treatment for treatment choices of dentinal hypersensitivity following scaling and root planing. The experimental group (15 patients) was treated with low-energy-level diode laser at each site of dentinal hypersensitivity following scaling and root planing. The control group (15 patients) received topical fluoride treatment (protective varnish for desensitization). All the patients were treated at baseline visit, and then at day 2 and 4 after the initial treatment; the pain was subjectively assessed by the patients as strong, medium, medium low, low, or no pain. Total absence of the dental hypersensitivity was reported in 26.66% of the examined group even after the second visit, compared to the control group where complete resolution of the hypersensitivity was not present after the second visit in any of the treated cases. Complete absence of pain was achieved in 86.6% of patients treated with laser and only in 26.6% in the fluoride treated group, after the third visit. Based on our findings, we conclude that low-energy biostimulative laser treatment can be successfully used for treatment of dental hypersensitivity following scaling and root planing. PMID: 19484401 [PubMed - in process]

Pop-Jordanov J, Pop-Jordanova N. Neurophysical substrates of arousal and attention. *Cogn Process.* 2009;10 Suppl 1:S71-9. Epub 2008 Oct 31.

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The study of arousal and attention could be of prominent importance for elucidating both fundamental and practical aspects of the mind-brain puzzle. Defined as "general activation of mind" (Kahnemann in Attention and effort. Prentice-Hall, New Jersey, 1973), or "general operation of consciousness" (Thacher and John in Functional neuroscience: foundations of cognitive processing. Erlbaum, Hillsdale, 1977), arousal can be considered as a starting point of fundamental research on consciousness. Similar role could be assigned to attention, which can be defined by substituting the attributes "general" with "focused". Concerning the practical applications, the empirically established correlation between

neuronal oscillations and arousal/attention levels is widely used in research and clinics, including neurofeedback, brain-computer communication, etc. However, the neurophysical mechanism underlying this correlation is still not clear enough. In this paper, after reviewing some present classical and quantum approaches, a transition probability concept of arousal based on field-dipole quantum interactions and information entropy is elaborated. The obtained analytical expressions and numerical values correspond to classical empirical results for arousal and attention, including the characteristic frequency dependence and intervals. Simultaneously, the fundamental (substrate) role of EEG spectrum has been enlightened, whereby the attention appears to be a bridge between arousal and the content of consciousness. Finally, some clinical implications, including the brain-rate parameter as an indicator of arousal and attention levels, are provided. PMID: 18975019 [PubMed - indexed for MEDLINE]

Pop-Jordanova N, Gucev Z. Game-based peripheral biofeedback for stress assessment in children. *Pediatr Int.* 2010;52(3):428-31. Epub 2009 Oct 23.

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BACKGROUND: Peripheral biofeedback is considered to be an efficient method for assessment and stress mitigation in children. The aim of the present study was to assess the levels of stress and stress mitigation in healthy school children (HSC), in children with cystic fibrosis (CF), general anxiety (GA) and attention-deficit-hyperactivity disorder (ADHD). **METHODS:** Each investigated group (HSC, CF, GA, ADHD) consisted of 30 school-aged children from both sexes. Psychological characteristics were evaluated on Eysenck Personality Questionnaire (EPQ). The lie scale was used to determine participant honesty. Four biofeedback games using a pulls detector were applied for assessment of the stress levels as well as to evaluate ability to relax. **RESULTS:** EPQ found more psychopathological traits ($P < 0.001$) and less extroversion ($P < 0.001$) in children with GA and ADHD. In addition, high neurotic tendencies were found in children with CF ($P < 0.01$) and GA ($P < 0.01$). Unexpectedly, the lie scale was lower in ADHD children ($P < 0.01$) than in all other groups (HSC, CF, GA). The Magic blocks score was significantly different in relaxation levels between control and CF children ($P < 0.05$). Speed in the game Canal was significantly different in relaxation levels between healthy controls

and all other groups, but no changes in pulls, as a relaxation measure, were found during the game. The CF group had much more commissions stemming from impulsivity ($t= 5.71$, $P < 0.01$), while the GA and ADHD children had more inattention omissions ($P < 0.05$). Strong negative correlation between age and pulls ($r= 0.49$, $P=0.003$) and strong negative correlation between age and omissions ($r=-0.86$, $P= 0.029$) were found among all groups analyzed. **CONCLUSIONS:** The ability to learn stress mediation is correlated with age. All three groups of children had significantly lower relaxation levels when compared to healthy controls. Relaxation was more difficult for children with GA or ADHD, and easier for children with CF. PMID: 19863753 [PubMed - in process]

Ristovska G, Gjorgjev D, Polozhani A, Kocubovski M, Kendrovski V. Environmental noise and annoyance in adult population of Skopje: a cross-sectional study. Arh Hig Rada Toksikol. 2009;60(3):349-55.

Institute of Public Health, Medical Faculty, University Sts. Cyril and Methodius, Skopje, Macedonia.

The aim of this study was to identify noise exposure indicators during day and night in the city of Skopje and to see if there is an association between these noise exposure indicators and annoyance. We have performed noise measurements and interviewed 510 adult subjects, using a questionnaire, prepared according to the ISO/TS-15666 standard. Average noise level over the day (Lday) was (62+/-6.45) dB(A) and over night (Lnight) (56+/-6.52) dB(A). Thirteen percent of subjects reported a high level, and 33.5% moderate level of annoyance. The most annoying noise sources were construction activities (34% of the subjects), road traffic (24%), and leisure/entertainment activities (18%). We found a significant association between exposure to Lday in the range 61 dB(A) to 65 dB(A) and annoyance in the exposed population (chi-square = 86.14; $p<0.001$; Spearman's $R=0.45$; $p<0.05$). During the night time annoyance was reported with exposure to Lnight above 46 dB(A). Levels of annoyance in Macedonia are similar to levels in developed European countries. Differences are in the source of noise. This study has shown that environmental noise is a significant hazard in urban environments, and assessment of annoyance may prove a useful tool for town planners and public health policy makers. PMID: 19789165 [PubMed - indexed for MEDLINE]

Samardziski M, Zafiroski G, Tolevska C, Konstadinova-Kunovska S, Vasilevska V. Parosteal osteosarcoma. Bratisl Lek Listy. 2009;110(4):240-4.

University Clinic for Orthopedic Surgery, University "St. Cyril and Methodius", Skopje, Macedonia. milan_samardziski@yahoo.com

In this retrospective clinical study, 6 cases of osteosarcoma of the bone have been analyzed. Five patients were with parosteal osteosarcoma and one with periosteal osteosarcoma. The study was performed at the Clinic for Orthopaedic Surgery in Skopje, Macedonia, from 1995 to 2005. This tumor represents 1.5% of all primary bone tumors treated at the Clinic in the 11 year period. The age of the 6 patients (2 female and 4 male) ranged from 8 to 39 years (average 23.8). The history analysis of the patients showed misinterpreted diagnosis in 50% of the cases, with 83.3% rate of local recurrence, 33.3% of metastases and 33.3% of mortality. Follow-up varied from 11 months to 9 years (average 4.5). The clinical and histopathological findings (identical with those reviewed in the literature) confirmed occurrence of two biologically different types of parosteal osteosarcoma: predominant type is originally "benign" but has a definite malignant potential, causing metastases after long symptom-free interval. The other type is highly malignant from the beginning. More radical surgery is recommended for the latter category of tumors, followed by chemotherapy. Compartmental, radical "en bloc" resection, followed by regular review of the patients, is recommended for the former (Tab. 1, Fig. 3, Ref. 20). Full Text (Free, PDF) www.bmj.sk. PMID: 19507652 [PubMed - indexed for MEDLINE]

Spasovski G, Beck BB, Blau N, Hoppe B, Tasic V. Late diagnosis of primary hyperoxaluria after failed kidney transplantation. Int Urol Nephrol. 2009 Dec 18. [Epub ahead of print]

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Primary hyperoxaluria type 1 (PH1) is a rare autosomal recessive inborn error of the glyoxylate metabolism that is based on absence, deficiency or mislocalization of the liver-specific peroxisomal enzyme alanine:glyoxylate aminotransferase. Hyperoxaluria leads to recurrent formation of calculi and/or nephrocalcinosis and often early end-stage renal disease (ESRD) accompanied by systemic calcium oxalate crystal deposition. In this report,

we describe an adult female patient with only one stone passage before development of ESRD. With unknown diagnosis of PH, the patient received an isolated kidney graft and developed an early onset of graft failure. Although initially presumed as an acute rejection, the biopsy revealed calcium oxalate crystals, which then raised a suspicion of primary hyperoxaluria. The diagnosis was later confirmed by hyperoxaluria, elevated plasma oxalate levels and mutation of the AGXT gene, showing the patient to be compound heterozygous for the c.33_34InsC and c.508G > A mutations. Plasma oxalate levels did not decrease after high-dose pyridoxine treatment. Based on this case report, we would recommend in all patients even with a minor history of nephrolithiasis but progression to chronic renal failure to exclude primary hyperoxaluria before isolated kidney transplantation is considered. PMID: 20020206 [PubMed - as supplied by publisher]

Spasovski G, Massy Z, Vanholder R. Phosphate metabolism in chronic kidney disease: from pathophysiology to clinical management. *Semin Dial.* 2009;22(4):357-62.

Department of Nephrology, Medical Faculty, University of Skopje, Skopje, Macedonia. gspas@sonet.com.mk

Hyperphosphatemia is considered as an independent risk factor for surrogate clinical endpoints like vascular calcification (VC) and bone disease, or hard clinical outcomes like cardiovascular events. To date, various treatment options for phosphate removal or reduction are available. The great expectations put into calcium-based phosphate binders were mitigated because of their possible contribution to progressive VC, particularly in patients treated simultaneously with active vitamin D derivatives. Thus, a paradigm change occurred whereby the main clinical concern shifted from the avoidance of hypocalcemia to that of the consequences of inducing a positive calcium balance. Sevelamer-HCl treatment allowed a comparable control of hyperphosphatemia with a lower risk of hypercalcemia than calcium-based phosphate binders, and a slower progression of VC; however, convincing evidence of improved clinical outcomes in dialysis patients is lacking. Although data on the safety and efficacy of lanthanum carbonate in the treatment of hyperphosphatemia have been provided in long-term clinical studies, there is still an ongoing scientific debate about its possible long-term toxicity. Moreover, there are no data from randomized clinical trials demonstrating beneficial ef-

fects of La carbonate treatment on VC or cardiovascular outcomes. In the absence of convincing clinical trials testing the effects of non-metal-based phosphate binders on cardiovascular and global outcomes it appears reasonable to maintain bone health and mineral homeostasis by mainly relying on adaptations of standard therapies. Noncalcium, non-aluminum-based binders might be reserved for patients with major mineral metabolism abnormalities and a high risk of VC. PMID: 19708981 [PubMed - indexed for MEDLINE]

Spasovski G, Masin-Spasovska J, Gjurchinov D. Successful treatment of severe secondary hyperparathyroidism (Brown tumor) by kidney transplantation and pulses of oral calcitriol. *Clin Transplant.* 2009;23(3):426-30.

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Brown tumor is an extreme form of severe hyperparathyroid bone disease in end-stage renal disease patients. The evolution of the tumor after renal transplantation and under conservative treatment is still unclear. Herein, we report a 22-yr-old girl with parathyroid glandular hyperplasia because of an inadequate compliance and control of the mineral metabolism and subsequently developed Brown tumor of the ribs. A gradual improvement in bone and parathyroid gland status was observed within three yr following successful kidney transplantation and treatment with pulses of oral calcitriol. To the best of our knowledge, this is the first case of such severe secondary hyperparathyroidism with successful conservative treatment in the setting of kidney transplantation with no evidence of vascular calcifications and graft failure. PMID: 19537305 [PubMed - indexed for MEDLINE]

Spasovski G. Strategies to manage low-bone turnover. *Nefrologia.* 2009;29(4):295-7. doi: 10.3265/Nefrologia.2009.29.4.5399.en.full.

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A change in paradigm occurred lately whereby not hypocalcemia but hypercalcemia and positive calcium balance were considered negative factors. Namely, the use of calcium-based binders in combination with vitamin D analogues, has been shown to lead to an over-suppression of parathyroid hormone (PTH) and devel-

opment of low-bone turnover adynamic bone disease (ABD). The changing prevalence of various types of bone diseases from a high to low-bone turnover goes in line with the presence of increased risk for vascular calcification (VC), morbidity and mortality in the dialysis population. The attenuation of the previous great expectations in calcium-based phosphate binders and vitamin D-analogues entailed a new treatment strategy to preserve bone and vascular health. Hence, a new evidence for treatment of ABD with various types of non calcium based binders and low calcium dialysate is presented. Sevelamer treatment has reduced calcium concentration and increased PTH levels, resulting in the improvement of markers of bone turnover, increased bone formation and improved trabecular architecture, providing a slower progression of VC. Data on lanthanum beneficial effect on ABD histology have been demonstrated in long-term clinical studies. Although there is a slow release of lanthanum from its bone deposits after discontinuation of the treatment and no association with aluminium- like bone toxicity, there is still an ongoing scientific debate about its long-term toxic potential. Finally, reducing the number of calcium based binders and low calcium dialysate (1.25 mmol/l) has been reported to have an impact on the evolution towards markers reflecting higher bone turnover. Then, adoption of the non calcium-based binders should be reserved to high risk patients with ABD and progression of vascular calcifications associated with increased morbidity and mortality. PMID: 19668299 [PubMed - indexed for MEDLINE]

Spiroska V, Kedev S, Antov S, Trajkov D, Petlichkovski A, Hristomanova S, Djulejic E, Paneva M, Senev A, Spiroski M. Association between 22 cytokine gene polymorphisms and dilated cardiomyopathy in Macedonian patients. *Kardiol Pol.* 2009;67(11):1237-47.

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

Comment in: *Kardiol Pol.* 2009 Nov;67(11):1248-9.

BACKGROUND: Inflammation is an important component in the pathogenesis of many cardiovascular diseases and one of the commonest mechanisms in cardiomyopathy. There have been several studies on the cytokine polymorphism and dilated cardiomyopathy (DCM), but the results obtained were contradictory. **AIM:** To examine a possible role of 22 cytokine gene polymorphisms in host susceptibility to or protection

against DCM in Macedonians. **METHODS:** In this study 301 healthy unrelated individuals and 52 patients with DCM were studied. Cytokine genotyping was performed by PCR with sequence-specific priming (PCR-SSP) (Heidelberg kit). **RESULTS:** After the Bonferroni adjustment, the IL-4 -1098/T, IL-4 -1098/T:T, IL-4/TCC, and IL-4/TCC:TTC cytokine genes were positively associated with DCM, while a negative association was identified for IL-4 -1098/G, IL-4 -1098/G:T, IL-1B +3962/C:C, IL-4/GCC, and IL-4/GCC:TTC. **CONCLUSIONS:** These results suggest that some cytokine gene polymorphisms are significantly associated and affect host susceptibility/resistance to DCM in Macedonians. PMID: 20024851 [PubMed - indexed for MEDLINE]

Spiroski I, Kedev S, Antov S, Trajkov D, Petlichkovski A, Dzhekova-Stojkova S, Kostovska S, Spiroski M. Investigation of SERPINE1 genetic polymorphism in Macedonian patients with occlusive artery disease and deep vein thrombosis. *Kardiol Pol.* 2009;67(10):1088-94.

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BACKGROUND: Raised SERPINE1 plasma levels are related to a 1-bp guanine deletion/insertion (4G5G) polymorphism in the promoter of the SERPINE1 (plasminogen activator inhibitor 1 - PAI1) gene. Evidence suggested that the plasma levels of SERPINE1 modulate the risk of coronary artery disease; furthermore, that the 4G5G polymorphism affects the expression of the SERPINE1 gene. **AIM:** To analyse association of SERPINE1 polymorphism with occlusive artery disease (OAD) and deep venous thrombosis (DVT) in Macedonians in order to investigate its role as a part of candidate genes in different vascular diseases in Macedonians. **METHODS:** Investigated groups consisted of 82 healthy patients, 75 with OAD, and 66 with DVT. Blood samples were collected after written informed consent was obtained, and DNA was isolated from peripheral blood leukocytes. Identification of SERPINE1 polymorphism was done with CVD StripAssay (ViennaLab, Labordiagnostica GmbH, Austria). The population genetics analysis package, PyPop, was used for analysis of the SERPINE1 data. Pearson's P-values, crude odds ratio and Wald's 95% CI were calculated with Bonferroni corrected p value. **RESULTS:** The frequency of 4G allele for SERPINE1 was 0.538 for DVT, 0.555 for healthy

participants, and 0.607 for OAD. The frequency of 5G allele for SERPINE1 was the smallest in patients with OAD (0.393) and was higher in healthy participants (0.445), and patients with DVT (0.462). Test of neutrality (Fnd) showed negative value, but was significantly different from 0 for SERPINE1 in healthy participants (p of $F = 0.041$) and in patients with DVT (p of $F = 0.030$). SERPINE1 genotypes in healthy participants and patients with OAD were not in Hardy Weinberg proportions ($p = 0.019$ and 0.001 , respectively). No association between SERPINE1 polymorphisms and OAD or DVT was found. CONCLUSION: There is no significant relationship between SERPINE1 polymorphisms and occlusive artery disease or deep venous thrombosis in Macedonian population. PMID: 20017074 [PubMed - indexed for MEDLINE]

Spiroski M, Trajkovski V, Trajkov D, Petlichkovski A, Efinska-Mladenovska O, Hristomanova S, Djulejic E, Paneva M, Bozhikov J. Family analysis of immunoglobulin classes and subclasses in children with autistic disorder. Bosn J Basic Med Sci. 2009;9(4):283-9.

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Autistic disorder is a severe neurodevelopment disorder characterized by a triad of impairments in reciprocal social interaction, verbal and nonverbal communication, and a pattern of repetitive stereotyped activities, behaviours and interests. There are strong lines of evidence to suggest that the immune system plays an important role in the pathogenesis of autistic disorder. The aim of this study was to analyze quantitative plasma concentration of immunoglobulin classes, and subclasses in autistic patients and their families. The investigation was performed retrospectively in 50 persons with autistic disorder in the Republic of Macedonia. Infantile autistic disorder was diagnosed by DSM-IV and ICD-10 criteria. Plasma immunoglobulin classes (IgM, IgA, and IgG) and subclasses (IgG1, IgG2, IgG3, and IgG4) were determined using Nephelometer Analyzer BN-100. Multiple comparisons for the IgA variable have shown statistically significant differences between three pairs: male autistic from the fathers ($p = 0,001$), female autistic from the mothers ($p = 0,008$), as well as healthy sisters from the fathers ($p = 0,011$). Statistically significant differences found between three groups regarding autistic disorder (person with autistic disorder, father/mother of a person with autistic disorder, and brother/sister) inde-

pendent of sex belongs to IgA, IgG2, and IgG3 variables. Multiple comparisons for the IgA variable have shown statistically significant differences between children with autistic disorder from the fathers and mothers ($p < 0,001$), and healthy brothers and sisters from the fathers and mothers ($p < 0,001$). Comparison between healthy children and children with autistic disorder from the same family should be tested for immunoglobulin classes and subclasses in order to avoid differences between generations. PMID: 20001993 [PubMed - indexed for MEDLINE]

Stafilov T, Sajn R, Pancevski Z, Boev B, Frontasyeva MV, Strelkova LP. Heavy metal contamination of topsoils around a lead and zinc smelter in the Republic of Macedonia. J Hazard Mater. 2010;175(1-3):896-914. Epub 2009 Oct 31.

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The results of a first systematic study of spatial distribution of different elements in surface soil over the Veles region (50 km²) known for its lead and zinc industrial activity in the recent past are reported. A total of 201 soil samples were collected according to a dense net in urban area and less dense net in rural area. The total of 42 elements were analyzed by epithermal neutron activation analysis (ENAA) and by atomic absorption spectrometry (AAS). The content of elements such as As, Au, Cd, Cu, Hg, In, Pb, Sb, Se, Zn in soil samples around the lead and zinc smelter and in the adjacent part of the town of Veles has appeared to be much higher than in those collected in the surrounding areas due to the pollution from the plant. Thus, the content of Cd (three times); Pb and Zn (two times) is even higher than the corresponding intervention (critical) values according to the Dutch standards. The results obtained by two complementary analytical techniques, AAS and ENAA, are discussed in terms of multivariate statistics. GIS technology was applied to depict the areas most affected by contamination from the lead and zinc smelter. PMID: 19944530 [PubMed - indexed for MEDLINE]

Stankov O, Ivanovski O, Popov Z. Artificial penile bodies-from kama sutra to modern times. J Sex Med. 2009;6(6):1543-8. Epub 2009 Mar 17.

University Clinic of Urology, University "Ss Cyril and

Methodius", Skopje, Macedonia.

INTRODUCTION: Artificial penile nodules are defined as inert objects inserted beneath the skin of the penis to enhance the pleasure of female/male sexual partners during intercourse. **AIM:** The aim of this article is to present our experience in dealing with artificial penile bodies. We have also reviewed the pertinent literature focusing on social, motivational, and occupational characteristics of individuals adopting this sexual practice, diagnostic dilemmas and the surgical and health side effects of the implantation of artificial penile nodules. **METHODS:** We performed a computerized MEDLINE search followed by a manual bibliographic review of cross-references. These reports were analyzed and the important findings summarized. **RESULTS:** The phenomenon of inserting self-made artificial nodules beneath the skin of the penis was first described in the Kama Sutra, the classic Indian treatise on love. It is most commonly observed among men from Southeast Asia. The occurrence is much less common in western cultures, but it has been reported to occur in Romania, Germany, and among Fijians and Russian immigrants in Israel. Furthermore, four cases of self-inserted artificial penile bodies from our clinical practice are presented and discussed. **CONCLUSIONS:** The most common motive associated with foreign artificial bodies on the penis is sexual or erotic in nature and that is to enhance the pleasure of female or male sexual partners during sexual intercourse. Most of the reports involve members of low economic groups like gang members, soldiers, drug addicts, sailors, labor workers, and prisoners. Men suffer no serious side effects after insertion, although fixed beads can cause rupture of condoms. For women, the beads can cause abrasions and a few days of postcoital vaginal pain. Penis implants and inserts and other penis augmentation devices are potentially dangerous to both men and women, and of questionable value in bringing pleasure to either, and should be discouraged. PMID: 19473473 [PubMed - indexed for MEDLINE]

Stefanovic V, Polenakovic M. Fifty years of research in Balkan endemic nephropathy: where are we now? Nephron Clin Pract. 2009;112(2):c51-6. Epub 2009 Apr 18.

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Despite broad investigations into the possible role of genetic factors, environmental agents and immune

mechanisms, the etiology of Balkan endemic nephropathy (BEN) is only partially understood. An increased incidence of upper urothelial cancer in patients with BEN and in populations from endemic settlements has been demonstrated. Genetic studies have landed support for genetic predisposition to BEN. The similarity of the morphological and clinical pattern of BEN and Chinese herbs nephropathy has raised the possibility of a common etiologic agent, aristolochic acid (AA), described in 1969 by Ivi and confirmed by a recent study of AA-DNA adducts. Ochratoxin A (OTA) is studied extensively as the etiologic agent of BEN. Weathering of low-rank coals nearby the endemic villages produces water-soluble polycyclic aromatic hydrocarbons and aromatic amines, similar to metabolic products of acetaminophen, which has a causal relationship with analgesic nephropathy. AA is confirmed as the etiologic agent of BEN; however, it may not be the sole risk factor. More research is needed on the patterns of BEN over time and between different endemic places. Therefore, it is important to test etiological hypotheses in different endemic foci, preferably as a multicentric research. An international approach to solving the etiology of BEN is needed in the coming years. The geographic correlation and presence of AA-DNA adducts in both BEN and associated urothelial cancer support the hypothesis that these diseases share a common etiology. PMID: 19390202 [PubMed - indexed for MEDLINE]

Sukarova Stefanovska E, Dejanova V, Tchakarova P, Petkov G, Efremov GD. Genetic inversions among hemophilia A patients from Macedonia and Bulgaria. Acta Haematol. 2008;120(3):192-4. Epub 2009 Jan 5.

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

No abstract available.

PMID: 19129691 [PubMed - indexed for MEDLINE]

Tasic V, Angjeleska M, Ristoska-Bojkovska N, Petrusevska G, Gucev Z. Autoimmune thyroiditis in a child with steroid-dependent nephrotic syndrome. Eur J Pediatr. 2009;168(2):229-31. Epub 2008 May 7.

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Autoimmune thyroiditis is rarely described in association with nephrotic syndrome. Herein we report a girl who developed autoimmune thyroiditis insidiously during the course of minimal change nephrotic syndrome. She was steroid-sensitive, but developed severe steroid dependency and did not respond to cyclophosphamide therapy. She went into stable remission with levamisole. Five months after introduction of levamisole a mild goiter was found on systematic examination at school. The diagnosis of autoimmune thyroiditis was established with typical ultrasound appearance of the thyroid gland along with significant titers of antithyroid antibodies. It is very unlikely that levamisole was responsible for thyroiditis because experimental animal administration of high doses of levamisole inhibited lymphocyte infiltration of the thyroid. Since levamisole has had a beneficial effect on the nephrotic syndrome in our patient we decided to continue the treatment. She has been receiving levamisole for 3 years, and no adverse effects have been observed during the treatment period. PMID: 18461358 [PubMed - indexed for MEDLINE]

Trajkov D, Mishevskaja-Perchinkova S, Karadzova-Stojanoska A, Petlichkovski A, Strezova A, Spiroski M. Association of 22 cytokine gene polymorphisms with rheumatoid arthritis in population of ethnic Macedonians. Clin Rheumatol. 2009;28(11):1291-300. Epub 2009 Aug 7.

Institute of Immunobiology and Human Genetics, University Ss. Kiril and Metodij, 1109, Skopje, P.O. Box 60, Republic of Macedonia.

To examine the possible role of 22 cytokine gene polymorphisms in host susceptibility to or protection against RA in Macedonians. In this study, 301 healthy unrelated individuals and 85 patients with RA were studied. Cytokine genotyping was performed by PCR with sequence-specific priming (PCR-SSP) (Heidelberg kit). Results showed susceptible association for four cytokine

alleles, six cytokine genotypes, one haplotype, and four combinations of haplotypes, while protective associations were found for four cytokine alleles, three cytokine genotypes, three haplotypes, and only one combination of haplotypes. These results suggest that IL-4 -1098, IL-4 -590, IL-10 -1082, IL-10 -819, IL-2 -330, IL-6 -174, and TNF-alpha -238 cytokine gene polymorphisms might be significantly associated and affect host susceptibility and/or resistance to RA in Macedonians. PMID: 19662331 [PubMed - indexed for MEDLINE]

Trajkov D, Trajchevska M, Arsov T, Petlichkovski A, Strezova A, Efinska-Mladenovska O, Sandevski A, Spiroski M. Association of 22 cytokine gene polymorphisms with tuberculosis in Macedonians. Indian J Tuberc. 2009;56(3):117-31.

Institute of Immunobiology and Human Genetics, Faculty of Medicine, University St. Kiril and Metodij, Skopje, Republic of Macedonia.

OBJECTIVE: To examine the possible role of 22 cytokine gene polymorphisms in host susceptibility to or protection against tuberculosis (TB) in Macedonians. METHOD: 301 healthy unrelated individuals and 75 patients with pulmonary TB were studied. Cytokine genotyping was performed by PCR with sequence-specific priming (PCR-SSP) (Heidelberg kit). RESULTS: TNF-alpha-238/G, IL-1R psti1970/C, IL-1beta + 3962/T:T, IL-4-1098/T:T, IFNgamma utr5644/A:A, IL-10-1082/G:G, IL-4-590/C:C, IL-10/ATC, IL-4/TCT, IL-4/TCC, IL-10/ATC:GCC, IL-4/TCT:TTT, IL-4/TCC:TTC, IL-10/GCC:GCC and IL-4/TCC:TCC were positively associated with TB, while protective association was identified for IL-4-098/G, IL-1beta + 3962/C, IFNgamma utr5644/T, IL-1beta + 3962/C:T, IL-4-1098/G:T, IL-4-590/C:T, IFNgamma utr5644/A:T, IL-4/GCC, IL-4/TTC and IL-4/GCC:TTC. CONCLUSION: These results suggest that some cytokine polymorphisms are significantly associated and affect host susceptibility/resistance to TB in Macedonians. PMID: 20349753 [PubMed - indexed for MEDLINE]

Trajkov D, Mirkovska-Stojkovicik J, Petlichkovski A, Strezova A, Efinska-Mladenovska O, Sandevska E, Sibinovska O, Hristomanova S, Djulejic E, Petrov J, Gogusev J, Spiroski M. Association of cytokine gene polymorphisms with chronic obstructive pulmonary disease in Macedonians. Iran J Allergy Asthma Immunol. 2009;8(1):31-42.

Institute of Immunobiology and Human Genetics, University School of Medicine Ss. Kiril and Metodij, Skopje, Republic of Macedonia.

The aim of this study was to examine the association of 22 cytokine gene polymorphism in Macedonians with chronic obstructive pulmonary disease (COPD). The sample of the population comprised of 301 normal respondents and 62 patients with COPD. Cytokine genotyping was performed by polymerase chain reaction with sequence-specific priming (PCR-SSP). Positive (susceptible) association was found between patient with COPD and IL-1alpha -889/C allele; where as

negative (protective) association among was found for the following alleles IL-1beta +3962/C; IL-12B -1188/A; IFNgamma +874/T; IL-2 -330/G; IL-4 -1098/G and IL-4-33/C. We found positive (susceptible) association between patients with COPD and following genotypes: IL4 -33/T:T; IFNgamma +874/A:A; IL-4 -1098/T:T; IL-1alpha -889/C:C; IL-1beta +3962/C:T; IL-12B -1188/C:C; IL-4Ralpha +1902/G:G; IL-10 -1082/G:G; IL-2 -330/T:T; IL-4 -590/C:C; and IL-1alpha -889/C:T. Negative (protective) association between patients with COPD and following genotypes was found: IFNgamma +874/A:T; IL-4 -33/C:T; IL-4 -1098/G:T; IL-2 -330/G:T; IL-1beta +3962/C:T; IL-4 -590/C:T; IL-10 -1082/A:G; and IL-4 -33/C:C. Positive (susceptible) association between patients with COPD and following haplotypes was found: IL-4/TCT; IL-10/ATC; and IL-2/TG, and negative (protective) association was found between the patients with COPD and haplotypes for: IL-4/TTC; and IL-4/GCC. It could be concluded that several cytokine polymorphisms are positively (susceptible), or negatively (protective) associated with COPD in Macedonians. PMID: 19279357 [PubMed - indexed for MEDLINE]

Trajkov D, Arsov T, Petlichkovski A, Strezova A, Efinska-Mladenovska O, Gogusev J, Spiroski M. Distribution of the 22 cytokine gene polymorphisms in healthy Macedonian population. Bratisl Lek Listy. 2009;110(1):7-17.

Institute of Immunobiology and Human Genetics, Faculty of Medicine, University St. Kiril and Metodij, Skopje, Republic of Macedonia.

BACKGROUND: Distribution of cytokine gene polymorphisms may vary significantly among different ethnic groups, and eventually contribute to observed differences in disease frequencies. **OBJECTIVES:** To genotype 22 cytokine polymorphisms in the Macedonian population. The Macedonian population consists of 301 healthy unrelated individuals. **METHODS:** Blood samples were collected after written consent, DNA was isolated from peripheral blood, and 22 polymorphisms were typed: IL-1alpha -889, IL-1beta -511, IL-1beta +3962, IL-1R psti1970, IL-1RN mspa11100, IL-4Ralpha +1902, IL-12 -1188, IFNgamma utr5644, TGF-beta1 cdn10, TGF-beta1 cdn25, TNF-alpha -308, TNF-alpha -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 (Heidelberg kit). The population genetics analysis package, PyPop, was used for analysis of the cytokine data.

RESULTS: Test of neutrality (Fnd) showed negative value, but was significantly different from 0 for TGF-beta1 1 cdn10 and IFNgamma utr5644 (p of F = 0.001, and 0.012 respectively). Several SNPs (IL-1alpha -889, IL-1beta +3962, IL-2 + 166, IL-4 -1098, IL-4 -590, IL-4 -33, and IL-10 -592) were not in HWP (p 0.005). Test of neutrality for cytokine haplotypes (TGF-beta1, TNFalpha, IL-2, IL-4, IL-6, and IL-10) showed significantly difference from 0 only for IL-2 haplotypes (p=0.020). **CONCLUSION:** The results of cytokine polymorphisms in Macedonian population can be used for anthropological comparisons, as well as for association studies with different diseases (Tab. 6, Ref. 34). Full Text (Free, PDF) www. bmj. sk. PMID: 19408823 [PubMed - indexed for MEDLINE]

Trajkovska S, Mbaye M, Gaye Seye MD, Aaron JJ, Chevreuil M, Blanchoud H. Toxicological study of pesticides in air and precipitations of Paris by means of a bioluminescence method. Anal Bioanal Chem. 2009;394(4):1099-106. Epub 2009 Apr 22.

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A detailed toxicological study on several pesticides, including chlorothalonil, cyprodynil, dichlobénil, pendimethaline, trifluraline, and alpha-endosulfan, present at trace levels in air and total atmospheric precipitations of Paris is presented. The pesticides contained in the atmospheric samples, collected during sampling campaigns in February-March 2007, are identified and quantified by a high-performance liquid chromatographic (HPLC)-UV detection method. The toxicity measurements are performed by means of the Microtox bioluminescence method, based on the evaluation of the bioluminescence inhibition of the *Vibrio fischeri* marine bacteria at two exposure times to the pesticide solutions. The specific toxicity, corresponding to the particular toxicity of the compound under study and represented by the EC(50) parameter, is determined for these pesticides. Also, the global toxicity, which is the toxicity of all micro-pollutants present in the sample under study, is estimated for the extracts of air and atmospheric precipitation (rainwater) samples. The specific toxicities strongly vary with the nature of the pesticide, the EC(50) parameter values being comprised between 0.17 and 0.83 mg/mL and 0.15 and 0.66 mg/mL, respectively, for exposure times of 5 and 15 min. The importance of the atmospheric samples' global

toxicity and the respective contribution of the toxic potency of the various pesticides contained in these samples are discussed. PMID: 19387620 [PubMed - indexed for MEDLINE]

V'ickova-Laskoska MT, Caca-Biljanovska NG, Laskoski DS, Kamberova SJ. Palmoplantar pustulosis treated with itraconazole: a single, active-arm pilot study. *Dermatol Ther.* 2009;22(1):85-9.

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Pustulosis palmoplantaris (PPP; synonyms: pustulosis palmaris et plantaris, palmoplantar amicrobic pustulosis) is a common chronic, relapsing, pustular eruption affecting the palms and soles. The authors report the successful treatment of six therapy-experienced patients with histologically confirmed PPP with oral itraconazole (100 mg/day for 1 month, followed by a month of 100 mg/day every other day). Three of six patients showed complete clearance of pustules, significant reduction of erythema, and unnoticeable desquamation, whereas the other three patients had no new pustules appearing and had modest reduction of erythema and desquamation. All patients experienced relapses within a month of therapy cessation. Two of the three complete responders reinitiated itraconazole therapy at 100 mg/day for another 2 weeks, followed by a maintenance dose of 50 mg/day until achieving remission. As complete responses are not commonly observed in placebo treatments in placebo-controlled trials for PPP, the authors believe that the present study shows that itraconazole is an effective treatment for treatment-resistant PPP. PMID: 19222520 [PubMed - indexed for MEDLINE]

Vasilevska V, Szeimies U, Stäbler A. Magnetic resonance imaging signs of iliotibial band friction in patients with isolated medial compartment osteoarthritis of the knee. *Skeletal Radiol.* 2009;38(9):871-5. Epub 2009 May 30.

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BACKGROUND: The purpose of this retrospective study was to assess the frequency of magnetic resonance imaging (MRI) signs of iliotibial band friction (ITBF) in

patients with advanced medial compartment knee osteoarthritis. **MATERIAL AND METHODS:** Proton density-weighted (PDw) fat-saturated (fatsat) MR images (1.5 T, slice thickness (SL) 2.5-3 mm, eight-channel phased array coil) of 128 patients with isolated advanced osteoarthritis of the medial knee compartment and complete or subtotal (>80%) loss of cartilage were evaluated. There were 41 men and 87 women. Mean age was 63 years, range 34-89 years. The control group consisted of 94 patients with medial meniscus degeneration without cartilage loss (56 men and 38 women, mean age 50 years, range 16-89 years). MRI signs of ITBF were evaluated in both groups [poorly defined abnormalities of signal intensity and localized fluid collection lateral, distal or proximal to the lateral epicondyle; signal intensity abnormalities superficial to or deep by the iliotibial band (ITB)]. Transverse images were evaluated separately. Consensus evaluation using all imaging planes was performed. **RESULTS:** Of 128 patients with osteoarthritis, 95 had moderate or advanced MRI signs of ITBF (74.2%). Eighty-nine patients (69.5%) had advanced degeneration of the meniscus. In the control group, 26 of 94 patients had only moderate MRI signs of ITBF. There was a statistically significant difference between both groups for the presence of MR signs of ITBF ($P \leq 0.01$). **CONCLUSION:** MRI signs of ITBF were frequently present in patients with severe medial compartment osteoarthritis of the knee. Joint space narrowing with varus knee deformity may be a cause of ITBF. PMID: 19484234 [PubMed - indexed for MEDLINE]

Zafirova B, Todorovska L. Anthropometric parameters of growth and nutritional status in children aged 6 to 7 years in R. Macedonia. *Adv Med Sci.* 2009;54(2):289-95.

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PURPOSE: Evaluation of age- and sex-specific differences of anthropometric parameters that were used as indicators of growth and nutritional status in children aged 6 and 7 years in R. Macedonia and their comparison with the WHO and NCHS reference values. **MATERIAL AND METHODS:** The study included 580 children aged 6 to 7 years from different regions of R. Macedonia. Eighteen anthropometric parameters were measured using standard equipment and measurement technique according to the International Biological Programme. The following nutritional indicators were calculated: BMI,

weight-for-height, weight-for-age and height-for-age. RESULTS: The majority of anthropometric parameters have shown significant age- and sex-specific differences in favour of male subjects, with exception of skin-folds that were apparently higher in female subjects. Values at the 50th percentile in our male subjects for the index weight-for-age were 23 kg and 26.95 kg, respectively, whereas in the female subjects they were 22 kg and 25 kg, respectively. The index height-for-age corresponding to the 50th percentile showed higher values in our male subjects (119.5 cm and 125.55 cm) than in our female subjects (118 cm and 124.5 cm, respectively). 50th percentile in our male subjects for BMI was 16.48 kg/m² and 16.75 kg/m², whereas in our female subjects it was 15.98 kg/m² and 16.25 kg/m², respectively. CONCLUSIONS: The found values are recommended to be applied for evaluation of deviations in the growth and nutritional status in children aged 6 and 7 years from Macedonian nationality. PMID: 20022859 [PubMed - indexed for MEDLINE]

Zlatanov N, Kocarev L. Random walks on networks: cumulative distribution of cover time. Phys Rev E Stat Nonlin Soft Matter Phys. 2009;80(4 Pt 1):041102. Epub 2009 Oct 2.

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We derive an exact closed-form analytical expression for the distribution of the cover time for a random walk over an arbitrary graph. In special case, we derive simplified exact expressions for the distributions of cover time for a complete graph, a cycle graph, and a path graph. An accurate approximation for the cover time distribution, with computational complexity of $O(2n)$, is also presented. The approximation is numerically tested only for graphs with $n \leq 1000$ nodes. PMID: 19905268 [PubMed - indexed for MEDLINE]