

Macedonian International Medical Publications

2007 year (PubMed search on June 30, 2008)

Andonov S, Ødegård J, Boman IA, Svendsen M, Holme IJ, Adnøy T, Vukovic V, Klemetsdal G. Validation of test-day models for genetic evaluation of dairy goats in Norway. J Dairy Sci. 2007 Oct;90(10):4863-71.

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Test-day data for daily milk yield and fat, protein, and lactose content were sampled from the years 1988 to 2003 in 17 flocks belonging to 2 genetically well-tied buck circles. In total, records from 2,111 to 2,215 goats for content traits and 2,371 goats for daily milk yield were included in the analysis, averaging 2.6 and 4.8 observations per goat for the 2 groups of traits, respectively. The data were analyzed by using 4 test-day models with different modeling of fixed effects. Model [0] (the reference model) contained a fixed effect of year-season of kidding with regression on Ali-Schaeffer polynomials nested within the year-season classes, and a random effect of flock test-day. In model [1], the lactation curve effect from model [0] was replaced by a fixed effect of days in milk (in 3-d periods), the same for all year-seasons of kidding. Models [2] and [3] were obtained from model [1] by removing the fixed year-season of kidding effect and considering the flock test-day effect as either fixed or random, respectively. The models were compared by using 2 criteria: mean-squared error of prediction and a test of bias affecting the genetic trend. The first criterion indicated a preference for model [3], whereas the second criterion preferred model [1]. Mean-squared error of prediction is based on model fit, whereas the second criterion tests the ability of the model to produce unbiased genetic evaluation (i.e., its capability of separating environmental and genetic time trends). Thus, a fixed struc-

ture with year (year, year-season, or possibly flock-year) was indicated to appropriately separate time trends. Heritability estimates for daily milk yield and milk content were 0.26 and 0.24 to 0.27, respectively.

Antevski BM, Smilevski DA, Stojovski MZ, Filipovski VA, Banev SG. Extreme gigantomastia in pregnancy: case report and review of literature. Arch Gynecol Obstet. 2007 Feb;275(2):149-53.

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We present an extreme case of Gigantomastia in pregnancy in a 24-year old woman, gravida 2, in a 28 weeks' of gestation, with a total breast weight of 33 kg, complicated by infection, ulcerations and subsequent hemorrhage. Thorough laboratory analyses did not reveal any hint as to the cause of this enormous breast enlargement. Gynecological examinations and ultrasound revealed a viable, progressive normal fetus. The severity of the problem is further emphasized by the patients' breathing problems and even big difficulty in standing and walking. We performed bilateral simple mastectomy as a life-saving procedure to prevent fatal complications. The procedure finished without any complications or large amount of blood loss. There are less than 100 cases of gravid gigantomastia reported, but never to such extreme breast weight. Etiology remains uncertain, and controversy exists in therapeutic modality. According to the literature the most reliable conservative treatment is bromocriptine therapy, but if the condition progresses surgical intervention, in the form of reduction mammoplasty or simple mastectomy, is the treatment of choice.

Antovska V, Iliev V, Stojcevski S, Kuzeska K. Combination of two anti-stress procedures: our original 4-corner deltoid-like vaginal suspension and suburethral duplication sec. Lazarevski in patients with genital prolapse. Bratisl Lek Listy. 2007;108(4-5):189-99.

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AIM: The effectiveness of the combination of two anti-stress procedures: 1) our original 4-corner deltoid-like vaginal suspension; and 2) suburethral duplication sec. Lazarevski are analysed. STUDY DESIGN: 144 women, undergoing vaginal hysterectomy, combined with our original 4-corner deltoid-like vaginal suspension and suburethral duplication sec. Lazarevski were divided into: SUIGP group (n = 48) with stress urinary incontinence (SUI) and genital prolapse (GP); and GP group (n = 96) with GP. All operations were performed by the first author of this study. RESULTS: At the last follow-up (mean 18.3 months for GP, and 18.7 months for SUIGP), point C was significantly higher in both groups and total vaginal length (tvL) longer in GP vs. preoperative positions (p < 0.05; p < 0.05; p < 0.05 respectively). There were no postoperative significant differences between groups. Regarding the severity of prolapse: stage I for anterior segment and stage 0 for most severe segment predominated in SUIGP (p < 0.05; p < 0.05 respectively). The recurrent prolapse was: 1) in anterior segment: stage I 6.25% in GP and 18.7% in SUIGP; stage II 6.25% in GP and 2.1% in SUIGP; 2) in posterior segment: stage I 18.7% in GP and 18.7% in SUIGP. There was no recurrent prolapse of the apical segment, and only one patient with stage III anterior segment. The recurrent SUI was 8.3% in SUIGP, and de novo SUI 1% in GP. CONCLUSION: This proposed combination seems to be safe and effective.

Bogdanska JJ, Todorova B, Labudovic D, Atanasovska E. Effect of clofibrate on the enzymes associated with oxidative stress in Wistar rat liver. Bratisl Lek Listy. 2007;108(2):56-64.

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BACKGROUND: A diversity of endogenous and exog-

enous compounds have been demonstrated to cause proliferation of peroxisomes and variety of associated effects in rodents. The aim of our study was to see the effect of clofibrate on the enzymes associated with oxidative stress. METHODS: Male Wistar rats weighing 250-350 g were treated with clofibrate in a dose of 250 mg/1000 g/ 24 h for 12 days. Whole liver homogenates and subsequent subcellular fractions were proceeded for enzyme measurements by spectrophotometric methods. RESULTS: The activity of hydrogen producing enzymes D-aminoacid oxidase, Urate oxidase and Palmitoyl CoA oxidase was statistically significantly increased in the treated group in comparison with the control one. On the contrary to the massive increase of the Palmitoyl CoA oxidase--a marker enzyme for peroxisomal proliferation, there was only a limited increase of catalase (which inactivates hydrogen peroxide) activity. On the other hand superoxide dismutase and glutathione peroxidase activities in experimental group were down regulated in the treated group. CONCLUSION: Our results support the hypothesis that clofibrate (peroxisomal proliferators) application might produce oxidative stress in rat livers

Bosevski M, Borozanov V, Georgievska-Ismail L. Influence of metabolic risk factors on the presence of carotid artery disease in patients with type 2 diabetes and coronary artery disease. Diab Vasc Dis Res. 2007 Mar;4(1):49-52.

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The aim of the study was to evaluate the prevalence of carotid artery disease in type 2 diabetes patients with coronary artery disease, and to establish the influence of metabolic factors on its occurrence. In all, 145 patients (aged 59.85±/8.43 years, diabetes duration 8.89±/6.29 years) were randomly selected in a cross-sectional study. Carotid ultrasound was used for evaluation of the presence of carotid plaque (CP) and stenosis (CS). A logistic regression model was constructed to define the influence of risk factors-- arterial hypertension, systolic blood pressure, weight, waist to hip ratio, high blood glucose and plasma lipid levels. Carotid artery disease was present in these patients with a prevalence of 81.9% for CP, 25.2% for unilateral CS and 13.5% for bilateral CS. The low-density lipoprotein (LDL) cholesterol level was an independent predictor for CS (OR 1.936; 95% CI 1.2413.026). Non-high density lipoprotein (HDL) cholesterol (OR 1.374; 95% CI 1.0351.825) and glycaemia (OR 1.214; 95% CI 1.0221.442) were predictors for carotid plaque.

Bosevski M, Borozanov V, Peovska I, Georgievskaismail L. Endothelial dysfunction correlates with plasma fibrinogen and HDL cholesterol in type 2 diabetic patients with coronary artery disease. Bratisl Lek Listy. 2007;108(7):297-300.

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OBJECTIVE: Assessment of endothelial dysfunction (ED) in type 2 diabetic patients with coronary artery disease (CAD) and estimation of correlation of ED with metabolic parameters: low HDL, hypertriglyceridemia, obesity, systolic blood pressure and with inflammatory-hemostatic parameters: CRP and fibrinogen. **PATIENTS AND METHODS:** 42 patients (age 60.0 +/- 8.5 years) with diagnosed type 2 diabetes and CAD were randomly included in a cross sectional study. B-mode ultrasound system with a linear transducer 7.5 MHz was used for evaluation of flow mediated vasodilation in brachial artery (FMV). FMV was presented as the percentage increase in brachial artery diameter, within 30 s after limb ischemia, previously provoked by cuff inflation. Percentage value up to 10% was defined as ED. **RESULTS:** Bivariate linear correlation model presented significant correlation between plasma fibrinogen and FMV percentage, with $r = -0.47$, $p < 0.01$. Presence of ED correlates linearly with plasma level of HDL < 1.03 mmol/L ($r = -0.35$, $p < 0.03$). Multivariate analysis using Backward Wald model presented fibrinogen (OR 3.14, 95% CI 0.87-11.28) and low HDL (OR 5.16, 95% CI 0.53-60.39) as factors correlated with the presence of endothelial dysfunction. **CONCLUSION:** These results presented plasma fibrinogen level and low HDL < 1.03 mmol/L as factors, independently correlated to the presence of endothelial dysfunction in type 2 diabetic patients with coronary artery disease.

Bosevski M, Borozanov V, Tosev S, Georgievskaismail L. Is assessment of peripheral endothelial dysfunction useful tool for risk stratification of type 2 diabetic patients with manifested coronary artery disease? Int J Cardiol. 2007 Oct 25. [Epub ahead of print]

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Endothelial dysfunction, per se, in coronary arteries can stratify a risk in coronary artery disease patients. Selected studies evaluating endotheliopathy as predictor of events in patients with type 2 diabetes, but without coronary artery disease. We hypothesized

that peripheral endothelial dysfunction could predict prognosis of type 2 diabetic patients who presented coronary artery disease. Our data presented endothelial dysfunction as prognostic marker of cardiovascular events in type 2 diabetic patients with manifested coronary artery disease, according univariate regression model.

Bosilkovski M, Krteva L, Dimzova M, Kondova I. Brucellosis in 418 patients from the Balkan Peninsula: exposure-related differences in clinical manifestations, laboratory test results, and therapy outcome. Int J Infect Dis. 2007 Jul;11(4):342-7. Epub 2007 Jan 22.

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OBJECTIVE: The aim of this study was to describe some demographic, clinical and laboratory characteristics, and to evaluate the outcome, in patients with brucellosis in an endemic area in the Balkan Peninsula, and to reveal the differences between patients with and without occupational exposure. **METHODS:** The study was carried out at the Clinic for Infectious Diseases in Skopje over a period of seven years. Four hundred and eighteen patients with brucellosis were enrolled and classified into two groups: patients with (251) and without (167) occupational exposure. **RESULTS:** Two hundred and twenty-eight (54.5%) of the patients had a positive family history. The most common clinical manifestations were arthralgia (81.8%), sweating (71.5%), localized disease (67.7%) and subjective fever (68.4%), whereas elevated values of C-reactive protein (78.9%) and circulating immune complexes (75.8%) were the most frequent laboratory abnormalities. Relapses and therapeutic failure were registered in 16.2% and 10.4%, respectively. Male gender, positive family history and arthralgia were more prevalent in those with occupational exposure, while pediatric age, fever and anemia were inversely correlated with occupational exposure. **CONCLUSIONS:** Human brucellosis is a serious problem in the Republic of Macedonia presenting with a high percentage of localized forms, relapses and therapeutic failures. The risk factor for acquiring the disease had no influence on the outcome.

Efremov GD. Thalassemias and other hemoglobinopathies in the Republic of Macedonia. Hemoglobin. 2007;31(1):1-15.

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This paper summarizes the results on the epidemiology and molecular basis of thalassemias and other hemoglobinopathies in the Republic of Macedonia. Over the past 40 years, population surveys of more than 22,000 participants (school children and workers) from all over the country, have shown that the average incidence of beta-thalassemia (thal) trait is 2.6%, ranging from less than 1% in the northeast to 10% in the south. The frequency of deltabeta-thal is 0.2%, while the frequency of the Swiss type of hereditary persistence of fetal hemoglobin (HPFH) is 0.3%. Screening of 9,619 newborns has shown that the frequency of alpha-thal trait is 1.5%, of which alpha-thal-2 is 1.45% and alpha-thal-1 is 0.05%. The molecular basis of the different forms of beta-thal and other hemoglobinopathies has been completely defined. Among the Macedonians, over 450 beta-thal chromosomes have been studied. Fifteen different beta-thal mutations have been detected, four of which [IVS-I-110 (G→A), IVS-I-6 (T→C), IVS-I-1 (G→A), codon 39 (C→T)] account for 85% of all beta-thal chromosomes. Among the Albanians, 48 beta-thal chromosomes have been studied. Eight different mutations have been detected, four of which [codon 39, -30 (T→A), IVS-I-110, IVS-I-1] account for 85% of all beta-thal chromosomes. Four new mutations [-101 (C→A), -87 (C→G), -30, polyadenylation signal (poly A) (AATAAA→AATGAA)] have been characterized. Molecular analyses of DNA from over 20 unrelated cases with deltabeta-thal have shown that this condition is caused by a 13 kb deletion (Sicilian type); in two families a deletion of 18 to 23 kb (Macedonian type of deltabeta-thal) was discovered. Molecular analyses of alpha-thal in the Republic of Macedonia have shown the following types of molecular defects: 20.5 kb deletion, 17.5 kb deletion, 3.7 kb deletion, poly A mutation (AATAAA→AATGAA), and Hb Icaria [alpha142, Term→Lys, TAA→AAA (alpha2)]. The incidence of abnormal hemoglobins (Hbs) in the Republic of Macedonia is 0.4%. Three different alpha chain variants among 10 families, seven different beta chain variants among 33 families, two gamma chain variants in two newborns, one variant with an extended alpha chain, and Hb Lepore among 105 families, have been observed. Structural analysis of numerous cases with Hb Lepore showed that the variant was of the Washington-Boston type.

Efremov GD. Dominantly Inherited beta-Thalassemia. Hemoglobin. 2007;31(2):193-207.

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Dominantly inherited beta-thalassemia (thal) or "inclusion body beta-thalassemias" are heterogeneous at the molecular level and are due to mutations at or near the beta-globin gene locus. Many of these involve mutations of exon 3 of the beta-globin gene. They include frameshifts, premature chain termination (nonsense) mutations, and complex rearrangements that lead to the synthesis of truncated or elongated and highly unstable beta-globin gene products. The resulting beta chain variants are very unstable, and in many cases, the products of the dominantly inherited beta-thal are not detectable. Hematological and clinical observations made in several families with comparable forms of beta-thal and with certain highly unstable hemoglobin (Hb) variants, have indicated a striking overlap; many subjects with detectable unstable Hb variants and with a dominant type of beta-thal without a detectable abnormal Hb, have similar phenotypes. Here, a review of dominantly inherited beta-thal is given, and new examples of hyperunstable Hbs (Hb Stara Zagora and Hb Jambol) are presented. The first example is a hyperunstable variant named Hb Stara Zagora that was found in a 2-year-old Bulgarian boy. The abnormal Hb is associated with severe hemolytic anemia as a consequence of its hyper instability. The anemia was noticed at the age of 2 months and since then he has been on a regular monthly blood transfusion regimen. Hemoglobin analysis revealed no abnormalities, except the presence of inclusion bodies. Sequencing of the beta-globin gene revealed a heterozygosity for a 6 bp deletion (-TGGCTA) at codons 137 (the second and third bp), 138 and 139 (the first bp), thus forming a new codon at position 139 (GAT). This event eliminates three amino acids (Val-Ala-Asn) and introduces a new residue (Asp). It creates a new restriction site for HphI. The parents and his twin brother had no history of hemolysis. The paternity of the child was confirmed by DNA analysis. The second example is a new hyperunstable variant named Hb Jambol, found as a de novo mutation in a 2-year-old Bulgarian girl with severe hemolytic anemia. The mutation was detected through RNA/DNA analysis. It represents a complex genomic rearrangement involving an insertion of 23 nucleotides (nts) after IVS-II-535, a deletion of 310 nts extending from IVS-II-550 to the first nt of codon 108, and an insertion of 28 nts at the deletion junctions (derived from inverted sequence between nts +3707 and +3734 3' to the beta-globin

gene termination codon). At the protein level, this mutation leads to a deletion of four amino acid residues (Leu-Leu-Glu-Asn) at positions 105, 106, 107 and 108, and an insertion of nine residues (Val-Pro-Ser-Val-Thr-Leu-Phe-Phe-Asp) at the same location, creating an abnormal elongated beta chain of 151 amino acid residues. The parents had no history of hemolysis. The paternity of the child was confirmed by DNA analysis.

Efremov GD, Simjanovska L, Plaseska-Karanfiliska D, Stanojevic E, Petkov GH. Hb Jambol: a new hyperunstable hemoglobin causing severe hemolytic anemia. Acta Haematol. 2007;117(1):1-7.

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We describe a new hyperunstable beta-chain variant due to a complex genomic rearrangement. The abnormal hemoglobin (Hb) was found as a de novo mutation in a 2-year-old Bulgarian girl with severe hemolytic anemia. The mutation was detected through RNA/DNA analysis. It represents a complex genomic rearrangement involving an insertion of 23 nts after IVS-II-535 (derived by triplication of the 12-nts adjacent sequence and subsequent deletion of 1 nt), a deletion of 310 nts extending from IVS-II-550 to the first nt of Cd 108 and an insertion of 28 nts at the deletion junctions (derived from the inverted sequence between nts +3,707 and +3,734 3' to the beta-globin gene termination codon). At the protein level this mutation leads to a deletion of 4 amino acid residues (Leu-Leu-Glu-Asn) at positions 105-108 and an insertion of 9 residues (Val-Pro-Ser-Val-Thr-Leu-Phe-Phe-Asp) at the same location, creating an abnormal elongated beta-chain of 151 amino acid residues. This highly unstable variant was named 'Hb Jambol' after the geographic location in which the patient resides.

Grcevaska L, Popovska MM, Dzikova S, Ristovska V, Polenakovic M. Role of mycophenolate mofetil in the treatment of lupus nephritis. Ann N Y Acad Sci. 2007 Sep;1110:433-8.

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Mycophenolate mofetil (MMF) is an immunosuppressive drug successfully used for the prevention of acute and chronic rejection of renal allografts, as well as in the therapy of glomerular disorders. We treated three

groups of patients with lupus nephritis: the first group of patients had a high histologic activity index (AI), 13.4 +/- 2.34; the second group of patients had a high histologic chronicity index (CI), 6.0 +/- 0.7; and the third group consisted of only two patients, one with low AI (3.5) and another with low CI (1.5). The patients were treated for 2 years. MMF was initiated at a dose of 2 g/daily for the first 6 months and the dose was decreased to 1.5 g/daily for the further 18 months. Steroids, 0.4 mg/kg/day, were the concomitant therapy for the first 6 months, with slow tapering for the further 18 months. Patients with high AI presented significant decrease of serum creatinine after 2 years, 286 +/- 112.95 to 131.2 +/- 44.65 micromol/L. Two of the patients, with acute oligoanuria, were withdrawn from dialysis treatment. Significant improvement was also noted, 6.97 +/- 1.81 to 0.9 +/- 0.31 g/day. Patients with high CI had nonsignificant decrease of serum creatinine, 178.5 +/- 47.73 to 129.25 +/- 22.88 micromol/L, and significant improvement of proteinuria, 4.63 +/- 1.57 to 1.14 +/- 0.39 g/day. The patient with low AI showed recovery of renal function (serum creatinine from 196 to 72 micromol/L) and alleviation of proteinuria, 7.93 to 3.4 g/day. The patient with low CI did not respond to the therapy and renal function slowly worsened. MMF has emerged as a promising therapeutic approach for both the induction and maintenance phase in patients with lupus nephritis.

Havas D, Jeran N, Efremovska L, Dordeviæ D, Rudan P. Population genetics of 15 AmpfISTR Identifiler loci in Macedonians and Macedonian Romani (Gypsy). Forensic Sci Int. 2007 Dec 20;173(2-3):220-4. Epub 2007 Feb 20.

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Allele frequencies of 15 AmpFISTR Identifiler STR loci (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TPOX, D18S51, D5S818 and FGA) were analysed in a sample of 100 unrelated autochthonous Macedonian and 102 Macedonian Romani individuals, representing different ethnic groups residing within the same country of Former Yugoslav Republic of Macedonia. The interpopulation comparisons between Macedonians and Macedonian Romani with four south eastern European populations, Kosovo Albanians, Serbians from Vojvodina Province, western Romanians and northern Greeks were performed as well as comparison between Macedonian Romani and Assam population from Asia (India). Reported data point that Macedonian

Romani, as an example of an endogamous population of Asian (Indian) origin, show significant allelic differences when compared to neighbouring south eastern European populations.

Ivanovski O, Stankov O, Kuzmanoski M, Saidi S, Banev S, Filipovski V, Lekovski L, Popov Z. Penile strangulation: two case reports and review of the literature. J Sex Med. 2007 Nov;4(6):1775-80.

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INTRODUCTION: Entrapment or strangulation of the penis is a rare emergency situation that can lead to a wide range of vascular and mechanical injuries. **AIM:** The aim of this article is to present our experience dealing with penile strangulation. A review of the literature is also summarized in this report. Current treatment options and outcomes are also evaluated. **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:** Penile strangulation has been first time reported in 1755. Since that time, sporadic reports have appeared in the literature describing a variety of foreign bodies on the penis that have in common only the property of circularity. We noted motives, types of objects, types of strangulation, symptomatology, trauma grades, diagnoses, including psychological involvement, as well as possible treatment options. Furthermore, two cases of penile strangulation from our clinical practice are presented involving different degrees of vascular insult leading to different pathogenesis, clinical presentation, and surgical approach. **CONCLUSION:** Penile strangulation is an unusual clinical condition and the consequences can be severe. Penile strangulation could lead to different degrees of vascular obstruction. Consequently, several clinical syndromes can occur: from mild nonsignificant vascular obstruction that resolves after decompression to severe gangrene of the penis accompanied with impaired renal function. The most common motive associated with foreign bodies on the penis is sexual or erotic in nature. The choice of method for removal depends upon type, size, incarceration time, trauma grade, and availability of the equipment. Prompt diagnosis and early treatment are essential to avoid the potential complications of ischemic necrosis and autoamputation.

Ivanovski V, Mayerhöfer TG, Popp J. Isosbestic-like point in the polarized reflectance spectra of monoclinic crystals--A quantitative approach. Spectrochim Acta A Mol Biomol Spectrosc. 2007 Nov;68(3):632-8.

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If two overlapping bands originate from transition moments that are perpendicular and lie along the principal axes of the infinity frequency dielectric tensor, an isosbestic-like point (ILP) appears in the overlaid polarized IR reflectance spectra of single crystals. These conditions can also be met in principle in case of the reflectance from the ac-plane of a monoclinic crystal despite of the crystal's low symmetry. In order to determine the transition moment directions, diagonalization of the infinity frequency dielectric tensor should be performed. It is shown that a critical magnitude for the appearance of ILP is the angle of incidence. An increase of this angle leads to a transformation of the ILP to an isosbestic-like region, which eventually vanishes at higher incidence angles. Polarized reflectance spectra of gypsum ($\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$), recorded from the ac crystal face, were used to verify the theoretical results.

Ivanovski V, Mayerhöfer TG, Popp J, Petrusovski VM. Polarized IR reflectance spectra of the monoclinic single crystal $\text{K}_2\text{Ni}(\text{SO}_4) \cdot 2.6\text{H}_2\text{O}$: dispersion analysis, dielectric and optical properties. Spectrochim Acta A Mol Biomol Spectrosc. 2008 Feb;69(2):629-41.

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Polarized IR reflectance spectra of $\text{K}_2\text{Ni}(\text{SO}_4) \cdot 2.6\text{H}_2\text{O}$ single crystal (belonging to the group of Tutton salts) were recorded at near-normal incidence. From the dispersion analysis performed on the spectra recorded from the ac crystal plane, mode parameters: transversal frequency, oscillator strength, attenuation constant and the orientation of the transition moment were determined. The polarized spectrum along the b crystallographic axis was also recorded and a dispersion analysis performed. Comparison between the spectroscopically obtained transition moment directions with those obtained from the structure data for

various modes is discussed. All dielectric tensor component values were obtained for the whole mid-IR frequency range. Also, the real and the imaginary parts of the complex indexes of refraction for the waves with wave vector in the direction of the b crystallographic axis and in the ac plane (when the direction of the electric vector is oriented along the b axis) were found as functions of frequency.

Janeska B, Stefova M, Alipieva K. Assay of flavonoid aglycones from the species of genus *Sideritis* (Lamiaceae) from Macedonia with HPLC-UV DAD. *Acta Pharm.* 2007 Sep;57(3):371-7.

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Flavonoids obtained from *Sideritis* species (Lamiaceae), *S. raeseri* and *S. scardica*, grown in Macedonia were studied. Qualitative and quantitative analyses of the flavonoid aglycones were performed using high-performance liquid chromatography (HPLC) with a UV diode array detector. Extracts were prepared by acid hydrolysis in acetone, re-extraction in ethyl acetate and evaporation to dryness; the residue dissolved in methanol was subjected to HPLC analysis. Isoscutellarein, chryseriol and apigenin were identified in the extracts. Also, a 4'-methyl ether derivative of isoscutellarein was found, together with hypolaetin and its methyl ether derivative, which were identified according to previously isolated glycosides and literature data. Quantitation was performed using calibration with apigenin. According to this screening analysis, the samples of the genus *Sideritis* from Macedonia are rich in polyhydroxy flavones and analogous with the previously studied Mediterranean *Sideritis* species from the Ibero-North African and Greek *Sideritis* species with respect to the presence of 8-OH flavones and their derivatives.

Jashari A, Hey-Hawkins E, Mikhova B, Draeger G, Popovski E. An improved synthesis of 4-chlorocoumarin-3-sulfonyl chloride and its reactions with different bidentate nucleophiles to give pyrido[1',2':2,3]- and thiazino[3',2':2,3]-1,2,4-thiadiazino[6,5-c]benzopyran-6-one 7,7-dioxides. *Molecules.* 2007 Aug 22;12(8):2017-28.

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An improved synthetic method affording 4-chlorocoumarin-3-sulfonyl chloride (4) in very good yield (ca. 85%) is reported. This compound was reacted with various bidentate nucleophiles such as 2-aminopyridines and 2-aminothiazoles in order to obtain substituted pyrido- and thiazino-1,2,4-thiadiazinobenzopyranone dioxides (potential anticancer and anti-HIV agents). These reactions occurred rapidly at room temperature giving yellowish precipitates, which are insoluble in common organic solvents, making the purification process challenging. Further investigation has shown that these fused heterocycles are not stable and decompose with opening of the 1,2,4-thiadiazine ring.

Jordanova M, Miteva N, Rocha E. A quantitative study of the hepatic eosinophilic granule cells and rodlet cells during the breeding cycle of Ohrid trout, *Salmo letnica* Kar. (Teloestei, Salmonidae). *Fish Shellfish Immunol.* 2007 Aug;23(2):473-8.

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Fundamental questions remain on the nature and role of fish eosinophilic granule cells (EGCs) and rodlet cells (RCs). A poorly studied aspect is their suspected seasonality of occurrence under normal circumstances. In the liver of female Ohrid trout, *Salmo letnica*, we detected EGCs and RCs associated with stromal components. Both cell types could be considered a normal liver component in that wild fish population. A stereological study was performed to investigate eventual seasonality / breeding-related alterations in the amount (relative and total volumes) of EGCs and RCs. Differences only existed in the quantity of RCs; increasing from the earliest stages to the more advanced stages of ovarian maturation. EGCs made a greater pool than RCs only at early- and late vitellogenesis. Based on the breeding related fluctuations we suggest there is a hormonal regulation, by sex steroids, of the RCs liver content. Moreover, our data endorses the idea that, when using changes in the RCs pool as a biomarker, the fish breeding status must be considered as a potential source of changes in the RCs pool.

Karadzinska-Bislimovska J, Minov J, Risteska-Kuc S, Stoleski S, Mijakoski D. Bronchial hyperresponsiveness in women cooks and clean-

ers. Arh Hig Rada Toksikol. 2007 Jun;58(2):223-31.

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The aim of this cross-sectional study was to assess the prevalence and characteristics of bronchial hyperresponsiveness (BHR) in 43 women cleaners (aged 26 to 57) and 37 women cooks (aged 29 to 55) and compare them with 45 controls (women office workers aged 27 to 58). The evaluation of all subjects included a questionnaire, skin prick tests to common aeroallergens, spirometry, and histamine challenge ($PC_{20} < \text{or} = 8 \text{ mg mL}^{-1}$). We found higher BHR prevalence in cleaners and cooks than in office workers (30.2 % and 29.7 %, vs. 17.7 %, respectively), but statistical significance was not reached. The prevalence of mild and moderate to severe BHR was similar in all groups. Borderline BHR prevalence was significantly higher in cleaners than in controls (16.2 % vs. 6.6 %, $P=0.032$) whereas the difference was on the verge of significance in cooks (13.5 % vs. 6.6 %, $P=0.081$). Moderate to severe BHR was strongly associated with positive family history of asthma and atopy in all groups. Mild BHR was significantly associated with daily smoking in cleaners ($P=0.031$) and cooks ($P=0.021$), as well as with the duration of exposure in cleaners ($P=0.038$). Borderline BHR was closely related to daily smoking and duration of exposure in both cleaners and cooks. Our findings indicate an important role of workplace exposure in borderline BHR development, as well as the significant effect of smoking on mild BHR development in women cleaners and cooks.

Kolevski G, Petrov I, Petrova V. Transcranial sonography in the evaluation of Parkinson disease. J Ultrasound Med. 2007 Apr;26(4):509-12.

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OBJECTIVE: With transcranial sonography (TS), it is possible to visualize hyperechoic signals in the substantia nigra (SN) in patients with Parkinson disease (PD). Our objective was to correlate the level of echogenicity in the SN with clinical status in patients with PD. **METHODS:** In our pilot study, using TS, we examined 15 patients with the confirmed presence of PD. Staging of the latest clinical status was evaluated according to the Hoehn and Yahr scale. According to TS, the level of echogenicity was graduated as hypoechogenicity, moderate hyperechogenicity, and

severe hyperechogenicity. **RESULTS:** Of the patients with severe hyperechogenicity (8 patients), 7 had Hoehn and Yahr stage III disease, and 1 had stage II disease. Of the patients with moderate hyperechogenicity (6 patients), 4 had stage II disease; 1 had stage III disease; and 1 had stage I disease. The patient with hypoechogenicity had stage I disease. Statistical analysis showed that there was a significant correlation between the level of echogenicity in the SN and the clinical stage ($r = 0.7735$; $P = .0007$). **CONCLUSIONS:** In our pilot study, although only a small number of patients were included, we confirmed the usefulness of TS in the evaluation of PD.

Kostadinova E, Nikolova D, Alipieva K, Stefova M, Stefkov G, Evstatieva L, Matevski V, Bankova V. Chemical constituents of the essential oils of *Sideritis scardica* Griseb. and *Sideritis raeseri* Boiss and Heldr. from Bulgaria and Macedonia. Nat Prod Res. 2007 Jul 20;21(9):819-23.

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The essential oils of two species of *Sideritis* growing spontaneously in Bulgaria and Macedonia are reported, *Sideritis scardica* and *Sideritis raeseri*. The oils of *S. scardica* from different locations differed significantly: in the Macedonian sample alpha-cadinol (20%) predominated, while in the oil of Bulgarian samples the main components were diterpenic compounds and octadecenol (over 20%). This is the first report of diterpenoids in essential oil of *S. scardica*. The oil of *S. raeseri* demonstrated a distinct chemical profile with its high concentration of sesquiterpenes, main components being germacrene (25%) and elemol acetate (15.9%). The observed qualitative variability of the oil composition of *S. scardica* of different geographic origin could be a result of different ecologic conditions but might also reflect the well-known tendency of some *Sideritis* species to hybridize.

Krstevska-Konstantinova M, Kocova M, Gucev Z, Sukarova-Angelovska E. Premature thelarche in Macedonia: a three-year follow-up. Bratisl Lek Listy. 2007;108(8):340-3.

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INTRODUCTION: Premature thelarche presents as an

appearance of breasts and glandular tissue in girls before the age of 8 years. It is mostly a benign and transitory variation of premature sexual development. **AIM OF THE STUDY:** We evaluated a group of girls with premature thelarche for clinical and auxologic characteristics for a period of three years. We investigated the duration of the condition and eventual progression toward true idiopathic central precocious puberty. **PATIENTS, MATERIALS, METHODS:** At the Department of Endocrinology and Genetics at the Pediatric Clinic in Skopje, 127 girls with premature thelarche, from all over the country, were analyzed and followed-up for a period of 3 years (2000-2003). **RESULTS AND CONCLUSIONS:** Premature thelarche as a partial form of premature sexual development, in our study included 98 girls, and showed to be a benign condition, the girls are with normal height, slightly elevated weight, but with increased bone maturation and height velocity in the first year. A progression toward central precocious puberty was not registered. The duration of the condition was about two years in most of the girls, with a regression of enlarged breasts in smaller patients and with occurrence of normal puberty in older patients.

Kuzmanovski I, Dimitrovska-Lazova S, Aleksovskaja S. Classification of perovskites with supervised self-organizing maps. Anal Chim Acta. 2007 Jul 9;595(1-2):182-9.

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In this work supervised self-organizing maps were used for structural classification of perovskites. For this purpose, structural data for total number of 286 perovskites, belonging to ABO₃ and/or A₂BB'O₆ types, were collected from literature: 130 of these are cubic, 85 orthorhombic and 71 monoclinic. For classification purposes, the effective ionic radii of the cations, electronegativities of the cations in B-position, as well as, the oxidation states of these cations, were used as input variables. The parameters of the developed models, as well as, the most suitable variables for classification purposes were selected using genetic algorithms. Two-third of all the compounds were used in the training phase. During the optimization process the performances of the models were checked using cross-validation leave-1/10-out. The performances of obtained solutions were checked using the test set composed of the remaining one-third of the com-

pounds. The obtained models for classification of these three classes of perovskite compounds show very good results. Namely, the classification of the compounds in the test set resulted in small number of discrepancies (4.2-6.4%) between the actual crystallographic class and the one predicted by the models. All these results are strong arguments for the validity of supervised self-organizing maps for performing such types of classification. Therefore, the proposed procedure could be successfully used for crystallographic classification of perovskites in one of these three classes.

Laban-Guceva N, Antova M, Bogoev M. No changes in serum concentrations of interleukin 10 (IL-10) and interferon gamma (IF-gamma) before and after treatment of the thyroid eye disease (TED). Bosn J Basic Med Sci. 2007 Nov;7(4):358-62.

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TED is a severe eye disease leading in rare cases to decrease of sight, optic nerve compression and blindness. Recently, significant progresses in understanding the disease have been done. Nevertheless, the treatment of the disease, especially in its severe form remains challenging. Glucocorticoids (GC) have been the basis of the treatment for a long time. Orbital irradiation (OI) and optical decompression (OD) are also used in managing the severe forms of TED. Somatostatin, intravenous immunoglobulin have been also used, with conflicting results. Regarding the potential for the treatment of TED with cytokine antagonists, controlled clinical studies are not available. Since cytokines play an important role in the pathogenesis of the TED, they seemed to be logical choice for modern TED treatment. It has been shown that both Th1 (interleukin-2, tumor necrosis factor gamma, interleukin gamma) and Th2 (interleukin-4, -5, -10) profile T cells are activated in the TED. We therefore measured interleukin-gamma, IF-gamma and interleukin-10 (IL-10) (Th1 and Th2 pattern) to assess its relationship to the course of the disease. This paper shows that both Th1 (IL-2) and Th2 (IF-gamma) pathways represented by those two cytokines are not involved (IL-10 before 2.29±/5.23 and after treatment 3.77±/8.44; IF gamma before 0.50±/0.24 and after treatment 0.35±/0.19). No relationship to the response to treatment was found. GC resulted in positive response in 8/22 patients, OI (12 patients) given after CS therapy, resulted in a response in all patients.

Increase in proptosis, loss of visual acuity in spite of CS treatment prompted OD in two patients, who both recovered visual acuity and proptosis fell under 25 mm Hertel.

Laban-Guceva N, Bogoev M, Antova M. Serum concentrations of interleukin (IL-)1alpha, 1beta, 6 and tumor necrosis factor (TNF-) alpha in patients with thyroid eye disease (TED). Med Arh. 2007;61(4):203-6.

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Serum proinflammatory cytokines were found to be altered in Graves disease (GD) and in TED. Serum values of IL1alpha, IL-1beta, IL-6, TNF-alpha were assessed in 22 patients with TED before and after treatment (aged 46.82 +/- 12.47, M:F=16:6). Free thyroxin was high, TSH low, thyroid ultrasound showed diffuse thyroid enlargement, treatment with antithyroid drugs propylthiouracil (PTU) or methimazole (MMI) resulted in clinical and hormonal remission. Several months after the initiation of the signs of hyperthyroidism, a progression in the ophthalmopathy was observed (Hertel up to 25 mm: normal 15-17 mm) while patients were clinically and hormonally euthyroid. Blood was collected in euthyroid state (with TED signs present, before corticosteroid therapy (CS) treatment) and after 3 months of treatment (patients without TED and without TED treatment). CS resulted in response of 8/22 patients. Ophthalmic irradiation (OI) given with CS therapy, resulted in a response in twelve patients (12/12). Lack of response to CS treatment, with rapid increase in proptosis, and loss of visual acuity prompted ophthalmic decompression (OD) in two patients. Both recovered visual acuity, while proptosis fell under 25 mm Hertel. The control group had 29 persons (aged 51.86 +/-10.52, M:F = 16:13). A significant difference was found in the serum levels of IL-1alpha between the groups of controls (0.74 +/-0.55 pg/ml) and patients before treatment (1.85 +/- 1.85 pg/ml; $p < 0.005$). This difference further increased after treatment to 5.08 +/- 4.42 pg/ml ($p < 0.05$). Serum IL-1beta was higher in patients before treatment (0.36 +/- 0.15 pg/ml) in comparison with controls (0.24 +/- 0.43 pg/ml; statistically not significant--NS), and its concentrations remained unchanged after treatment (0.39 +/- 0.18 pg/ml; NS). IL-6 also had lower concentrations in patients at the start of the treatment (1.28 +/- 0.92; controls 1.72 +/- 1.9 pg/ml; NS). After the completion of TED treatment its concentration raised to 2.07 +/- 1.82 pg/ml (higher than the pretreatment; NS). For patients

with low Clinical Activity Score (CAS) scores (1-5) there was no change in IL-6 concentrations before (1.03 +/- 0.64 pg/ml) and after treatment (1.07 +/- 0.63 pg/ml). Patients with higher CAS scores (6-10) had a change in IL-6 levels (from 1.32 +/- 1.00 to 2.67 +/- 4.84; $p > 0.05$). In addition, patients with pathological VEP had no changes in IL-6 (from 0.93 +/- 0.53 to 0.97 +/- 0.32 pg/ml), while patients with normal VEP had increased IL-6 serum concentrations (1.36 +/- 0.98 to 2.32 +/- 4.17 pg/ml; NS). No stimulatory effect of IL-1beta on IL-6 was observed: IL-1beta was unchanged while IL-6 levels were increased after treatment. In general, when compared to controls TNF-alpha was twofold lower in patients than in the controls (0.18 +/- 0.034 and 0.34 +/- 0.41 pg/ml respectively; $p < 0.05$). In addition, serum TNF-alpha concentration did not change with treatment (0.18 +/- 0.03 pg/ml; $p < 0.05$). Increasing serum concentrations of TNF-alpha before and after treatment were associated with more severe forms of TED (treated with OD and OI with CS). Smoking did not alter the serum concentrations of cytokines.

Masin-Spasovska J, Spasovski G, Dzikova S, Petrusevska G, Lekovski Lj, Ivanovski N, Popov Z. Do we have to treat subclinical rejections in early protocol renal allograft biopsies? Transplant Proc. 2007 Oct;39(8):2550-3.

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The aim of the present study was to evaluate whether treatment of subclinical, borderline rejections (SR/BR) or histological findings of chronic allograft nephropathy (CAN) in protocol biopsies in the first month posttransplantation after living related kidney transplantation has a beneficial effect on graft histology and renal function at 6 months. Among the 40 paired biopsies, only 6/80 showed no histological lesions. BR was found in 13/40 and 12/40, and SR in 15/40 and 21/40 of patients on the 1- and 6-month biopsies, respectively. The mean histological index/total sum of scores for acute and chronic changes (HI) increased at 6-month biopsy: 5.3 +/- 2.9 vs 7.8 +/- 3.6 ($P < .001$). Similarly, the mean sum of histological markers for chronicity (CAN score) of 2.1 +/- 1.5 increased to 4.6 +/- 2.3 ($P < .001$) on the 6-month biopsy. When divided according to whether there was treatment of BR and SR, the treated BR/SR group on 1-month biopsy had a mean HI score of 7.11 +/- 1.9, which remained almost the same (7.11 +/- 2.32) at 6 months. Among the

untreated BR/SR group it increased from 4.95 +/- 1.99 to 8.16 +/- 4.30. However, there was no difference in graft function between the groups from 1 to 6 months. In conclusion, a protocol 1-month biopsy may be valuable to establish the prevalence of BR/SR in stable allografts. The presence of an untreated BR/SR upon a 1-month biopsy showed greater susceptibility for histological deterioration on the 6-month biopsy due to an accelerated CAN process.

Minov J, Karadzinska-Bislimovska J, Vasilevska K, Risteska-Kuc S, Stoleski S. Occupational asthma in subjects occupationally exposed to herbal and fruit tea dust. Arh Hig Rada Toksikol. 2007 Jun;58(2):211-21.

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We performed a cross-sectional study to detect occupational asthma (OA) in 63 subjects occupationally exposed to herbal and fruit tea dust and in 63 corresponding controls. The evaluation included a questionnaire, skin prick tests to workplace and common inhalant allergens, spirometry, and histamine challenge test. The evaluation of the work-relatedness of asthma in the exposed workers was based on serial peak expiratory flow rate (PEFR) measurements and bronchoprovocation tests. We found a higher prevalence of respiratory symptoms in the exposed workers, whereas spirometric parameters were significantly lower. The prevalence of sensitisation to allergens and of bronchial hyperresponsiveness (BHR) did not differ significantly between the groups. The prevalence of asthma was also similar in both groups (8.0% vs. 6.4%; $P=0.540$). Work-relatedness of symptoms was reported by all asthmatic tea workers and by no control with asthma. Significant work-related changes in PEFR diurnal variations and in non-specific BHR, suggesting allergic OA, were found in one tea worker with asthma (1.6%). No specific workplace agent causing OA in the affected subject was identified. None of the tea workers with asthma met the criteria for medical case definition of the reactive airway dysfunction syndrome (RADS). Our data confirm workplace exposure to herbal and fruit tea dust as a risk factor for OA.

Mitrev Z, Belostotskii V, Hristov N. Suture line reinforcement using suction-assisted bioglue application during surgery for acute aortic dissec-

tion. Interact Cardiovasc Thorac Surg. 2007 Apr;6(2):147-9.

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Bioglue has been widely and variously applied in treating acute aortic dissection according to the pathological process and surgeon's preference. This publication outlines a new hemostatic technique using suction-assisted bioglue application for aortic suture line reinforcement during surgery on acute aortic dissection. Twenty consecutive patients were treated in our center for acute aortic dissection using this technique. There were no bleeding complications during surgery and there were no re-explorations or early deaths as a result of bleeding. Average daily chest tube drainage was 582 +/- 150 ml/day, with the duration of drainage of 2 +/- 0.9 days. In conclusion, this new hemostatic technique is simple to use and demonstrates excellent, immediate and early postoperative results.

Mladenovska K, Craud O, Richomme P, Belamie E, Raicki RS, Venier-Julienne MC, Popovski E, Benoit JP, Goracinova K. 5-ASA loaded chitosan-Ca-alginate microparticles: Preparation and physicochemical characterization. Int J Pharm. 2007 Dec 10;345(1-2):59-69.

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The objective of the work was to prepare chitosan-Ca-alginate microparticles that can effectively deliver 5-ASA to the colon after peroral administration. For these requirements, a spray-drying technique was applied to 5-ASA/sodium alginate aqueous solution to obtain spherical particles having a mean diameter less than 10 microm. The microparticles formed were cross-linked and coated into solution of CaCl₂ and chitosan to obtain stable microsystem. (1)H NMR and UV-vis spectra of 5-ASA have shown no degradation when working in adequate conditions, such as light protection, freshly prepared solution and use of nitrogen to prevent the oxidative self-coupling of 5-ASA moieties. By imaging with SEM, acceptable spherical morphology was observed, but also flattened, disk-shaped particles of smooth surface and low porosity. CLSM imaging showed dominant localization of chitosan in the particle wall, while for alginate, a homogeneous distribution throughout the particle was observed giving the particles negative charge. In the FTIR spectra of 5-

ASA loaded Ca-alginate microparticles the characteristic peaks of 5-ASA were not altered indicating no covalent interaction between the drug and the polymer. DSC and X-ray diffraction studies revealed that 5-ASA was molecularly dispersed within the chitosan-Ca-alginate microparticles during the production process.

Mladenovska K, Raicki RS, Janevik EI, Ristoski T, Pavlova MJ, Kavrovski Z, Dodov MG, Goracinova K. Colon-specific delivery of 5-aminosalicylic acid from chitosan-Ca-alginate microparticles. Int J Pharm. 2007 Sep 5;342(1-2):124-36.

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Chitosan-Ca-alginate microparticles for colon-specific delivery and controlled release of 5-aminosalicylic acid after peroral administration were prepared using spray drying method followed by ionotropic gelation/polyelectrolyte complexation. Physicochemical characterization pointed to the negatively charged particles with spherical morphology having a mean diameter less than 9 microm. Chitosan was localized dominantly in the particle wall, while for alginate, a homogeneous distribution throughout the particles was observed. (1)H NMR, FTIR, X-ray and DSC studies indicated molecularly dispersed drug within the particles with preserved stability during microencapsulation and in simulated in vivo drug release conditions. In vitro drug release studies carried out in simulated in vivo conditions in respect to pH, enzymatic and salt content confirmed the potential of the particles to release the drug in a controlled manner. The diffusional exponents according to the general exponential release equation indicated anomalous (non-Fickian) transport in 5-ASA release controlled by a polymer relaxation, erosion and degradation. Biodistribution studies of [(131)I]-5-ASA loaded chitosan-Ca-alginate microparticles, carried out within 2 days after peroral administration to Wistar male rats in which TNBS colitis was induced, confirmed the dominant localization of 5-ASA in the colon with low systemic bioavailability.

Panovska-Stavridis I, Ivanovski M, Siljanovski N, Cevreska L, Efremov DG. Chronic lymphocytic leukemia patients with a V1-69 gene rearrangement do not have inferior survival with respect to patients that express other unmutated V(H) genes. Leuk Res. 2007 Feb;31(2):245-8.

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Recent studies indicate that V(H) gene usage in B-CLL may have prognostic impact independently of V(H) gene mutation status. The V1-69 gene is the most frequently rearranged V(H) gene in B-CLL and is almost always unmutated. We therefore investigated whether patients with a V1-69 gene rearrangement differ in clinical course and outcome with respect to patients expressing other unmutated V(H) genes. We show that V1-69 B-CLLs constitute a uniform group of patients that more often present at advanced clinical stages and require early treatment, but their survival does not differ significantly from patients with other unmutated V(H) genes.

Panovska TK, Kulevanova S, Gjorgoski I, Bogdanova M, Petrushevska G. Hepatoprotective effect of the ethyl acetate extract of *Teucrium polium* L. against carbontetrachloride-induced hepatic injury in rats. Acta Pharm. 2007 Jun;57(2):241-8.

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Hepatoprotective activity of the ethyl acetate extract of *Teucrium polium* L. was investigated using rats with CCl₄-induced liver damage. Specific biochemical parameters (glutathione peroxidase, superoxide dismutase, reduced glutathione and total antioxidative status) were estimated in blood and in liver homogenate. Lipid peroxidation in CCl₄-intoxicated rats was evidenced by a marked increment in the levels of thiobarbituric acid reactive substances. Histopathological examinations of the liver were undertaken to monitor the liver status. Silymarin was used as a standard to compare the hepatoprotective activity of the extract. Some biochemical parameters in groups treated with the *Teucrium polium* extract at a dose of 25 mg kg⁻¹, showed significantly different values than that of the CCl₄-treated group. The liver biopsy of all experimental rat groups treated with the *Teucrium polium* ethyl acetate extract showed significant restoration of the normal histomorphological pattern of liver cells. The study substantiates the potential hepatoprotective activity of the ethyl acetate extract of *Teucrium polium* L.

Pejov L, Jovanovski G, Grupce O, Soptrajanov B.

Anharmonicity of water stretching vibrations in series of isomorphous crystalline hydrates Copper and manganese saccharinates hexahydrates. Spectrochim Acta A Mol Biomol Spectrosc. 2007 Feb;66(2):419-26.

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On the basis of the experimentally obtained frequencies of isotopically isolated OH and OD species, the anharmonicity constants, as well as the harmonic eigenvalues of the OH and OD stretching vibrations for two members of the isomorphous series of metal(II) saccharinates hexahydrates (those of Mn and Cu) were calculated using several theoretical models [B. Berglund, J. Lindgren, J. Tegenfeldt, J. Mol. Struct. 43 (1978) 169, M.G. Sceats, S.A. Rice, J. Chem. Phys. 71 (1979) 973, H. Engstrom, J.B. Bates, L.A. Boatner, J. Chem. Phys. 73 (1980) 1073]. The anharmonicity constants and the $\nu(\text{OH})/\nu(\text{OD})$ isotopic ratios correlate well with the stretching frequencies of the isotopically isolated OH and OD oscillators. Both anharmonicity constants and isotopic ratios as criteria for the anharmonicity of the OH (OD) vibrations show that, with a very few exceptions, it increases with the increase in the hydrogen bond strength. The exceptions from the trend are explained in terms of local electrostatic field differences and force constant changes due to the coordination to the metal ion. The obtained regression equations were used to predict the anharmonicity constants of the $\nu(\text{OD})$ modes in other members of the series. Within the three-particle model of the hydrogen bonded complex, the parameters characterising the coupling of the $\nu(\text{OH})/\nu(\text{OD})$ modes with the low-frequency $\nu(\text{Ocdots, three dots, centered O})$ ones were estimated. The positions of the overtones of OH and OD stretching vibrations in the compounds of copper and manganese were estimated using the calculated anharmonicity parameters. The predicted values for the OD oscillators were compared with the experimentally obtained data. Model calculations of the described type are shown to be valuable in the assignment of the second-order transitions, especially in complex systems.

Pereska Z, Dejanova B, Bozinovska C, Petkovska L. Prooxidative/antioxidative homeostasis in heroin addiction and detoxification. Bratisl Lek Listy. 2007;108(9):393-8.

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BACKGROUND: Long-term heroin abuse is related to pathological changes in many organs mediated by oxidative stress (OS). **OBJECTIVES:** Estimation of systemic OS and antioxidant capacity in heroin addiction and detoxification provides information about prooxidant/antioxidant homeostasis in heroin misuse and need for antioxidant supplementation. **METHODS:** OS was evaluated by the measurement of plasma reactive oxygen metabolites using spectrophotometric method and plasma lipid peroxidation by its end product--malondyaldehyd using Tiobarbituric Acid Reactions Substances method. The extracellular antioxidant capacity was estimated using OXY-adsorbent test. **RESULTS:** This cross-sectional study includes 68 patients: 46 heroin addicts (20 patients on chronic heroin abuse, 19 patients on conventional method of detoxification and 7 patients on opioid antagonist--naltrexone (and 22 patients as a control) group. Increased OS was found in the heroin group (d-ROMs 349.3 +/- 102.2 UCarr, MDA 4.0 +/- 0.4 micromol/L) compared to the group on detoxification (d-ROMs 230.2 +/- 96.4 UCarr; MDA 3.6 +/- 0.3 micromol/L) and control group (d-ROMs 264.1 +/- 30.9 UCarr; MDA 3.7 +/- 0.2 micromol/L). TAC was decreased in the heroin group (324.5 +/- 75.0 micromol HClO/ml) and restored during conventional detoxification (371.8 +/- 25.1 micromol HClO/ml), but not completely in the group with naltrexone treatment (335.6 +/- 16.9 micromol HClO/ml) compared with controls (395.4 +/- 35.6 micromol HClO/ml). **CONCLUSION:** Long-term heroin abuse stimulates a progressive systemic oxidative stress which increases the extracellular antioxidants consumption and develops conditions for chronic heroin toxicity.

Petreska I, Ivanovski G, Pejov L. The perturbation theory model of a spherical oscillator in electric field and the vibrational stark effect in polyatomic molecular species. Spectrochim Acta A Mol Biomol Spectrosc. 2007 Apr;66(4-5):985-93.

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The effect of external electrostatic fields on the spherical oscillator energy states was studied using stationary perturbation theory. Besides the spherical oscillator with ideal symmetry, also a variety of the deformed systems were considered in which the deformations may be induced by the external fields, but also by the short-range crystal lattice forces. The perturbation theory analysis was carried out using the field-depend-

ent basis functions. Predicted spectral appearances and band splittings due to the deformations and external field influences were shown to be helpful in interpreting the experimental spectra of molecular oscillator possessing subsets of mutually orthogonal triply degenerate normal modes (such as, e.g. tetrahedral species). To verify the results of the perturbation theory treatments, as well as to provide a further illustration of the usefulness of the employed technique, a numerical HF/aug-cc-pVTZ study of the vibrational states of methane molecule in external electrostatic field was performed.

Popov Z, Ivanovski O, Kolevski P, Stankov O, Petrovski D, Cakalaroski K, Ivanovski N. De novo malignancies after renal transplantation—a single-center experience in the Balkans. *Transplant Proc.* 2007 Oct;39(8):2589-91.

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The occurrence of malignancies is a well-known serious complication after organ transplantation. Despite the fact that many factors may be involved, the pathogenesis is still unclear. The aim of the present study was to examine the incidence and clinical characteristics of de novo malignancies that arise after renal transplantation over a 13-year experience in a single center in the Balkan Peninsula. During this period, 185 renal transplantations (139 living related and 46 cadaveric) were followed in our department. Overall, 19 malignancies (9.78%) were observed in 15 patients (7.8%). The mean age of these patients was 45 years (range, 21-53 years). Ten patients (55%) developed skin cancers: 8 squamous and 2 basal cell. Kaposi's sarcomas were found in 3 patients (16.6%, 1 visceral form). We also detected 1 breast cancer, 1 seminoma, 1 colon cancer, 1 urogenital-transitional cell-like cancer, 1 renal cell carcinoma, 1 plasmacytoma, and 1 retroperitoneal sarcoma after an ABO incompatible transplantation. All cancers were de novo malignancies that presented at a mean time of 21 months (range, 2-52 months) after surgery. In conclusion, the incidence of malignancy in the present series was similar to that reported elsewhere. The predominance of skin cancers was understandable bearing in mind the sunshine. The appearance of skin malignancies in our group of patients was earlier, more severe, and multiple sites. No cases of posttransplantation lymphoproliferative disorders were observed. Careful clinical examination and long-term screening protocols are needed for early detection and treatment of this life-

threatening complication among the transplant population.

Sikole A, Dzekova P, Selja N, Gaseva M, Nikolov IG, Zabzun M, Muharemi S, Asani A, Amitov V, Mena S, Grunevska V, Ivanovski L, Polenakovic M. Treatment of hepatitis C in hemodialysis patients with pegylated interferon alpha-2a as monotherapy. *Ren Fail.* 2007;29(8):961-6.

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BACKGROUND: The high prevalence of hepatitis C virus (HCV) infection in hemodialysis patients is of great concern because they have a higher rate of mortality than HCV-negative hemodialysis patients. The aim of the study was to evaluate the efficacy and safety of pegylated interferon alpha-2a monotherapy in hemodialysis patients with chronic HCV infection. **METHODS:** Fourteen dialysis patients with chronic HCV infection were scheduled to receive 135 mug pegylated interferon alpha-2a subcutaneously, once a week, after dialysis session for a period of 48 weeks. Efficacy and safety were assessed by end of treatment viral response, sustained viral response, biochemical response, and adverse events. Serum HCV RNA levels were assessed using reverse transcriptase polymerase chain reaction (RT-PCR), while HCV genotype was analyzed by RT-PCR followed by hybridization of amplified products. **RESULTS:** Of the 14 patients enrolled in the study, 9 completed treatment. Eight patients (57%) had undetectable levels of HCV RNA at the end of treatment, while one patient remained positive. Two (14.3%) patients were discontinued because of insufficient therapeutic response. Three patients (21.34%) did not finish treatment because serious adverse events occurred: one patient with bronchopneumonia and one with pericarditis were discontinued from treatment, while one patient died due to cerebral hemorrhage. Sustained viral response was present in 36% of the patients (5/8 patients) at the end of the follow up period. Biochemical response with normalization of serum ALT levels during treatment was observed in all treated patients (83 +/- 20.1 U/L at baseline vs. 23.4 +/- 4.6 U/L at week 48). The most common adverse events were flu-like syndrome, myalgia, arthralgia, and pancytopenia. Most of the adverse events were manageable. The serious adverse events were believed to be unrelated to the therapy, but rather to the co-morbidities of the hemodialysis patients. **CONCLUSIONS:** Pegylated interferon alpha-2a treatment was effective in a considerable proportion of the

treated hemodialysis patients with hepatitis C, and it was reasonably safe to use.

Spasovski GB. First two AB-incompatible living kidney transplantations in the Balkans—should it be a procedure of choice in a developing country? *Int J Artif Organs*. 2007 Feb;30(2):173-5.

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Kidney transplantation is the best available medical intervention for the treatment of end-stage renal failure. However, as a consequence of the growing gap between organ supply and demand, many patients die waiting for an organ each year. In order to increase the number of organs, living donor (LD) transplantation from unrelated and ABO-incompatible (ABOi) donors have been introduced over the last few decades. While in the past ABOi transplantation resulted in hyperacute or acute antibody-mediated rejection, the tremendous progress in this area in recent years has shown that it can be overcome by careful patient management, including protocols to remove or lower antibodies, along with stronger immunosuppression and intensive monitoring. The organ shortage problem is even more prominent in regions such as the Balkans where cadaver transplantation has not been well developed. In addition to the introduction of expanded criteria for living donation (elderly and marginal donors), we performed the first two ABOi/LD transplantations in the Balkans in the last 2 years using an already established preconditioning regimen and maintenance therapy with cyclosporine, mofetil mycophenolate and prednisolon. We report our modest experience of a case in which the patient developed lymphadenopathy, sarcomatosis and died after one year; and a second case with accelerated acute rejection and hemorrhagic necrosis with explantation of the graft after a month. Taking into account the high cost of the desensitization procedure and induction therapy as well as the need for intensive monitoring throughout the standardized procedures and facilities, we might reconsider whether ABOi living kidney transplantation should be a procedure of choice in developing countries.

Spasovski GB. Bone health and vascular calcification relationships in chronic kidney disease. *Int Urol Nephrol*. 2007;39(4):1209-16.

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Abnormal bone in chronic kidney disease (CKD) may adversely affect vascular calcification via disordered calcium and phosphate metabolism. In this context, bone health should be viewed as a prerequisite for the successful prevention/treatment of vascular calcification (VC) along with controlled parathyroid hormone (PTH) secretion, the use of calcium-based phosphate binders and vitamin D therapy. In CKD patients, VC occurs more frequently and progresses more rapidly than in the general population, and is associated with increased cardiovascular disease (CVD) morbidity and mortality. A number of therapies aimed at reducing PTH concentration are associated with an increase of calcaemia and Ca x P product, e.g. calcium-containing phosphate binders or active vitamin D. The introduction of calcium-free phosphate binders has reduced calcium load, attenuating VC and improving trabecular bone content. In addition, a major breakthrough has been achieved through the use of calcimimetics, as first agents which lower PTH without increasing the concentrations of serum calcium and phosphate. Nowadays, it is becoming evident that even early stage CKD is recognised as an independent CVD risk factor. Moreover, the excess of CVD among dialysis patients cannot be explained entirely on the basis of abnormal mineral and bone metabolism. Hence, much controversy has surrounded the cost-effectiveness of treatment with the new phosphate-binding drugs as well as new vitamin D analogs and calcimimetics. Thus, it seems prudent and reasonable that maintaining bone health and mineral homeostasis should rely on some modifications of standard phosphate binding and calcitriol therapy. Hypophosphataemia and hypercalcaemia in adynamic bone disease (ABD) might be treated by reducing the number of calcium carbonate/acetate tablets in order to increase serum phosphate and decrease serum calcium, which, in turn, might positively stimulate PTH secretion. The same rationale is assumed for the use of a low calcium dialysate. On the other hand, secondary hyperparathyroidism with hyperphosphataemia and hypocalcaemia should be treated with a substantial number of calcium carbonate/acetate tablets in combination with calcitriol and low calcium dialysate in order to decrease serum phosphate and maintain the Ca x P product within K/DOQI guidelines (<4.4 mmol l(-1)). Finally, it becomes apparent that prevention, with judicious use of calcium-based binders, vitamin D and a low calcium dialysate without adverse effects on Ca x P or oversuppression of PTH, provides the best management of VC and mineral and bone disorder in

CKD patients.

Spasovski G, Gelev S, Masin-Spasovska J, Selim G, Sikole A, Vanholder R. Improvement of bone and mineral parameters related to adynamic bone disease by diminishing dialysate calcium. *Bone*. 2007 Oct;41(4):698-703.

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BACKGROUND: The existence of adynamic bone disease (ABD) as most prevalent form of renal osteodystrophy in recent years and its reduced ability to handle an exogenous calcium load has implied a higher risk for vascular and soft-tissue calcifications. The effect of low dialysate calcium (LCD) on parathyroid hormone (PTH) secretion in ABD patients has not yet sufficiently been clarified. This randomized, prospective study aimed to compare the effects of LCD and high calcium dialysate (HCD) on the evolution of bone and mineral parameters related to ABD in dialysis patients. **METHODS:** 52 out of 60 patients with predialysis intact PTH < 100 pg/ml completed this study and were equally distributed over LCD (1.25 mmol/l) or HCD (1.75 mmol/l) treatment. The duration of the study was 6 months and the only peroral phosphate binder administered was calcium carbonate. Total and ionised calcium were measured monthly in serum before and after dialysis while serum parameters relevant to bone were measured at the enrollment and at 3-month intervals. **RESULTS:** There were no differences in predialysis mean phosphate or calcium x phosphorus product (Ca x P). The most common side effects of both treatments were comparable. Hypotension occurred in 16% and 17% and cramps in 6% and 8% of the dialysis sessions, in the HCD and LCD group, respectively. The groups did not differ in the mean tCa before dialysis, but this parameter was significantly higher in the HCD group vs. LCD at the end of dialysis (2.59±/0.18 vs. 2.44±/0.19 mmol/l; p<0.01). The patients of the HCD group also had a significantly higher mean iCa both before (1.08±/0.05 vs. 1.04±/0.06 mmol/l; p=0.02) and at the end of dialysis (1.18±/0.04 vs. 1.48±/0.04 mmol/l; p<0.01). There were no differences within the LCD group between baseline and end of dialysis treatment values of tCa and iCa. However, the mean tCa and iCa were markedly increased at the end of dialysis in the HCD group [2.40±/0.21 vs. 2.59±/0.18 mmol/l (p<0.01); 1.08±/0.05 vs. 1.18±/0.04 mmol/l (p<0.01)]. Mean serum levels of iPTH and total alkaline phosphatase in the LCD group

were increased at 3 months and at the end of the study compared with the baseline levels [(38.6±/22.9 vs. 63.3±/46.0 vs. 78.6±/44.7 pg/ml); (59.5±/18.7 vs. 75.9±/26.7 vs. 84.0±/35.4 U/l)], respectively, and bone alkaline phosphatase increased also only after 6 months of treatment (23.4±/7.3 U/l vs. 35.6±/22.3). The bone markers in the HCD group did not change. At the end of the study all bone parameters in the LCD group were significantly higher than in the HCD group. **CONCLUSION:** There was an evolution towards parameters reflecting higher bone turnover in patients treated with dialysate calcium of 1.25 mmol/l, probably by prevention of a positive calcium balance and enabling sustained stimulation of PTH secretion. Hence, LCD might be considered a valuable therapeutic option for ABD patients.

Stankovska E, Stafilov T, Sajn R. Monitoring of trace elements in honey from the Republic of Macedonia by atomic absorption spectrometry. *Environ Monit Assess*. 2007 Sep 26. [Epub ahead of print]

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Contents of Zn, Cu, Fe, Mn, Cd, Na, K, Ca and Mg in 123 honey samples from different regions of the Republic of Macedonia were determined by atomic absorption spectrometry. A microwave digestion system was applied for digestion of the samples. The mean content for the elements determined was found to be: 2.252, 0.696, 1.885, 1.752, 0.004, 29.52, 984.8, 40.11, 18.24 mg kg⁻¹ for Zn, Cu, Fe, Mn, Cd, Na, K, Ca and Mg, respectively. Based on a comparison of statistical parameters, the spatial distribution of particular elements in Macedonian honey and the results of factor analysis, two natural and one anthropogenic geochemical associations were identified. The natural geochemical associations (Mg, Mn, Ca, K and Fe, Zn, Ca, -K, -Na) are influenced mainly by lithology. The anthropogenic associations (Cd and -Cu) are mostly a result of metallurgical activities, namely lead production in the town of Veles.

Tanevska V, Kuzmanovski I, Grupce O. Provenance determination of Vinica terra cotta icons using self-organising maps. *Ann Chim*. 2007 Jul;97(7):541-52.

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In the Vinica Fortress, Republic of Macedonia, 50 undamaged terra cotta icons and 100 fragments, all dated 6th-7th century, were found. In order to determine the provenance of these unique terra cotta icons, the mass fractions of 19 different chemical elements were previously determined in ten fragments of the terra cotta icons and thirty three samples of clays from eight different sites from the region. Due to the dimensionality and complexity of the experimental data, the archaeometric results were treated with self-organising maps (SOM). The results obtained using SOM were compared with the ones obtained using principal component analysis. Both chemometric methods revealed that Vinica terra cotta icons were made from clay from Grncarka, 2.5 km South-East from the Vinica Fortress.

Tosheska K, Labudovic D, Alabakovska S, Handziski Z, Spiroski M, Todorova B. Lipoprotein (a) and apolipoprotein (a) phenotypes in healthy Macedonian children. Bratisl Lek Listy. 2007;108(4-5):179-83.

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BACKGROUND: Plasma levels of lipoprotein(a) [Lp(a)] are determined largely by genetic variation in the gene encoding apolipoprotein(a) [apo(a)], the unique protein component of Lp(a). High plasma levels of Lp(a) increase the risk of premature atherosclerosis. However, the association of apo(a) phenotypes with the development of these diseases remains largely unexplored. **OBJECTIVES:** Determination of Lp(a) levels and apo(a) isoforms (phenotypes) in 100 (51 boys, 49 girls) Macedonian healthy children aged 9-18. **METHODS:** We used 3-15% gradient SDS-PAGE for separation of apo(a) isoforms. According to the different apo(a) electrophoretic mobilities, Apo(a) was classified into five single and respective double-band phenotypes. **RESULTS:** Each individual expressed a single (homozygotic), double-band (heterozygotic) or no band (null phenotype). The apo(a) phenotype frequencies revealed that the frequency of single-band phenotype expression (64 %) was higher than that of double bands (32 %) and that the frequency of phenotypes representative of low molecular weight was very low (4%). The most frequent phenotype was S4 (42.65%). The distribution of plasma Lp(a) levels was skewed, with the highest frequencies at low levels. The mean Lp(a) concentration was 11.95 (SD of 5.98 and median of 9.62 mg/dL). We did not find differences in the mean

and median plasma Lp(a) levels between boys and girls ($p > 0.05$). A strong inverse relationship was found between the apparent molecular weight of apo(a) phenotypes and plasma Lp(a) concentration ($r = -0.4257$). **CONCLUSIONS:** Determination of Lp(a) levels and apo(a) phenotypes in children, may help in preventing and reducing the risk of atherosclerotic development.

Vavlukis M, Borozanov V, Georgievska-Ismail L, Bosevski M, Taneva B, Kostova N, Peovska I. Arterial hypertension in patients with coronary artery disease treated with surgical myocardial revascularization. Bratisl Lek Listy. 2007;108(7):301-6.

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OBJECTIVES: To evaluate the incidence and prognostic power of arterial hypertension in patients with coronary artery disease treated with surgical myocardial revascularisation, before and after the operation. **BACKGROUND:** Arterial hypertension is one of the leading modifiable risk factors in CAD patients who underwent CABG surgery with the major impact on clinical outcome in these patients. **METHODS:** 749 patients with mean age of 55 +/- 8 years, (639 male/119 female) were analyzed for their preoperative: demographic, clinical, left ventricular morphologic and functional and angiographic, perioperative: type of operation, type and number of applied conduits, in-hospital morbidity and mortality, and post-operative: demographic, clinical, left ventricular morphologic and functional and angiographic characteristics. Mean postoperative follow-up period was 5.97 +/- 4.27 years. **RESULTS:** Hypertension was found in 52.7% of patients before the operation, and it was the most frequent risk factor, without any differences between different age groups, but significantly more often in females ($p = 0.0001$), diabetics ($p = 0.0001$), and patients with preserved LV function ($p = 0.011$). Although significantly correlated with in-hospital morbidity ($r = 0.085$ and $p = 0.023$), HTA was not identified as independent predictor. The most predictable was the occurrence of early neurological complications. HTA was also found to be a predictor of long life prognosis in CABG patients, but not as independent prognostic factor. Significant reduction in incidence was found in post-CABG patients (30.1%), which is most likely a result of applied pharmacologic treatment. ACE-inhibitors, Ca-antagonists and B-blockers were applied in

39.44%, 30.1% and 33.6% of patients respectively, with significant positive correlations found for all of them as follows: $r = 0.221$, $p = 0.0001$, $r = 0.316$, $p = 0.0001$ and $r = 0.093$, $p = 0.031$. **CONCLUSION:** Hypertension is the most powerful risk factor in CAD patients who undergo CABG surgery in our country, and a powerful prognostic factor of early and late clinical outcome. There is a trend toward decreasing the incidence of HTA in post-CABG patients, as a result of improved pharmacologic treatment after the operation.

Vlaski E, Stavric K, Isjanovska R, Seckova L, Kimovska M. Acetaminophen intake and risk of asthma, hay fever and eczema in early adolescence. Iran J Allergy Asthma Immunol. 2007 Sep;6(3):143-9.

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A positive association between acetaminophen intake and allergic diseases has recently been reported in developed countries with impaired oxidant/antioxidant balance and promotion of atopy as proposed underlying mechanisms. The aim of the study was to explore the relationship between acetaminophen intake and asthma, hay fever, and eczema in The Republic of Macedonia as a country with acetaminophen intake not physician-controlled, high passive smoke exposure and dietary antioxidant intake, and moderately low prevalence of allergic diseases. Self-reported data obtained through the standardized International Study of Asthma and Allergies in Childhood Phase Three written questionnaires of 3026 adolescents aged 13/14 years from randomly selected schools in Skopje, the capital of Macedonia, were used. The frequency of current acetaminophen intake—both unadjusted and adjusted for confounding factors—was correlated to current and ever-diagnosed asthma, hay fever and eczema by odds ratios (OR, 95% CI) in binary logistic regression. Use of acetaminophen at least once monthly increased the risk of current wheeze (adjusted OR 2.04, 1.31-3.20 $p=0.002$), asthma 'ever' (adjusted OR 2.77, 1.06-7.26 $p=0.039$), current allergic rhinoconjunctivitis (adjusted OR 2.95, 1.79-4.88 $p=0.000$) and hay fever 'ever' (adjusted OR 2.25, 1.36-3.70 $p=0.002$). A significant association between frequent acetaminophen intake and atopic eczema and also between infrequent acetaminophen intake and investigated allergic diseases was not established. The findings suggest an increased risk of asthma and hay

fever, but not atopic eczema associated with frequent acetaminophen use in a developing country.

V'ickova-Laskoska MT, Laskoski DS, Kamberova S, Caca-Biljanovska N, Volckova N. Epidemiology of pemphigus in Macedonia: a 15-year retrospective study (1990-2004). Int J Dermatol. 2007 Mar;46(3):253-8.

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BACKGROUND: Pemphigus is an autoimmune blistering skin disease mediated by auto-antibodies directed against desmoglein proteins. There are only a few epidemiological studies on pemphigus. Our objective was to determine the epidemiological features of pemphigus in Macedonia, and to compare the results with those reported elsewhere. **METHODS:** Diagnosis in all cases was confirmed by histopathology and direct immunofluorescence. Binomial distribution testing and Fisher's exact-test at the 0.01 level of significance were used to determine if particular demographic groups were over-/under-represented among the pemphigus patients. **RESULTS:** One hundred and thirty-three new pemphigus cases were diagnosed in Macedonia from 1990-2004. The average annual incidence was 0.44/100,000 inhabitants (SD=0.17). The incidence doubled to 0.89 in 2001 during the local armed unrest. The disease did not affect either gender to a greater extent. The average annual incidence was 0.51 for ethnic Macedonians. Roma (Gypsies) had a statistically significantly higher incidence of pemphigus at 2.4 cases/100,000 individuals. Ethnic Albanians had statistically significantly lower incidence of 0.1 cases/100,000 individuals. The most common variant was pemphigus vulgaris (77.4%). **CONCLUSIONS:** The annual incidence for pemphigus in Macedonia is 0.44 cases/100,000 inhabitants. Most common form was pemphigus vulgaris. An epidemiological peak occurred in 2001 during the local armed conflict. Macedonian Roma had a sixfold higher incidence of pemphigus compared with the overall population; ethnic Albanians had a fourfold lower incidence.

Zlatanovic N, Kedev S, Gjorgov N, Miletic B, Georgiev A, Kovacevic D, Trajkov I, Kaev M, Borozanov V, Boskov V. Pulse amplitude adjustment provides immediate pacemaker longevity gain. Anadolu Kardiyol Derg. 2007 Jul;7 Suppl 1:216-8.

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OBJECTIVE: Adjusting pacemaker pulse amplitude influences the longevity of the pacemaker. Our aim was to establish the initial longevity gain. **METHODS:** Forty randomly selected patients with implanted pacemakers were analyzed. Mean age was 65.58±13.7 years. All pacemakers were working on factory settings of pulse amplitude 3.5 V and pulse width of 0.4 ms for average of 3 years before the adjustment. Initial mean longevity was projected to 68.61±18.86 months, mean battery voltage 2.78 V, and mean battery current 14.21±2.61 microA. **RESULTS:** Pulse amplitude threshold test was performed and average value of

0.632±0.22 V was obtained. Pulse amplitude was programmed to 2.5 V and pulse width was left unchanged. New readings of battery data were obtained. Battery voltage did not show immediate changes, and battery current decreased to 11.53±1.98 microA. New average longevity was projected to 81.03±19.82 months, which presents a 12.42 months of initial longevity gain with statistical significance at 95% confidence interval (p=0.003). Positive correlation was found between the new pulse amplitude and new values of battery current (p<0.01). **CONCLUSION:** Pulse amplitude decrease of only 1 V provides significant initial longevity gain of more than a year. If found correlations would have any impact on further longevity gains over longer period of time is yet to be established.