

Božina N¹, Rojnić Kuzman M², Medved V², Jovanović N², Sertić J¹, et al. Associations between MDR1 gene polymorphisms and schizophrenia and therapeutic response to olanzapine in female schizophrenic patients. J Psychiatr Res 2006 Nov 17; [Epub ahead of print].

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Multidrug resistant protein (MDR1) gene, which codes for P-glycoprotein and functions as an efflux transporter in different cells, is widely localized in normal tissues including the gastrointestinal tract, blood cells, biliary tract, kidney and brain and plays a major role in absorption, distribution and elimination of various xenobiotics. Therefore, MDR1 gene variants were proposed as potential susceptibility factors for diseases and as determinants of treatment response to various drugs. We investigated the relationships between exon 21 G2677T and exon 26 C3435T genetic variants of MDR1 gene with susceptibility and treatment response in female schizophrenic patients. The study was conducted in two steps. We first compared allele, genotype and haplotype distributions between 117 female schizophrenic patients and 123 control female subjects. Afterwards, we studied treatment response to olanzapine, in 87 out of 117 previously unmedicated female patients. Overall, we found lower representation of G2677/C3435 haplotype in schizophrenic female patients compared to controls. Test result for linkage disequilibrium between loci was found to be significant. Furthermore, we found significant associations between MDR1 exon 21 G2677T genotypes and treatment response measured with positive PANSS percentage changes, with T allele and TT genotype being associated with significantly better treatment response. A borderline, non-significant statistical association was found between MDR1 exon 26 C3435T genotypes and treatment response, with TT genotype being associated with better treatment response. Our data support functional importance of the MDR1 mutations for the susceptibility and treatment response in female schizophrenic patients.

Nikolić-Heitzler V¹, Rabuzin F², Tatzber F³, Vrkić N¹, Bulj N¹, Borović S², et al. Persistent oxidative stress after myocardial infarction treated by percutaneous coronary intervention. Tohoku J Exp Med 2006;210:247-55.

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Acute myocardial infarction causing cardiac ischemia is responsible for the majority of cardiac related deaths. Medical interventions that ensure rapid reperfusion, such as percutaneous coronary intervention, are aimed to allow myocardial re-oxygenation. However, this generates reactive oxygen species, resembling ischemia-reperfusion type of injury based on oxidative stress. In the present study we monitored dynamic changes of total serum peroxides, total antioxidant capacity and soluble intercellular adhesion molecule-1 as well as the titer of antibodies against oxidized low-density lipoproteins in the blood during the convalescence period of 32 patients with acute myocardial infarction treated by percutaneous coronary intervention. Samples were taken at admittance and at two hours, four hours, three days and seven days following percutaneous coronary intervention. Total antioxidant capacity dropped to 82% ($p < 0.05$). The titer of antibodies against oxidized low-density lipoproteins transiently decreased within the first three days, and increased afterwards. The values of serum peroxides and soluble intercellular adhesion molecule-1 increased continuously in respect to the initial levels reaching the maximum at the time of release from hospital. These findings indicate a persistent oxidative stress that might be associated with intravascular inflammation in patients during convalescence and release from hospital.

Jasprica I¹, Mornar A¹, Debeljak Ž², Smolčić-Bubalo A¹, Medić-Šarić M¹, Mayer Lj³, et al. In vivo study of propolis supplementation effects on antioxidative status and red blood cells. J Ethnopharmacol 2007;110:548-54.

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In vivo study has been conducted on 47 healthy women and men in order to investigate whether daily intake of powdered propolis extract during 30 days has any influence on the following blood parameters: activity of superoxide dismutase, glutathione peroxidase and catalase, concentration of plasma malondialdehyde, total cholesterol, low- and high-density lipoprotein cholesterol, triglycerides, glucose, uric acid, ferritin and transferrin, to-

gether with routine red blood cell parameters. The effect of daily propolis intake seems to be time and gender related. For the men test group after the initial 15 days of propolis treatment, 23.2% ($p=0.005$) decrease in concentration of malondialdehyde was observed. After 30 days of treatment, statistically significant ($p=0.010$) 20.9% increase in superoxide dismutase activity and change in some of the red blood cell parameters were detected. For the women test group, the propolis treatment did not induce a change in any of the measured parameters.

Šegvić Klarić M¹, Pepeljnjak S¹, Domijan AM³, Petrik J². Lipid Peroxidation and Glutathione Levels in Porcine Kidney PK15 Cells after Individual and Combined Treatment with Fumonisin B₁, Beauvericin and Ochratoxin A. Basic Clin Pharmacol Toxicol 2007;100:157-64.

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Abstract: Individual and combined effects of the mycotoxins fumonisin B₁, beauvericin and ochratoxin A on cell viability, lipid peroxidation (TBARS) and intracellular glutathione (GSH) were studied on porcine kidney epithelial cells (PK15). Cells were treated with 0.05, 0.5 and 5 µg/ml of each mycotoxin or the combinations of two or all three applied in equal concentrations for 24 and 48 hr. Changes in cell viability, GSH and TBARS levels showed that the cytotoxic effects of these mycotoxins were concentration- and time-dependent. After 24 hr, cell viability was significantly decreased by the exposure to 5 µg/ml of fumonisin B₁ (25%), beauvericin (30%) and ochratoxin A (35%), as compared to controls. Only ochratoxin A (5 µg/ml) increased TBARS (56%), with further significant increase (85%) after 48 hr exposure. Fumonisin B₁ and beauvericin significantly increased TBARS (57% and 80%, respectively) only when the highest dose was applied for 48 hr. After 24 hr, GSH was significantly decreased (18%) by ochratoxin A (0.05 µg/ml), whereas fumonisin B₁ and beauvericin significantly decreased GSH at the concentration of 0.5 µg/ml. Combined treatment with fumonisin B₁, beauvericin and ochratoxin A resulted mostly in additive effects especially after a 24-hr exposure, although synergistic as well as antagonistic interactions could not be excluded depending on toxin concentrations and time of exposure. This is the first report on beauvericin-induced effects on lipid peroxidation and GSH in animal cells.

Kovač K¹, Dodig S¹, Tješić-Drinković D², Raos M¹. Correlation between Asthma Severity and Serum IgE in Asthmatic Children Sensitized to *Dermatophagoides pteronyssinus*. Arch Med Res 2007;38:99-105.

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BACKGROUND: We undertook this study to test the possible correlation between serum concentration of total and specific IgE antibodies and asthma severity in asthmatic children sensitized to the house dust mite *Dermatophagoides pteronyssinus*. **METHODS:** The study included 157 asthmatic children aged 5-15 years (8 +/- 3 years). Clinical diagnosis was based on personal and family history, physical examination, pulmonary function testing and skin tests. Asthma severity was determined according to GINA guidelines. *In vitro* tests included serum concentration of total and specific IgE. **RESULTS:** All asthmatic children had elevated serum concentration of total IgE. The children with elevated serum concentration of total IgE also showed an increased serum concentration of specific IgE. Asthma of higher higher severity was present in patients with total IgE concentration >288.0 kIU/L (AUC = 0.736) and specific IgE to *Dermatophagoides pteronyssinus* >44.1 kIU/L (AUC = 0.843). Intermittent asthma was present in 76.9% of children with specific IgE concentration <44.1 kIU/L. The positive predictive value suggested with 79.2% probability that a child with a concentration of specific IgE to *Dermatophagoides pteronyssinus* >44.1 kIU/L would have a more severe form of asthma. **CONCLUSIONS:** Asthmatic children with higher asthma severity have a higher serum concentration of both total IgE (>288.0 kIU/L) and specific IgE to *Dermatophagoides pteronyssinus* (>44.1 kIU/L), respectively.

Rački S¹, Zaputović L², Vujičić B³, Crnčević-Orlić Ž⁴, Dvornik Š⁵, Mavrić Ž². Comparison of survival between diabetic and non-diabetic patients on maintenance hemodialysis: A single-centre experience. Diabetes Res Clin Pract 2007;75:169-75.

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We analyzed survival rates of 144 prevalent patients on maintenance hemodialysis from 1998 to 2003 at the De-

partment of Nephrology and Dialysis, Rijeka University Hospital, Rijeka, Croatia, and evaluated risk factors predicting their survival. Included were only end-stage renal disease (ESRD) patients on maintenance hemodialysis treatment dialysed more than 6 months before entering the study and who were clinically stable. The patients were randomised in two groups according to the presence or absence of diabetic nephropathy as the cause of ESRD and followed-up. The patient's death as outcome measure was recorded. The survival rates were estimated by the Kaplan-Meier method. The major causes of death were cardiovascular disease in 40 (60.6%) patients. An acute myocardial infarction in 15 (22.7%) patients was the major single cause of death. We found a significantly lower survival of diabetic patients than non-diabetic patients ($P=0.0013$). The most important predictors of death among diabetic patients on maintenance hemodialysis were hyperglycaemia ($P<0.001$), ischemic heart disease ($P=0.004$), hypercholesterolemia ($P=0.013$), and low delivered dialysis dose ($P=0.013$). The survival of diabetic patients undergoing hemodialysis was much worse than survival of non-diabetic patients. The cardiovascular disease remained the major cause of death in both groups. Early detection of pre-existing cardiovascular risk factors and diseases, and treatment of infections leading to sepsis, are of great importance, as they may influence the survival rates. Intensive management of diabetic patients is essential.

Domitrović R, Tota M, Milin Č. Oxidative stress in mice: effects of dietary corn oil and iron. Biol Trace Elem Res 2006;113:177-91.

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The aim of this study was to analyze the effect of high dietary Fe on liver antioxidant status in mice fed a corn-oil-enriched diet. Male Balb/c mice were fed for 3 wk with a standard diet enriched with 5% by weight of corn oil with adequate Fe (FCO diet) or supplemented with 1% carbonyl Fe (FCOFe diet). The control group was fed a standard diet. The high-Fe diet induced a twofold increase of hepatic Fe level. However, an increase of thymic Fe level has been induced solely by dietary fat. The hepatic copper (Cu) level slightly decreased in the FCO diet. In the spleen, the high-Fe diet-induced increase of Fe level was negatively correlated with the Cu level. The antioxidant status was influenced by both dietary fat and Fe. Mice fed corn-oil-enriched diets had a higher concentration of thiobarbituric acid-reactive substances (TBARS), with a greater increase in the FCOFe diet. Fatty acid analysis showed decreased n-3 and n-6/n-3 ratio, particularly in the FCO-

Fe diet. Hepatic Cu/Zn superoxide dismutase (CuZn-SOD) activity was decreased in FCO diet, and Fe supplementation caused a further decrease in the enzyme activity. These results suggest that feeding with corn oil-enriched diet increases oxidative damage by decreasing antioxidant enzyme defense. The high-Fe diet additionally affects the antioxidant defense system, further increasing the tissue's susceptibility to lipid peroxidation. Additionally, both corn-oil- and Fe-enriched diets have increased the Cu requirement in mice.

Laškaj R, Slavica D, Čepelak I, Kuzman I. Gamma-Glutamyltransferase Activity and Total Antioxidant Status in Serum and Platelets of Patients with Community-acquired Pneumonia. Arch Med Res 2007;38(4):424-31.

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BACKGROUND: We undertook this study to analyze serum and platelet gamma-glutamyltransferase (GGT) activity and total antioxidant status (TAS) concentration during the course of pneumonia and to compare them between patients with normal platelet count and those who developed reactive thrombocytosis. **METHODS:** Platelet count, GGT activity and TAS concentration in serum (S) and platelet (Plt) isolates were measured in 60 patients with community-acquired pneumonia (CAP) on admission and at discharge. **RESULTS:** At the end of treatment, platelet count increased significantly from the value recorded on admission. By the end of treatment, 42% of patients developed reactive thrombocytosis. Serum and platelet GGT activity was higher, whereas (S)TAS was significantly lower in CAP patients than in control subjects. On admission, (Plt)TAS was significantly higher in CAP patients as compared with control subjects; at discharge, (Plt)TAS was lower in comparison with either patient admission and control subjects. GGT activity and TAS concentration in serum and platelet isolate on admission did not differ significantly between patients with and without thrombocytosis. At discharge, (S)GGT activity showed no significant changes, whereas (Plt)GGT decreased significantly in patients with thrombocytosis as compared with those without thrombocytosis. In patients with thrombocytosis, (S)TAS concentration showed no significant difference, whereas (Plt)TAS concentration measured at discharge was significantly lower in patients with thrombocytosis as compared to those with normal platelet count. **CONCLUSIONS:** The pattern of changes in (Plt)GGT catalytic activity and TAS concentration might be indicative of a certain role of thrombocytosis during treatment in patients with CAP. Further investigations are necessary to clarify these changes.