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**CIP**

**\*Catipovic-Veselica K, Djurijancek J, Bracic-Kalan M, Amidzic V, Mrdjenovic S, Kozmar D, et al. Heart rate and heart-rate variability in patients with acute coronary heart disease classified on Bortner's scale as type A and type B. Psychol Rep 1997;80:775-84.**

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We investigated heart rate and heart-rate variability in 82 patients (60 men and 22 women) with acute coronary heart disease and scores on Bortner's scale at hospital admission and discharge. Patients with acute coronary heart disease classified as Type A (n=48) had a significantly lower mean heart rate than patients classified as Type B during the day of hospital admission and discharge and during the night of hospital discharge. Mean heart rate variability was significantly higher in patients classified as Type A than in the patients classified as Type B during the day of hospital admission and discharge. The patients classified as Type A on Bortner's scale had higher vagal tone and more favorable sympathovagal balance than patients of Type B. The finding may have implications for the treatment of patients with acute coronary heart disease and may suggest some explanation about the protective effect of Type A behavior.

**\*Dumic M, Brkljacic L, Plavsic V, Zunec R, Ille J, Wilson RC, et al. Prenatal diagnosis of congenital adrenal hyperplasia (21-hydroxylase deficiency) in Croatia. Am J Med Genet 1997;72:302-6.**

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We report on the prenatal diagnosis of congenital adrenal hyperplasia due to 21-hydroxylase in 20 at risk pregnancies (16 salt-wasting and 4 simple virilizing families). We diagnosed 3 affected fetuses (2 males and 1 female), 3 healthy homozygotes (2 males and 1 female), and 14 healthy heterozygotes (7 females and 7 males). In 16 fetuses, the diagnosis was made with measurements of 17-hydroxyprogesterone (17-OHP) and delta-4-androstenedione (delta) in amniotic fluid (AF), human leukocyte antigen (HLA) typing of amniotic cells, as well as karyotypes between the 16th and 18th weeks of gestation. In 4 fetuses, DNA analysis of AF cells was also performed. In 3 pregnancies, in which affected fetuses were suspected (HLA typing and 17-OHP and delta in AF), the fetuses were electively aborted between the 17th to 19th weeks of gestation by parental decision. In all aborted fetuses, diagnosis was confirmed with HLA typing, autopsy findings of hyperplastic adrenal glands, and ambiguous genitalia in female fetuses. Postnatal diagnosis was confirmed in healthy fetuses with HLA typing and serum 17-OHP concentrations, and in 4 of them with DNA analysis. In 3 of the 4 families, DNA analyses revealed the following mutations: in family 1, the index case mutation was Intron 2, Exon 3/Exon 6, and the fetus was Normal/Exon 6; in family 2, the index case mutation was Ex1 Int2 Ex3/Int2, and the fetus was Ex1 Int2 Ex3/Normal; and in family 3, the index case mutation was Ex8(356)/Ex8(356), and the fetus was Ex8(356)/Normal.

**\*Demarin V, Rundek T, Hodek B. Maternal cerebral circulation in normal and abnormal pregnancies. Acta Obstet Gynecol Scand 1997;76:619-24.**

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The aim of this study was to evaluate maternal cerebral blood flow velocity (CBFV) changes in normal and abnormal pregnancies, and to correlate CBFV findings with the severity of symptoms in abnormal pregnancies. A group of 40 gravidas with pre-eclampsia were analyzed by Transcranial Doppler (TCD), Color Doppler Flow Imaging of carotid arteries and Transcranial Color Coded System once a week, starting from the 32nd week of pregnancy up to the period of 2 months after the delivery. Some 70% of abnormal pregnancies had impaired TCD findings, mostly increased CBFV. The degree of toxemia measured by Goecke's index significantly correlated with abnormal CBFV. Nine gravidas with increased CBFV on the first examination developed vasospasm during 34 to 36 weeks of gravidity. No statistically significant difference in the M1 segment of MCA diameters was found between normal

( $3.8 \pm 0.7$  mm) and abnormal pregnancies ( $4.1 \pm 0.9$  mm). In conclusion, the increase in the maternal CBFV was the most frequent finding in abnormal pregnancies. The most important observation was that significant changes in CBFV preceded neurological symptoms, emphasizing the predictive role of TCD in abnormal pregnancies.

**\*Kapitanovic S, Radosevic S, Kapitanovic M, Andjelinovic S, Ferencic Z, Tavassoli M, et al. The expression of p185(Her-2/Neu) correlates with the stage of disease and survival in colorectal cancer. Gastroenterology 1997;112: 1103-13.**

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This study was designed to investigate HER-2/neu gene expression in benign and malignant colorectal lesions and to evaluate its prognostic importance in colorectal cancer. Two hundred twenty-one samples of normal colon, benign lesions, and colorectal adenocarcinomas were studied for expression of HER-2/neu oncoprotein. Immunohistochemical staining of formalin-fixed, paraffin-embedded tissue sections of primary tumor and lymph nodes was performed. Immunoprecipitation followed by Western blotting of freshly frozen samples of the same tumors were also performed. Normal colon mucosa, benign lesions, and adenocarcinomas clearly differed in the expression levels and histological distribution of p185(HER-2/neu). Normal mucosa was mostly negative, but significant number of benign lesions and adenocarcinomas overexpressed HER-2/neu protein. Adenocarcinomas were significantly more positive than benign lesions. The results show significant correlation with the epithelial abnormality degree and clinical parameters including Dukes' classification and relapse-free and postoperative survival period. In conclusion, the p185(HER-2/neu) rate expression could serve as an independent prognostic factor in patients with p185(HER-2)/(neu)-positive colorectal malignancies.

**Kubat M, Furac I, Strinovic D, Zecevic D. Short tandem repeat polymorphism at the humcd4 and humf13B loci in a Croatian population. Int J Legal Med 1997;110:230-1.**

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Population studies were carried out on unrelated individuals of Croatian ancestry. Genomic DNA was amplified by the polymerase chain reaction (PCR) at the polymorphic microsatellite loci HUMCD4 ( $n=105$ ) and HUMF13B ( $n=108$ ). After horizontal polyacrylamide gel electrophoresis followed by silver staining, 6 alleles and 12 genotypes were observed for HUMCD4, and 6 alleles and 13 genotypes could be identified for HUMF13B. Data obtained were in concordance with the prediction of Hardy-Weinberg equilibrium. The allele frequency data were compared with Austrian and Italian population samples and no significant deviations between these populations were observed.

**Müller WEG, Romero FJ, \*Perovic S, Pergande G, Pialoglou P. Protection of flupirtine on beta-amyloid-induced apoptosis in neuronal cells in vitro: prevention of amyloid-induced glutathione depletion. J Neurochem 1997;68:2371-7.**

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Cortical neurons from rat embryos were treated with the toxic fragment A beta 25-35 at 1 mM in the presence or absence of flupirtine, triaminopyridine, successfully applied clinically as a nonopioid analgesic drug. Five days later, 1 mM A beta 25-35 caused a reduction in cell viability to 31.1%. Preincubation of cells with flupirtine (1 or 5 mg/mL) resulted in a significant increase in the percentage of viable cells (74.6 and 65.4%, respectively). During incubation with A beta 25-35, the neurons underwent apoptosis as determined by the appearance of the characteristic stepladder-like DNA fragmentation pattern and by the TUNEL technique. A beta 25-35-induced DNA fragmentation could be abolished by preincubation of the cells with 1 mg/mL flupirtine. Incubation with A beta 25-35 reduces the intraneuronal level of GSH from 21.4 to 7.4 nmol/ $10^6$  cells. This depletion could be partially prevented by preincubation of the cells with flupirtine. Thus, flupirtine may be adequate for the treatment of the neuronal loss in Alzheimer's disease (where A-beta accumulates in senile plaques) and probably other neurological diseases such as amyotrophic lateral sclerosis.

**Opelz G, Vanrenterghem Y, Kirste G, Gray DWR, Horsburgh T, Lachance JG, Largiader F, Lange H, \*Vujaklija-Stipanovic K, et al. Prospective evaluation of pretransplant blood transfusions in cadaver kidney recipients. *Transplantation* 1997;63:964-7.**

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A beneficial effect of pretransplant transfusions on graft survival was demonstrated in the early 1970s. In the mid-1980s, however, retrospective studies showed that transfusions had lost their graft-protective effect in the cyclosporine era. During the last 10 years, deliberate transfusion pretreatment of transplant patients has been discontinued. Within a collaborative project of 14 transplant centers, prospective recipients of cadaver kidney grafts were randomized to receive either three pretransplant transfusions or transplants without transfusions. The graft survival rate was significantly higher in the 205 transfusion recipients than in the 218 patients who did not receive transfusions (at 1 year:  $90\pm 2\%$  vs.  $82\pm 3\%$ ,  $p=0.020$ ; at 5 years:  $79\pm 3\%$  vs.  $70\pm 4\%$ ,  $p=0.025$ ). Cox regression analysis showed that this effect was independent of age, gender, underlying disease, prophylaxis with antilymphocyte antibodies, and preformed lymphocytotoxins. In conclusion, transfusion pretreatment improves the outcome of cadaver kidney transplants even with the use of modern immunosuppressive regimens.

**Puljevic D, Smalcelj A, Durakovic Z, Goldner V. QT dispersion, daily variations, QT interval adaptation and late potentials as risk markers for ventricular tachycardia. *Eur Heart J* 1997;18:1343-9.**

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The aim of the study was to determine the value and correlation between QT dispersion, daily variations in the QT interval and late potentials as risk markers for ventricular tachycardia. One hundred and forty-five patients were included in the study 3 months after myocardial infarction. QT dispersion significantly increased with the severity of arrhythmia (modified Lown's classification;  $p<0.001$ ). The level of 80 ms was associated with ventricular tachycardia with a sensitivity of 72.7% and a specificity of 86.4%. The greater daily variability of the QTc interval in patients with ventricular tachycardia was insignificant. QT interval adaptation did not discriminate between patients with ventricular tachycardia and those in other groups. Late potentials were associated with ventricular tachycardia with a sensitivity of 50% and a specificity of 90.3%. In conclusion, large QT dispersion and late potentials were risk markers for ventricular tachycardia, but there was no correlation between QT dispersion, daily variations in the QT interval, and late potentials in patients 3 months after myocardial infarction.

**Rukavina T, Ticac B, \*Susa M, Jendrike N, Jonjic S, Lucin P, et al. Protective effect of antilipopolysaccharide monoclonal antibody in experimental Klebsiella infection. *Infect Immun* 1997;65:1754-60.**

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An O-antigen-specific murine monoclonal antibody (MAb) directed against an immunodominant epitope expressed on Klebsiella O1, O6, and O8 lipopolysaccharides (LPS) was examined with respect to its binding to nonencapsulated and encapsulated bacterial cells and its ability to protect against lethal murine Klebsiella sepsis. In a model of experimental Klebsiella peritonitis and sepsis induced by a virulent O1:K2 serogroup strain, higher doses of anti-LPS MAb Ru-O1 than of a previously described anticapsular MAb specific for the K2 capsular polysaccharide were needed to provide protection. However, high-dose (40 mg/g of body weight) pretreatment with anti-LPS MAb Ru-O1 significantly reduced bacterial dissemination to various organs as well as macroscopic and histologic pulmonary alterations. Thus, since the number of Klebsiella capsular antigens occurring in clinical material is too large to be completely "covered" by a K-antigen-specific hyperimmunoglobulin preparation, O-antigen-specific antibodies may supplement K-antigen-specific immunoprophylaxis and therapy of clinical Klebsiella infection.

**Vuckovic J, Ilic A, \*Knezevic N, Marinkovic M, Zemunik T, Dubravcic M. Prognosis in monoclonal gammopathy of undetermined significance. Br J Haematol 1997;97:649-51.**

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Eighty-seven patients with monoclonal gammopathy of undetermined significance (MGUS) were followed for a period of 1-20 years, median 91 months. Transformation to multiple myeloma occurred in 14 patients of whom 7 died as a consequence of the disease. There were 13 unrelated deaths. The actuarial probability of survival was 80% at 10 years and 44% at 15 years, and the probabilities of malignant conversion for the same periods were 17% and 30%, respectively. The most significant factor influencing the probability of malignant conversion was the increase of monoclonal protein above the level of 30 g/L during the observation period ( $p < 0.001$ ), followed by an increase of M-protein to more than 50% above the baseline level ( $p = 0.02$ ) and a decreased level of uninvolved immunoglobulins ( $p = 0.054$ ).