

Kukura V, Zovko G, Ciglar S, Markulin-Grgić L, Šantek F, Podgajski M, et al. Serum CA-125 tumor marker in endometrial adenocarcinoma. Eur J Gynaecol Oncol 2003;24:151-3.

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One hundred and seventy-four patients, mean age 61.23±9.41 years old, with irregular perimenopausal haemorrhage were included in the study. Fractional curettage was performed in all patients. When the pathohistologic findings were adenocarcinoma the concentration of CA-125 tumor marker was determined. Hysterectomy with bilateral salpingo-oophorectomy was determined. In 142 cases carcinoma was restricted to the uterus and in 32 patients extrauterine metastatic disease was found. In the former group CA-125 was positive in 130 patients with a mean value of 64.12±22.41 U/mL serum. In the latter group the cancer antigen was positive in 29 patients with a mean value of 244.82±68.11 U/mL. High production is associated with increased metastatic potential.

Škrabić V, Zemunik T, Šitum M, Terzić J. Vitamin D receptor polymorphism and susceptibility to type 1 diabetes in the Dalmatian population. Diabetes Res Clin Pract 2003;59:31-5.

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Several studies have found a relationship between polymorphisms of the vitamin D receptor gene (VDR) and development of type 1 diabetes (T1DM). The meaning of this observation remains unclear and its relevance must be checked in different population samples. To examine the association of VDR polymorphisms and susceptibility to T1DM in the Dalmatian population of South Croatia the authors studied 134 individuals with type 1 diabetes and 132 control subjects. VDR genotyping was performed using PCR and BsmI, Apal and TaqI restriction enzymes. Data were analysed using the chi²-test. The genotype combination which conferred strongest susceptibility to T1DM was BBAAAt (p=0.002). Interestingly, the BA haplotype was found to be a risk factor in a German population, the only European population tested thus far. The results indicate that VDR polymorphisms are associated with increased risk of T1DM in the Dalmatian population of South Croatia and warrant further studies.

Turk N, Milas Z, Margaletić J, Starešina V, Slavica A, Riquelme-Sertour N, et al. Molecular characterization of *Leptospira* spp. strains isolated from small rodents in Croatia. Epidemiol Infect 2003;130:159-66.

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The authors report the isolation and characterization of 16 *Leptospira* spp. strains isolated from small rodents captured in 11 different regions of inland Croatia. Large NotI and SgrAI restriction fragment allowed to assign 10 isolates to the serovar

istrica, 5 isolates to the serovar tsaratsovo and 1 isolate to the serovar lora. The phylogenetic analysis conducted from the sequences of the first 330 bp from the 16S rDNA gene revealed that the strains belonged to three different species, *L. borgpetersenii*, *L. kirschneri* and *L. interrogans*. Carrier rates in eight rodent species varied from 0 to 71.4%. *Mus musculus* showed the highest infection level and confirmed its role as a major reservoir of the serogroup Sejroe. For the first time we reported the occurrence of serovars tsaratsovo and lora in Croatia.

Zoričić S, Marić I, Bobinac D, Vukičević S. Expression of bone morphogenetic proteins and cartilage-derived morphogenetic proteins during osteophyte formation in humans. J Anat 2003;202(Pt 3):269-77.

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The authors used immunohistochemical methods to investigate the distribution of bone morphogenetic protein (BMP)-2, -3, -5, -6, -7, and cartilage-derived morphogenetic protein (CDMP)-1, -2, -3 in human osteophytes (abnormal bony outgrowths) isolated from osteoarthritic hip and knee joints from patients undergoing total joint replacement surgery. All osteophytes consisted of three different areas of active bone formation: 1) endochondral bone formation within cartilage residues; 2) intramembranous bone formation within the fibrous tissue cover and 3) bone formation within bone marrow spaces. The immunohistochemistry of certain BMPs and CDMPs in each of these three different bone formation sites was determined. The results indicate that each BMP has a distinct pattern of distribution. Immunoreactivity for BMP-2 was observed in fibrous tissue matrix as well as in osteoblasts; BMP-3 was mainly present in osteoblasts; BMP-6 was restricted to young osteocytes and bone matrix; BMP-7 was observed in hypertrophic chondrocytes, osteoblasts and young osteocytes of both endochondral and intramembranous bone formation sites. CDMP-1, -2 and -3 were strongly expressed in all cartilage cells. Surprisingly, BMP-3 and -6 were found in osteoclasts at the sites of bone resorption. Since a similar distribution pattern of bone morphogenetic proteins was observed during embryonal bone development, it is suggested that osteophyte formation is regulated by the same molecular mechanism as normal bone during embryogenesis.

Ćorović N, Duraković Z, Mišigoj-Duraković M. Dispersion of the corrected QT interval in the electrocardiogram of the ex-prisoners of war. Int J Cardiol 2003;88:279-83.

Institute for Medical Research and Occupational Health, Zagreb, Croatia

The study of electrocardiograms (ECGs) was performed in a subgroup of 181 men, ex-prisoners of war with mean age 35.8±11.0 years and mean duration of imprisonment 164.5±87.1 days, chosen at random from the total sample of released prisoners (n=1458). The control group was pair-matched. The analysis of ECGs was done according to the Minnesota code, and Bazett's formula gave the values of the corrected QT interval (QT(c)). The dispersion of the QT(c) interval is determined

by the difference between the longest and the shortest measured QT(c) interval in each ECG lead. The results of descriptive statistics in the group of ex-prisoners showed the range of QT(c) dispersion of 8.0-122.0 ms (mean 52.4±21.6 ms), while in the control group the range was 6.0-72.0 ms (mean 30.4±13.8 ms) (df=360, t=11.536; p<0.001). The QT(c) interval from 422.0 to 480.0 ms had 60.2% ex-prisoners and 30.4% controls, while a QT(c) interval over 480.0 ms had 19.3% ex-prisoners and 1.10% controls (p<0.0001). In the ex-prisoners group, the QT(c) dispersion over 50 ms was present in 51.4%; of those, a dispersion of 95 ms and more was found in 3.9%, while in the controls a QT(c) dispersion over 50 ms was found in 8.3%, but a dispersion of 95 ms and more was not recorded (p<0.0001). The odds ratio estimated for the prolonged QT(c) interval was 8.467 and for enlarged QT(c) dispersion it was 11.695 in the ex-prisoners versus controls (p<0.001). In conclusion, persons exposed to long-term maltreatment in detention camps have significantly greater QT(c) dispersion, as well as a higher relative risk of prolonged QT(c) interval and greater QT(c) dispersion than a control group.

Mustajbegović J, Žuškin E, Schachter EN, Kern J, Luburić-Milas M, Pucarin J. Respiratory findings in tobacco workers. Chest 2003;123:1740-8.

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The aim of this study was to screen for respiratory symptoms and lung function impairment in workers occupationally exposed to tobacco dust in a tobacco-processing plant. One hundred twenty-one tobacco workers (97 women and 24 men) were included in the study. In addition, a group of 98 control workers (73 women and 25 men) were studied. Acute and chronic respiratory symptoms were recorded in all tobacco workers. Lung function was measured by recording the maximum expiratory flow-volume curves on which FVC, FEV₁, and flow rates at 50% of FVC (FEF₅₀) and the last 25% of FVC (FEF₂₅) were read. There was a high prevalence of chronic respiratory symptoms among these workers, and this prevalence was significantly higher in exposed female workers than in female or male control workers (p<0.01 and p<0.05, respectively). Occupational asthma was recorded in 6 female tobacco workers (6.2%) and in none of the control subjects (p<0.05). None of the male workers were found to have occupational asthma. There was also a high prevalence of acute symptoms that were noted during the work shift. Among these tobacco workers, the odds ratios for respiratory symptoms were frequently significant for employment and smoking among male tobacco workers but were not significant in general for female tobacco workers. The ventilatory capacity data in tobacco workers showed statistically significant reductions in FEV₁, FEF₅₀ and FEF₂₅ in relation to predicted values. These reductions were demonstrated in smokers as well as in nonsmokers. Regression analysis suggested that there were significant changes according to employment status for FVC, FEV₁, and FEF₂₅ in female tobacco workers. Measurements of ventilatory capacity during the course of the work shift in 38 female tobacco workers demonstrated significant mean acute reductions in FEV₁ (-5.7%), in FEF₅₀ (-15.7%), and in FEF₂₅ (-23.4%). These data indicate that tobacco workers may develop respiratory disorders related to tobacco dust in their work environment.

Krmpotić-Nemanić J, Vinter I, Kelović Z, Suknaić S. The neglected maxillary process of the palatine bone. Ann Anat 2003;185:53-6.

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In most recent anatomy textbooks as well as in the latest anatomical nomenclature, the maxillary process of the palatine bone is not mentioned at all. The maxillary process is, however with rare exceptions, always present as an important part of the closure of the hiatus sinus maxillaris. In our material consisting of 200 disarticulated, macerated skull bones and 25 specimens of maxillary sinus, the maxillary process was missing in only 5 cases (2.2%). This process develops in the second year of life

and displays different shapes. It can be long and slender or wide and round shaped. Its upper margin is more or less concave, corresponding to the margin of the hiatus over which it is bent. Its inferior margin can be smooth or irregular. In instances in which maxillary sinus is double, the os palatinum has two maxillary processes, so that both sinuses are partly closed with the maxillary process of the palatine bone.

Balog T, Marotti T, Šverko V, Marotti M, Krolo I, Ročić B, et al. Enkephalin degrading enzymes in pheochromocytoma patients. Oncol Rep 2003;10:253-8.

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It has been demonstrated that pheochromocytoma of the adrenal gland might be associated with altered concentration of enkephalin-like peptides. The effect of these peptides can be either prolonged or abbreviated by two neutrophil membrane bound enzymes; aminopeptidase N (APN) and neutral endopeptidase (NEP). The authors assumed that altered enkephalin level in pheochromocytoma patients (but not in patients with non-functional adenomas or tumors of different origin) might result in differently regulated APN and/or NEP activity. They measured APN and NEP activity on surface of neutrophils, level of lipid peroxidation (LPO) in plasma and enkephalin concentration in plasma in patients with pheochromocytomas, non-functional adenomas, malignant renal tumors and healthy controls. Catecholamines and vanillylmandelic acid (VMA) were measured in 24-h urine of pheochromocytoma patients. NEP and APN activity on neutrophils from all pheochromocytoma patients was significantly increased as compared with healthy controls, non-functional adenomas and malignant renal tumors. In all pheochromocytoma patients NEP activity was reduced almost to the control level after surgery. At the same time APN activity was in some patients up- and in others down-regulated. In comparison, elevated levels of catecholamines and VMA were found after multiple determinations in 6 out of 10 pheochromocytoma patients. Although preliminary, this study has shown specifically and consistently up-regulated NEP activity on neutrophils from pheochromocytoma patients, and uniformly decreased NEP activity in these patients after adrenalectomy.

Branović K, Forčić D, Ivančić J, Strancar A, Barut M, Košutić-Gulija T, et al. Application of short monolithic columns for improved detection of viruses. J Virol Methods 2003;110:163-71.

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Monolithic chromatography media represent a novel generation of stationary phases introduced in the last 10-15 years providing a chromatography matrix with enhanced mass transfer and hydrodynamic properties. These features allow for an efficient and fast separation of especially large biomolecules like e.g., DNA and viruses. In this study, the enrichment of virus RNA on short monolithic columns prior to molecular detection of viruses is described. Measles and mumps viruses were chosen as model viruses. The results show that it is possible to bind viral RNA on monoliths and concentrate viral nucleic acids from a fairly dilute sample. Consequently, a potential application of short monolithic columns is the concentration of virus RNA to improve the sensitivity and selectivity of viral detection with the possibility of isolating viral RNA from cell-free biological fluids.

Korbler T, Gršković M, Dominis M, Antica M. A simple method for RNA isolation from formalin-fixed and paraffin-embedded lymphatic tissues. Exp Mol Pathol 2003;74:336-40.

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Gene activation that lies beneath lymphoid cell differentiation has been one of the most explored issues in immunology in the recent years. However, the analysis of this molecular event in

lymphoproliferative diseases is often hampered by the lack of fresh material. Most tissues available for routine histological investigation are formalin fixed and paraffin embedded. Gene expression in such specimens could be analyzed using reverse transcription of mRNA and the polymerase chain reaction (RT-PCR). The authors adjusted and established a method for mRNA isolation from such specimens by a combination of previously reported protocols and a modification of the phenol/chloroform extraction method. Given the significance of transcription factors in the human hemopoietic system, the authors investigated whether mRNA could be successfully isolated from archival tissue for a study on expression of Ikaros family transcription factors in lymphatic tissue. Although quantitative analysis of RNA isolated from archival tissue is probably not feasible due to the unpredictable degree of RNA isolation varying from sample to sample, the authors show that screening analysis is possible and simple.

Milović F, Uravić M, Raguž K, Depolo A, Rahelić V, Bačić G, et al. Penetrating liver war injury: a report on 172 cases. *Mil Med* 2003;168:419-21.

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During the 4-year military conflict in Croatia, the authors treated operatively 7,928 casualties. Of those casualties, 172 (2.2%) had penetrating liver injury, mostly sustained by explosive devices. Of these injuries, 90.7% were associated with the trauma of other abdominal and extra-abdominal organs. Seventy-five percent of injuries belonged to grades III and IV on the Liver Injury Scale. The main method of treatment was debridement with ligation of severed vessels and bile ducts. In 8.1% of cases with detrimental bleeding, the authors used liver packing. Fifty percent of these patients have survived but with a high incidence of septic complications. This method was proven salutary in the most detrimental injuries that could not be treated in any other way. Postoperative hemorrhage and intra-abdominal abscesses were complications that needed surgical and ultrasound-guided aspiration, respectively. Numerous heavy injuries of the liver combined with associated trauma of other vital organs are responsible for the high mortality rate of 28.5%.

Šlaus M, Strinović D, Škavić J, Petrovečki V. Discriminant function sexing of fragmentary and complete femora: standards for contemporary Croatia. *J Forensic Sci* 2003;48:509-12.

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Determining sex is one of the first and most important steps in identifying decomposed corpses or skeletal remains. Previous studies have demonstrated that populations differ from each other in size and proportion and that these differences can affect metric assessment of sex. This paper establishes standards for determining sex from fragmentary and complete femurs in a modern Croatian population. The sample is composed of 195 femora (104 male and 91 female) from positively identified victims of the 1991 War in Croatia. Six discriminant functions were generated, one using seven variables, three using two variables, and two employing one variable. Results show that complete femora can be sexed with 94.4% accuracy. The same overall accuracy, with slight differences in male/female accuracy, was achieved using a combination of two variables defining the epiphyses, and with the variable maximum diameter of the femoral head.

Jakovljević M, Sagud M, Mihaljević-Peješ A. Olanzapine in the treatment-resistant, combat-related PTSD – a series of case reports. *Acta Psychiatr Scand* 2003;107:394-6.

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Nightmares and insomnia in combat-related post-traumatic stress disorder (PTSD) might be resistant to treatment with selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines. The authors describe five case reports of patients suffering from long-lasting and intractable nightmares and insomnia. They were given different psychotropic agents in past few years, with no improvement in their sleep disturbance. Olanzapine was added to the current treatment regimen. Both nightmares and insomnia improved rapidly after olanzapine institution in all of five patients. No adverse events of olanzapine were reported. In conclusion, olanzapine augmentation might be useful in alleviating treatment-resistant nightmares and insomnia in patients with combat-related PTSD.

Škrobonja A, Muzur A, Škrobonja A Jr. Two examples of reimplantation from Croatian sacral patrimony. *Ann Plast Surg* 2003;50:412-5.

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In the current article, two paintings related to the topic of reimplantation from Croatian sacral patrimony are presented. The first one is "The Kiss of Judas," the fresco by Vincent of Kastav (1474) in Beram in Istria – a Gospel scene with Jesus performing reimplantation of the ear to Malchus after it was cut off by Apostle Peter. The second one is an old oil on canvas from the island of Rab, presenting St. Anthony of Padua performing reimplantation of a boy's amputated foot. Although in both cases the primary function of the painting is to convey a moral message, they are interesting from the medical-historical point of view for their view of universal popular imagination and the conception of healing severe wounds during the absence of modern medical knowledge.

Halassy B, Krstanović M, Frkanec R, Tomašić J. Adjuvant activity of peptidoglycan monomer and its metabolic products. *Vaccine* 2003;21:971-6.

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Peptidoglycan monomer (PGM) is a natural compound of bacterial origin. It is a non-toxic, non-pyrogenic, water-soluble immunostimulator potentiating humoral immune response to ovalbumin (OVA) in mice. It is fast degraded and its metabolic products – the pentapeptide (PP) and the disaccharide (DS) – are excreted from the mammalian organism upon parenteral administration. The present study investigates: a) whether PGM could influence the long-living memory generation; and b) whether metabolic products retain adjuvant properties of the parent compound and contribute to its adjuvanticity. The authors report that mice immunised twice with OVA + PGM had significantly higher anti-OVA IgG levels upon challenge with antigen alone 6 months later in comparison to control group immunised with OVA only. PP and DS were prepared enzymatically in vitro as apyrogenic and chemically pure compounds. When mice were immunised with OVA plus PP and DS, respectively, the level of anti-OVA IgGs in sera was not higher than in mice immunised with OVA alone, while PGM raised the level of specific antibodies. Results implicate that the adjuvant active molecule, capable of enhancing long-living memory generation, is PGM itself, and none of its metabolic products.