

Croatian International Publications

> Croat Med J. 2008;49:288-90

Grazio S, Babić-Naglić D, Kehler T, Čurković B.
Persistence of weekly alendronate: a real-world study in Croatia. Clin Rheumatol. 2008;27:651-3.

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The aim of this study was to assess real-world persistence (long-term adherence) with weekly alendronate. Persistence data were collected according to World Health Organization criteria for the prior month and year for 102 consecutive patients with osteoporosis at three outpatient clinics in Croatia. Persistence was assessed using medication possession ratios (MPR). Adequate persistence was defined as sufficient medication supply to ensure anti-fracture efficacy (MPR \geq 80%). Self-reported persistence data were compared with resupply prescription data from primary care physicians (PCPs). The effect of patient age, co-therapy, co-morbidity, and time since osteoporosis was diagnosed were evaluated. A diagnosis of osteoporosis was established 3.21 ± 1.83 years prior for the 96 women and six men enrolled (mean age 66.92 ± 8.05 years). During the previous year, 86.3% patients reported not missing any tablets. Age correlated with the number of missed tablets, with older patients missing more tablets ($p=0.038$). Patients with co-therapy ($p=0.042$) missed more tablets. PCPs reported that 65.7% of the patients were issued prescriptions for 52 tablets. A total of 68.7% had MPR $>$ 80%. Patients with rheumatoid arthritis did not impact MPR ($p=0.936$). Previous fractures or number of fractures were not associated with persistence ($p>0.05$). In Croatia, persistence was superior with weekly-administered alendronate than has been reported elsewhere, perhaps due to socio-cultural factors. Larger, longitudinal studies are needed to confirm these results.

Jonjić S, Krmpotić A, Arapović J, Koszinowski UH.
Dissection of the antiviral NK Cell response by MCMV mutants. Methods Mol Biol. 2008;415:127-49.

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Our understanding of virus control by natural killer (NK) cells relies mainly on in vitro observations. The significance of these findings for virus control in vivo is not yet fully understood. Complexity is added by the fact that many viruses, particularly herpesviruses, are equipped with sets of genes that, dependent on the genetic background of the host, modify the NK cell response. The advent of recombinant DNA technology and mutagenesis procedures for BAC-cloned viral genomes has made it possible not only to screen for viral proteins with such functions but also to assess their biological relevance. Mutant viruses with gene defects reveal the efficacy and complexity of NK cell control. Here, the authors describe procedures to assess the NK cell response to mouse cytomegalovirus (MCMV), a prominent virus model for studying NK cell functions in vivo.

Mlinarić-Galinović G, Welliver RC, Vilibić-Čavlek T, Ljubić-Sternak S, Draženović V, Galinović I, et al.
The biennial cycle of respiratory syncytial virus outbreaks in Croatia. Virol J. 2008;5:18.

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The paper analyses the epidemic pattern of respiratory syncytial virus (RSV) outbreaks in children in Croatia. Over a period of 11 consecutive winter seasons (1994-2005) 3,435 inpatients from Zagreb County aged from infancy to 10 years who were hospitalised with acute respiratory tract in-

fections were tested for RSV-infection. RSV was identified in nasopharyngeal secretions of patients by virus isolation in cell culture and by detection of viral antigen with monoclonal antibodies. In the Zagreb area, RSV outbreaks were proven to vary in a two-year cycle, which was repeated every 23-25 months. This biennial cycle comprised one larger and one smaller season. Climate factors correlated significantly with the number of RSV cases identified only in the large seasons, which suggests that the biennial cycle is likely to continue regardless of meteorological conditions. Knowledge of this biennial pattern should be useful in predicting the onset of RSV outbreaks in Croatia, and would facilitate planning for the prevention and control of RSV infections in the region.

Čurić J, Vukelić-Marković M, Marušić P, Hrkač-Pustahija A, Brkljačić B. Influence of bladder distension on opacification of urinary collecting system during CT urography. Eur Radiol. 2008;18:1065-70.

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The purpose of the study was to evaluate and compare opacification of the renal collecting system and ureters detected by computed tomographic urography (CTU) performed 20 min and 1 h after the ingestion of 1,000 mL of water. CTU was performed on 89 patients (55 men, 34 women; age 28-77 years) and 168 collecting systems and ureters were evaluated. A 16-detector-row scanner (Sensation 16, Siemens) was used; a two-phase protocol with a split bolus of contrast agent (total 120 mL) was applied. A combined nephrographic-excretory phase was obtained 100 s after the second injection. Three-dimensional reconstructions of the excretory phase were created and used to evaluate the degree of opacification of the collecting system and ureters. In 44 patients, water was administered 20 min before examination, and in 45 patients, 1 h before examination. CTU performed 1 h after water ingestion demonstrated complete opacification of calices in 87.5%, of renal pelvis in 97.5%, of upper ureter in 91.8% and of lower ureter in 87.5% of patients. CTU performed 20 min after water ingestion demonstrated complete opacification of calices in 79.5%, of renal pelvis in 85%, of upper ureter in 62.5% and of lower ureter in 54.5% of patients. Complete opacification of the proximal and distal ureter in the group with a 1-h delay was statistically higher ($P < 0.01$). CTU performed on the distended bladder, 1 h after the oral ingestion of water, enables excellent opacification of collecting system, including distal ureters.

Mladina R, Čujić E, Šubarić M, Vuković K. Nasal septal deformities in ear, nose, and throat patients: an international study. Am J Otolaryngol. 2008;29:75-82.

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The purpose of this study was to investigate the incidence and characteristics of nasal septum deformities in ear, nose, and throat (ENT) patients in various geographic regions in the world. Anterior rhinoscopy without nasal decongestion was performed in 17 ENT centers in 14 countries. The septal deformities were classified according to the classification system proposed by Mladina. A total of 2589 adult ENT patients (1500 males and 1089 females) were examined. Septal deformities were found in 89.2% of subjects. Left-sided deformities were slightly more prevalent than right-sided deformities (51.6% and 48.4%, respectively). The most frequent type of deformity was type 3 (20.4%). Straight septum was found in 15.4% of females and 7.5% of males. Almost 90% of the subjects showed 1 of the 7 types of septal deformity. There were no statistically significant differences in the incidence of their appearance among particular geographic regions. Type 3 was the most frequent type. Straight septum was twice as frequent in females than in males.

Pezer Z, Ugarković D. Role of non-coding RNA and heterochromatin in aneuploidy and cancer. Semin Cancer Biol. 2008;18:123-30.

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Abnormal chromosome content known as aneuploidy is the most common characteristic of human solid tumours. The molecular roots of aneuploidy lie in defective centromere/kinetochore assembly and function leading to improper chromosome segregation. These defects can be caused by mutations and/or by altered expression of diverse kinetochore proteins. In addition to proteins, non-coding RNA deriving from centromeric repeats plays an active role, mostly through the RNAi pathway, in the formation of pericentromeric and centromeric heterochromatin, both of them important for proper centromere function. The authors propose that stoichiometric expression of major kinetochore components such as non-coding centromeric RNA and proteins is crucial for centromere/kinetochore assembly and function. Slight changes in expression of non-coding RNA or mutations in the RNA metabolic pathways induce chromosome instability, mis-segregation and aneuploidy, facilitating finally tumourigenesis.

Štefanić M, Papić S, Suver M, Glavaš-Obrovac L, Karner I. Association of vitamin D receptor gene 3'-variants with Hashimoto's thyroiditis in the Croatian population. *Int J Immunogenet.* 2008;35:125-31.

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With respect to the biological function of the vitamin D receptor (VDR) and functionally plausible gene-expression data, the authors sought to test whether particular 3'-restriction fragment length polymorphisms (RFLP) and haplotypes previously directly or indirectly associated with VDR mRNA 3'-allelic imbalance phenotype and differences in total VDR mRNA expression are implicated in Hashimoto's thyroiditis (HT) susceptibility. Thus, 145 Croatian HT patients and 145 age-, sex- and ethnically matched euthyroid controls were genotyped for VDR rs1544410 (BsmI), rs7975232 (ApaI) and rs731236 (TaqI) polymorphisms by polymerase chain reaction-RFLP method. Covariate-adjusted single-locus and haplotype-phenotype regression analyses were performed. Permutation corrections [P(c)] and Akaike Information Criteria were used for model comparisons. The best-fit [global P(c)=7.2x10⁻⁴] BsmI-TaqI BT haplotype was found significantly more often in subjects without HT [12.2% vs. 3.7%; odds ratio (OR, 95% confidence intervals) = 0.28 (0.14-0.56), P(c)=8x10⁻⁴], whereas the bT haplotype was significantly more frequent in individuals with HT [45.7% vs. 61.8%; OR=1.91 (1.37-2.65), P(c)=4x10⁻⁴]. Two extended BsmI-ApaI-TaqI RFLP haplotypes, the common baT [35.7 vs. 47.3%, OR=1.63 (1.17-2.27), P(c)=0.012] and rare BaT variants [6.5 vs. 1.2%, OR=0.17 (0.06-0.55), P(c)=1.2x10⁻³] were associated with HT, representing predisposing and protective haplotypes, respectively. In single-RFLP association analyses, only rs1544410 polymorphism was associated with HT phenotype (allelic P(c)=0.0078) and appeared to function under the recessive model, with decreased risk of HT among the BB homozygotes [OR=0.39 (0.21-0.7), P(c)=0.0052] when compared to the reference

b(+)-genotypes. These data suggest that common haplotypic variants within the VDR gene 3'-region previously linked to VDR mRNA expression and allelic imbalance could be associated with HT in the general population, and thus, may be involved in the pathogenesis of HT.

Čičin-Šain L, Matošić A, Mokrović G, Balija M, Marušić S, Jernej B. Platelet monoamine oxidase kinetics, alcoholism subtypes and cigarette smoking. *Neuropsychobiology.* 2007;56:138-45.

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In trying to dissociate the effect of alcohol and tobacco use on platelet monoamine oxidase-B (MAO-B) activity, the authors compared the enzyme kinetics in controls (n = 66) and alcohol-dependent patients (n = 81), subdivided according to the severity of both, alcohol and tobacco use. Platelet MAO-B kinetics was measured spectrophotofluorimetrically in chronic alcohol intoxication and after 3 weeks abstinence. In alcoholic patients, an increased Michaelis-Menten constant (16%, p < 0.01) was shown, notwithstanding smoking status. Maximal velocity did not differ between patients and controls when adjusted for smoking. In cigarette smokers, a highly significant dose-dependent reduction of platelet MAO velocity (40%, p < 0.001) was demonstrated, with a similar degree of reduction in patients and controls. Tobacco use itself had no influence on MAO affinity. No differences were shown between subtype 1 and 2 alcoholics, or between the day of admission and the 21st day of abstinence. In conclusion, it seems that both, alcohol and tobacco consumption, may contribute to the lowering of overall platelet MAO-B activity. The effect of alcohol is small, due to interference with substrate binding, and not alteration of catalytic activity. In contrast, the effect of cigarette smoking is pronounced and relates to the dose-dependent reduction of platelet MAO velocity, with no influence on its affinity.