

1. Bresnihan B, Alvaro-Gracia JM, Cobby M, Doherty M, \*Domljan Z, Emery P, et al. Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. *Arthritis Rheum* 1998;41:2196-204.

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The aim of the study was to evaluate the efficacy and safety of interleukin-1 receptor antagonist (IL-1Ra) in patients with rheumatoid arthritis (RA). Patients with active and severe RA (disease duration <8 years) were recruited into a 24-week, double-blind, randomized, placebo-controlled, multicenter study. Doses of nonsteroidal antiinflammatory drugs and/or oral corticosteroids remained constant throughout the study. Any disease-modifying antirheumatic drugs were discontinued at least 6 weeks prior to enrollment. Patients were randomized to 1 of 4 treatment groups: placebo or a single, self-administered subcutaneous injection of IL-1Ra at a daily dose of 30 mg, 75 mg, or 150 mg. A total of 472 patients were recruited. At 24 weeks, of the patients who received 150 mg/day IL-1Ra, 43% met the American College of Rheumatology criteria for response, 44% met the Paulus criteria, and statistically significant improvements were seen in the number of swollen joints, number of tender joints, investigator's assessment of disease activity, patient's assessment of disease activity, pain score on a visual analog scale, duration of morning stiffness, Health Assessment Questionnaire score, C-reactive protein level, and erythrocyte sedimentation rate. IL-1Ra was well tolerated and no serious adverse events were observed. This study confirmed both the efficacy and the safety of IL-1Ra in a large cohort of patients with active and severe RA. IL-1Ra is the first biologic agent to demonstrate a beneficial effect on the rate of joint erosion.
2. Èèùk-Jelièæ E, Grubiæ Z, Žunec R, Labar B, Kerhin-Brkljaèæ V, Kaštelan A. Implication of molecular analysis of HLA-A\*02 subtyping for unrelated bone-marrow donor selection. *Bone Marrow Transplant* 1998;22 Suppl 4:S27-30.

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The HLA-A\*02 allele is the most heterogeneous allele at HLA-A locus with 22 different subtypes so far identified. All of these subtype polymorphisms are located in alpha 1 and alpha 2 domains which are responsible for peptide binding and HLA restricted recognition by T-cell receptor. The aim of the present study was to determine the frequency of different HLA-A\*02 alleles in 33 healthy unrelated Croatians. HLA-A\*02 subtyping has also been retrospectively performed in 2 recipient-unrelated donor pairs and in 4 recipient-HLA phenotypically identical parent pairs. All subjects, previously typed as HLA-A2 by serology were tested using HLA-A\*02 ARMS-PCR kit which discriminates 17 different A\*02 alleles. Among 17 A\*02 alleles we have found 4 different A\*02 subtypes in healthy unrelated Croatians. The most frequent A\*02 allele was A\*0201 (84%). The frequency of the remaining A\*02 alleles were as follows: A\*0205 (3%), A\*0207 (6%) and A\*0213 (6%). Among 6 tested bone-marrow transplantation (BMT) pairs, only one has been found to be A\*02 subtype incompatible (A\*0201/A\*0205). Four different A\*02 alleles are found in Croatian population with the predominance of A\*0201. However these results suggest that A\*02 subtyping is also necessary for optimal matching of HLA-A\*02 positive donor-recipient pairs in HLA incompatible BMT.
3. Ivandiæ A, Prpiæ-Križevac I, Jakiaè M, Baèun T. Changes in sex hormones during an oral glucose tolerance test in healthy premenopausal women. *Fertil Steril* 1999;71:268-73.

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The objective was to assess the effect of an acute elevation in circulating insulin on serum androgen levels in healthy obese women with different body-fat distributions. Seventy healthy premenopausal women participated: 27 women with upper-body obesity, 22 women with lower-body obesity, and 21 normal-weight women as controls. A 75-g oral glucose tolerance test (OGTT) was performed for all participants. Anthropometry and serum concentrations of glucose, insulin, free T, DHEAS, androstenedione, E2, and sex hormone-binding globulin (SHBG) at fasting, 60 minutes, and 120 minutes after oral glucose loading were investigated. Although androgens and E2 levels in all three groups declined modestly, there were no statistically significant differences in response of the sex hormones to an OGTT in the two obese groups and normal-weight women. No correlation was found between changes in sex-

hormone levels during an OGTT and insulin rise. Increased body mass index and more pronounced abdominal fat localization resulted in basal hyperinsulinemia, markedly exaggerated glucose-induced insulin levels, and hyperandrogenism, as was evident by significantly elevated free T and low SHBG serum levels. There were no statistically significant differences in androgen response to acute hyperinsulinemia during an OGTT between obese women with different regional fat distributions and lean controls.

4. Mahovliæ V, Audy-Jurkoviæ S, Ovanin-Rakiæ A, Bilušiæ M, Veldiæ M, Babiæ D, et al. Digital image analysis of silver-stained nucleolar organizer region-associated proteins in endometrial cytologic samples. *Anal Quant Cytol Histol* 1999;21:47-53.  
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Digital image analysis was applied to determine the number, area and size of silver-stained nucleolar organizer regions (AgNORs) in cytologic samples from curettage in normal, hyperplastic and malignant endometrium. Thirty-two archival cytologic smears from curettage (previously stained by the Papanicolaou method) with the histologic diagnosis (4 inactive endometrium, 5 secretion, 5 proliferation, 5 simple hyperplasia, 5 complex hyperplasia, 3 atypical hyperplasia, 5 adenocarcinoma, grade 1) were analyzed with the AgNOR technique. Quantitative analysis was performed on an SFORM digital imaging system. The average value of AgNOR count increased from normal to hyperplastic endometrium and well-differentiated adenocarcinoma. Differences were significant except between atypical hyperplasia and adenocarcinoma. Four, five and more AgNORs in 40% or more of the nuclei were found in complex and atypical hyperplasia and adenocarcinoma. Proliferation, and simple and atypical hyperplasia had similar mean values of AgNOR area. The mean total AgNOR area value increased from normal to hyperplastic and well-differentiated adenocarcinoma. Differences were statistically significant. AgNOR size in well-differentiated adenocarcinoma was significantly different from that in normal endometrium and different grades of hyperplasia. In conclusion, digital image analysis of AgNOR count, area and size enabled a distinction to be made between normal, hyperplastic and malignant endometrium.
5. Miriæ D, Fabijaniæ D, Giunio L, Eteroviæ D, Æuliæ V, Božiæ I, et al. Dermatological indicators of coronary risk: a case-control study. *Int J Cardiol* 1998;67:251-5.  
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We examined the association of dermatological signs such as baldness, thoracic hairiness, hair greying and diagonal earlobe crease with the risk of myocardial infarction in men under the age of 60 years. A hospital-based, case-control study included 842 men admitted for the first non-fatal myocardial infarction, the controls were 712 men admitted with noncardiac diagnoses, without clinical signs of coronary disease. The relative risks were estimated as odds ratios. Logistic regression was used to control for the confounding variables. After allowing for age and other established coronary risk factors, the relative risk of myocardial infarction for fronto-parietal baldness compared with no hair loss was 1.77 (95% CI 1.27-2.45) and it was 1.83 (95 CI 1.4-2.3) for men with thick, extended thoracic hairiness. The presence of a diagonal earlobe crease yielded a relative risk of 1.37 (95% CI 1.25-1.5), while hair greying was associated with myocardial infarction only in men under the age of 50 years. It appears that baldness, thoracic hairiness and diagonal earlobe crease indicate an additional risk of myocardial infarction in men under the age of 60 years, independently of age and other established coronary risk factors.
6. Muiæ V, Ljubièiæ M, Vodopija I. Bayes' theorem-based assessment of VDRL syphilis screening miss rates. *Sex Transm Dis* 1999;26:12-6.  
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Interlaboratory differences in syphilis screening strategies (serial versus parallel test combinations) prompted us to determine an estimate of the diagnostic miss rate in the detection of (1) infected persons and (2) infected but untreated persons potentially affected by late active syphilis. We set out to establish the most efficient syphilis screening strategy for two routine tests (VDRL and *Treponema pallidum* hemagglutination assay [TPHA]) with regard to our tested public health population. Retrospective analysis covered the results of a routine parallel VDRL and TPHA testing on 24,863 persons done in four public health laboratories. Nosologic sensitivity of the VDRL test (18.32%) was determined using the TPHA test as reference. The percentage of VDRL nonreactors among infected persons (TPHA reactors) was considered as the VDRL false negative rate (81.68%). We estimated the proportion of persons infected but untreated with potential late active syphilis using our own Bayes theorem-based procedure. The Bayes theorem-based estimate showed a significantly

higher value for persons at risk of active late syphilis than the number of suspected cases obtained using the classical approach (25.1% versus 18.32%, or 83 persons versus 61 of the 330 infected). In screening an older population, the VDRL test alone (or as the first of a series with TPHA as a confirmation test) may produce a diagnostic miss rate higher than the syphilis detection rate. Another miss in such a population is detected by the Bayes theorem-based method.

7. Pavloviæ M, Simiæ D, Krstiæ-Buriæ M, Èoroviæ N, Živkoviæ D, Rožman A, et al. Wartime migration and the incidence of tuberculosis in the Zagreb region, Croatia. *Eur Respir J* 1998;12:1380-3.  
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The objective of the present study was to investigate the rate of decline in the incidence of tuberculosis (TB) in residents (1985-1994) and in refugees and displaced persons (1992-1994) during prewar and war periods (1985-1994) in the region of Zagreb, Croatia, and to examine a possible change in the trend of decline in the resident population. Data on the incidence of TB were obtained from the Epidemiology Department, Institute for Lung Diseases, Zagreb, Croatia. The sample comprised two groups of subjects: residents (800,000-1,000,000 inhabitants) and all refugees and displaced persons temporarily residing in the Zagreb region (78,000-95,000 persons). Data were analysed by stepwise logistic regression. The most significant predictors of the TB incidence rate were the square of the year and residence status. The rate of TB incidence in nonresidents was significantly higher than in residents. The decline in incidence in residents was significantly slower than in the nonresident group. The results did not indicate a potential change in the natural decline of the incidence of tuberculosis in the resident population during the study periods. The difference between the regression trends of the incidence of tuberculosis in residents and nonresidents was the result of various concomitant factors, including artefacts of the war.
8. Poljak M, Brenèiæ A, Seme K, \*Vince A, Marin IJ. Comparative evaluation of first- and second-generation digene hybrid capture assays for detection of human papilloma viruses associated with high or intermediate risk for cervical cancer. *J Clin Microbiol* 1999;37:796-7.  
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In the present study we comparatively evaluated the first- and second-generation Digene Hybrid Capture assays for detection of human papillomaviruses (HPV) associated with high or intermediate risk for cervical cancer in cervical specimens. Concordant results were obtained with 468 of 483 (96.8%) specimens. All 15 specimens which gave repeatedly discordant results were positive by the second-generation test only, and 14 of them tested PCR positive. The enhanced sensitivity of the second-generation assay is mainly a result of the reformulation of hybridization reagents and, to a lesser extent, a result of the addition of new HPV probes.
9. Poropat M, Batinæ D, Bašæ M, Nižiæ LJ, Dodig D, Miloševiæ D, et al. Tc-99m DTPA renal scintigraphy using deconvolution analysis with six functional images of the mean time to evaluate acute pyelonephritis. *Clin Nucl Med* 1999;24:120-4.  
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In 38 children with proved P-fimbriated *E. coli* acute pyelonephritis, Tc-99m DTPA dynamic renal scintigraphy in the zoom mode using deconvolution analysis was performed, and the results were compared with those of Tc-99m DMSA scans. From the dynamic study, six functional images of the mean time were generated. Each functional image was analyzed separately to search for focal areas of increased mean time within the kidney contour. Tc-99m DMSA scintigraphy showed generalized or focal decreased uptake in 32 (41.8%) kidneys, and deconvolution analysis of Tc-99m DTPA scintigraphy revealed pathologic renographic curves in 58 (77.6%) kidneys. Prolonged whole- kidney and normal renal parenchymal transit times (dilatation without obstruction) were found in 38 (50%) kidneys, whereas prolonged whole-kidney and renal parenchymal transit times (dilatation with obstruction) were observed in 20 (27.6%) kidneys. Separate analysis of each of the six functional images of the mean time showed focal areas of increased mean time in the kidney parenchyma of 11 kidneys. In five cases, time-activity curves from these areas showed a sharp increase of activity on the descending part of the curve, which might reflect the return of urine from the collecting system into kidney cortex (i.e., intrarenal reflux). These results showed that in a urinary tract with acute pyelonephritis, urodynamic changes may lead to obstructive nephropathy and intrarenal reflux. Tc-99m DTPA renal scintigraphy has proved to be a valuable method to evaluate acute

pyelonephritis, thus allowing dynamic and morphologic analysis of the urinary tract at the same time.

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