

Ružić B, Tomašković I, Trnski D, Kraus O, Bekavac-Bešlin M, Vrkić N. Systemic stress responses in patients undergoing surgery for benign prostatic hyperplasia. BJU Int. 2005;95:77-80.

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The objective of this study was to determine differences in systemic stress responses in patients undergoing three different types of surgery for benign prostatic hyperplasia (BPH), evaluated by measuring levels of stress variables, i.e. cortisol; acute-phase reactants (CRP and fibrinogen) and antioxidants, i.e. total antioxidant status (TAS) and superoxide dismutase (SOD). The study included 80 patients who fulfilled the inclusion criteria for surgery for BPH. Based on an ultrasonographic estimate of the prostate volume before surgery, all patients were allocated to one of three groups; group 1, prostate < or = 30 g and treated with transurethral incision of the prostate (TUIP); group 2, prostate 30-80 g, treated with transurethral resection of the prostate (TURP); and group 3, prostate > 80 g, treated with a suprapubic transvesical prostatectomy (TP). There were significantly higher levels of cortisol, CRP and TAS, and significantly lower levels of fibrinogen and SOD in all study groups after surgery than before. Surgery and associated conditions, e.g. excitement, fear, blood loss, etc., lead to traumatic and oxidative stress, followed by a strong systemic stress response during and after surgery. Low fibrinogen levels after surgery had a different pattern from the other acute-phase reactants, as a result of increased fibrinolytic activity after TURP and TP. In conclusion, the extent of the systemic stress response correlated fairly well with the degree of tissue damage, which differed in the three groups. Suprapubic TP caused the most tissue trauma and triggered the strongest systemic stress response. This response was moderate after TURP, while TUIP (a minor intervention) caused the least stress. Specific changes in stress markers could be used to improve surgery for BPH.

Hasan M, Krmpotić A, Ruzsics Z, Bubić I, Lenac T, Halenius A, et al. Selective down-regulation of the NKG2D ligand H60 by mouse cytomegalovirus m155 glycoprotein. J Virol. 2005;79:2920-30.

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Both human and mouse cytomegaloviruses (CMVs) encode proteins that inhibit the activation of NK cells by down-regulating cellular ligands for the activating NK cell receptor NKG2D. Up to now, three ligands for the

NKG2D receptor, named RAE-1, H60, and MULT-1, have been identified in mice. The resistance of mouse strains to murine CMV (MCMV) infection is determined by their ability to generate an effective NK cell response. The MCMV gene m152, a member of the m145 gene family, down-regulates the expression of RAE-1 in order to avoid NK cell control in vivo. Here the authors report that the m155 gene, another member of the m145 gene family, encodes a protein that interferes with the expression of H60 on the surfaces of infected cells. Deletion of the m155 gene leads to an only partial restoration of H60 expression on the cell surface, suggesting the involvement of another, so far unknown, viral inhibitor. In spite of this, an m155 deletion mutant virus shows NK cell-dependent attenuation in vivo. The acquisition of endo-beta-N-acetylglucosaminidase H resistance and the preserved half-life of H60 in MCMV-infected cells indicate that the m155-mediated effect must take place in a compartment after H60 exits from the ERGIC-cis-Golgi compartment.

Sirotković-Skerlev M, Križanac S, Kapitanović S, Husnjak K, Unušić J, Pavelić K. Expression of c-myc, erbB-2, p53 and nm23-H1 gene product in benign and malignant breast lesions: coexpression and correlation with clinicopathologic parameters. Exp Mol Pathol. 2005;79:42-50.

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The aims of this study were to assess the expression of protein products of c-myc, erbB-2, p53 and nm23-H1 gene in benign and malignant breast lesions, to estimate their possible coexpression and to correlate the results of immunohistochemical analysis with various clinicopathologic parameters. The method used was the immunohistochemical detection of the corresponding protein. Expression of c-myc protein was high in both malignant and benign lesions (95% and 100%). Expression of erbB-2 and mutated p53 proteins in malignant lesions was 27% and 34%. These proteins were present in benign lesions as well: 7.8% of benign lesions were positive for erbB-2 protein and 19.6% for p53 protein. The expression of nm23-H1 protein was similar in benign and malignant lesions: 47% and 54%. The coexpression of nm23-H1 and mutated p53 protein was found in 14 carcinomas (16.5%). The authors found a tendency of negative correlation between the expression of these two proteins. In addition, there was a negative correlation between the size of breast carcinomas and the expression of nm23-H1, a higher proportion of nm23-H1-positive carcinomas in the group of erbB-2-negative, p53-negative carcinomas and a higher propor-

tion of nm23-H1-positive carcinomas in the group of malignant lesions with negative axillary lymph nodes. These results support the hypothesis that in women with breast cancer the expression of nm23-H1 gene may contribute to more favorable phenotype. The authors also showed that some changes found in malignant breast tumors such as the presence of mutated p53 protein and the expression of erbB-2 protein may be found in benign lesions as well

Hudolin T, Hudolin I. The role of primary repair for colonic injuries in wartime. Br J Surg. 2005;92:643-7.

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The study reviewed an experience of selective primary repair for penetrating colonic injuries incorporating a number of procedures during the 1992-1995 Bosnia-Herzegovina conflict. Of 5370 casualties, 259 (4.8%) had injuries to the colon. The patients were divided into two groups: those who had primary repair and those who needed a colostomy. The patients' records were reviewed to determine the cause of injury (explosive weapons or bullets), the position and type of colon injury, associated injuries, the surgical procedure(s) done, complications related to the colonic wound or its management, and mortality. A total of 122 (47.1 %) patients had primary colonic repair and 137 (52.9%) had a colostomy. One hundred and fifty (57.9%) were injured by explosive weapons, 108 (41.7%) had bullet wounds and one (0.4%) a stab injury. Associated injuries were seen in 249 (96.1%) patients. Complications related to the colonic wound or its management developed in 27% of patients after primary repair and 30% after colostomy. Mortality rates were 8.2% and 7.2%, respectively. In conclusion, primary repair was a safe and effective treatment for penetrating colonic injuries during war.

Bedenić B, Vraneš J, Šuto S, Žagar Ž. Bactericidal activity of oral beta-lactam antibiotics in plasma and urine versus isogenic Escherichia coli strains producing broad- and extended-spectrum beta-lactamases. Int J Antimicrob Agents. 2005;25:479-87.

Department of Microbiology, Andrija Štampar School of Public Health, Zagreb University School of Medicine, Zagreb, Croatia

The aim of this investigation was to assess the bactericidal activity of oral beta-lactam antibiotics available in Croatia (amoxicillin/clavulanate, cephalexin, cefuroxime, cefadroxil and ceftibuten), in biological fluids against isogenic Escherichia coli strains producing broad-spectrum (TEM-1, TEM-2 and SHV-1) and extended-spectrum beta-lactamases (SHV-2, SHV-3, SHV-4, SHV-5, SHV-12). Bactericidal activity of oral beta-lactams in plasma and urine was tested in time-kill experiments and by determining bactericidal titres at different time intervals post-dose. The killing rate of antibiotics in urine was slower than in plasma, but faster than in Mueller-Hinton

broth. High bactericidal titres in urine were only maintained throughout the whole dosing interval by ceftibuten against strains producing broad-, SHV-2 and SHV-3 beta-lactamases. The older generation cephalosporins can be considered for the therapy of urinary tract infections caused by E. coli harbouring TEM-1, TEM-2 and SHV-1 beta-lactamases but a shorter dosing interval is needed. Ceftibuten can be recommended with caution in ESBL producing E. coli except those producing SHV-4, SHV-5 and SHV-12 that confer resistance to it. If these enzymes are produced, fluoroquinolones or carbapenems could be considered.

Borčić J, Anić I, Smojver I, Čatić A, Miletić I, Ribarić SP. 3D finite element model and cervical lesion formation in normal occlusion and in malocclusion. J Oral Rehabil. 2005;32:504-10.

Rijeka University School of Dental Medicine, Rijeka, Croatia

The aim of this study was to develop a three-dimensional (3D) finite element model (FEM) of the first maxillary premolar in order to compare the stress profiles in the buccal and palatal cervical regions. The 3D geometry of the tooth was reconstructed, the solid model was transferred into a finite element program where a 3D mesh was created, and the stress distribution analysis was performed. Two typical cases have been considered: the tooth under normal occlusion (case I) and the tooth under malocclusion (case II). In case I, larger compressive stresses were found in the cervical enamel and dentine. Tensile stresses were found in the fissure system, adjacent area, and at the vestibular surface of the buccal cusp. The peak values for the principal stress ranged from -259 to +2.25 MPa in the cervical areas. In the case II, larger compressive stresses were found in the palato-cervical enamel and dentine. Tensile stresses were found inside the enamel in the fissure system, adjacent area, at the vestibular surface of the buccal cusp, and in the bucco-cervical enamel. The peak values for the principal stress ranged from -501.947 MPa in palatal region to +82.4 MPa in the buccal region. This study implies a role of occlusal forces in development of non-carious lesions. In the case of malocclusion, tensile stresses generated on the cervical areas were higher compared with the stresses generated in the case of normal occlusion and it is probably capable of producing non-carious cervical lesion.

Pibernik-Okanović M, Peroš K, Szabo S, Begić D, Metelko Z. Depression in Croatian Type 2 diabetic patients: prevalence and risk factors. A Croatian survey from the European Depression in Diabetes (EDID) Research Consortium. Diabet Med. 2005;22:942-5.

Vuk Vrhovac University Hospital, Zagreb, Croatia

The aim of this study was to determine the prevalence rate of and risk factors for depression in Croatian Type 2 diabetic patients. Depressive mood was examined in

384 randomly selected outpatients with Type 2 diabetes. Center for Epidemiological Studies Depression Scale (CES-D) and Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) were used to identify depressive disturbances. The groups with CES-D ≥ 16 and < 16 were compared with respect to demographic, psychological and clinical characteristics. Regression analysis was used to determine risk factors for depression. Of the examined patients, 22% had CES-D scores ≥ 16 , and in 33% of them clinical depression was confirmed by the psychiatric interview. Depressed patients compared with the non-depressed ones reported more diabetes-related problems and poorer well-being ($t=6.71$, $P<0.001$ and $t=11.98$, $P<0.001$, respectively). Multiple regression analysis indicated female gender, experienced support and the level of emotional well-being to predict depression ($R=0.74$, $F=15.3$, $P<0.001$). The obtained data indicate that the prevalence rate in Croatian Type 2 diabetic patients is comparable to findings from other cultural settings. Depressive symptoms can be predicted by psychological rather than disease-related variables. Psychological care for diabetic patients may be necessary to prevent depressive symptomatology.

Parnham MJ, Čulić O, Eraković V, Munić V, Popović-Grle S, Barišić K, et al. Modulation of neutrophil and inflammation markers in chronic obstructive pulmonary disease by short-term azithromycin treatment. Eur J Pharmacol. 2005;517:132-43.

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The anti-inflammatory potential of azithromycin in chronic obstructive pulmonary disease (COPD) patients was explored following a standard oral dosing regimen. Patients with moderate and severe COPD were treated with azithromycin (500 mg, $n=16$) or placebo ($n=8$) once daily for 3 days in a randomized, double blind design, to compare effects on inflammation markers with those seen in a previous study in healthy volunteers. A battery of tests was made on serum, blood neutrophils and sputum on days 1 (baseline), 3, 4, 11, 18 and 32. In comparison to placebo, azithromycin resulted in an early transient increase in serum nitrites plus nitrates (day 3), associated with a tendency towards an increase in the blood neutrophil oxidative burst to phorbol myristic acetate. Subsequently, prolonged decreases in blood leukocyte and platelet counts, serum acute phase protein (including C reactive protein) and soluble E-selectin and blood neutrophil lactoferrin concentrations and a transient decrease in serum interleukin-8 were observed. Blood neutrophil glutathione peroxidase activity showed a prolonged increase after azithromycin treatment. The biphasic facilitatory-then-inhibitory response to azithromycin seen in healthy volunteers is not so clearly detectable in COPD patients, only potential anti-inflammatory effects. Treatment for longer periods may give therapeutic anti-inflammatory benefit in these patients.

Babić Z, Svoboda-Beusan I, Kučišec-Tepeš N, Dekaris D, Troškot R. Increased activity of Pgp multidrug transporter in patients with Helicobacter pylori infection. World J Gastroenterol. 2005;11:2720-5.

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The aim of this study was to determine whether local antibiotic resistance involves P-glycoprotein (Pgp)-mediated active drug out-pumping during *Helicobacter pylori* (H. pylori) infection treatment with classic antibiotic therapy. Pgp activity was determined in gastric mucosa biopsy specimens obtained from 53 patients with pathohistologically verified gastritis and microbiologically confirmed H. pylori infection, and compared with the Pgp-activity in 12 control subjects with normal endoscopic findings. The H. pylori positive patients were treated with short-term 7-d therapy consisting of two antibiotics (amoxicillin and azithromycin/metronidazole and clarithromycin) and a proton pump inhibitor. Pgp-activity was determined by flow cytometry in the test of rhodamine dye efflux and quantified as mean fluorescence ratio (RMF). Upon the first cycle, H. pylori was successfully eradicated in 20 patients, whereas therapy was continued in 33 patients. In the course of antibiotic therapy, RMF increased ($P<0.05$) and gastric cells showed higher rhodamine dye efflux. The mean pre-treatment RMF values were also higher ($P<0.0001$) in patients with multiple therapeutic failure than in those with successful H. pylori eradication and control subjects. Pgp might be one of the causes of therapy failure in patients with H. pylori and antibiotic therapy could be chosen and followed up on the basis of the Pgp-transporter local activity.

Lugović L, Lipozenčić J, Jakić-Razumović J. Prominent involvement of activated Th1-subset of T-cells and increased expression of receptor for IFN-gamma on keratinocytes in atopic dermatitis acute skin lesions. Int Arch Allergy Immunol. 2005;137:125-33.

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The objective of the study was to evaluate humoral and cellular immunological factors in the blood and the skin lesions of atopic dermatitis (AD) patients, and to analyze the presence of inflammatory cell-surface markers in blood and skin biopsies. The parameters for monitoring of 40 AD patients included results of prick test to inhalant allergens and epicutaneous (patch) test to contact allergens; values of total IgE, serum immunoglobulins (IgG, IgA, IgM) and different cell markers in the sera (CD3, CD4, CD8, CD20, CD21, CD23, HLA-DR). The authors also analyzed inflammatory cell-surface markers (CD3, CD4, CD8, CD20, CD20, CD1a, CD23, CD29, CD45RO, IFN γ) in the biopsies of skin lesions from 10 AD patients and 5 healthy controls (HCs) by immunohistochemical analysis. Beside increased total serum IgE and positive skin tests, a significantly

higher percentage of CD23+ cells with lower percentage of CD21+ cells was revealed in peripheral blood of AD patients in comparison to HCs. A positive epidermal expression of the majority of markers of T cells (CD3+, CD4+, CD8+, CD29+, CD45RO+, IFN γ +) and those of Langerhans' cells (LCs) (CD1a, CD23+), without those of B cells (CD20+) were noted in AD patients, but no in the skin of HCs. Furthermore, significant difference was also found between the two groups for increased expression of CD3, CD4, CD8, CD29, CD45RO, IFN γ + markers (markers for IFN γ receptor) and higher intraepidermal CD23+ LCs and intradermal CD1a+ LCs in AD skin lesions. These results suggest involvement of various humoral factors with increased production of IgE and cooperation between Th subsets and LCs, with higher production of related cytokines, and disturbed cellular immunity, including epidermal LCs with IgE receptors of high and low affinity in AD. The annotation of activated Th1 cells with increased producing of IFN γ in acute AD skin lesions is notable, and might lead to IFN γ binding to keratinocytes and consequently inflammatory skin changes in the disease.

Ivančić-Baće I, Salaj-Šmic E, Brčić-Kostić K. Effects of recJ, recQ, and recFOR mutations on recombination in nuclease-deficient recB recD double mutants of Escherichia coli. J Bacteriol. 2005;187:1350-6.

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The two main recombination pathways in Escherichia coli (RecBCD and RecF) have different recombination machineries that act independently in the initiation of recombination. Three essential enzymatic activities are required for early recombinational processing of double-stranded DNA ends and breaks: a helicase, a 5'→3' exonuclease, and loading of RecA protein onto single-stranded DNA tails. The RecBCD enzyme performs all of these activities, whereas the recombination machinery of the RecF pathway consists of RecQ (helicase), RecJ (5'→3' exonuclease), and RecFOR (RecA-single-stranded DNA filament formation). The recombination pathway operating in recB (nuclease-deficient) mutants is a hybrid because it includes elements of both the RecBCD and RecF recombination machineries. In this study, genetic analysis of recombination in a recB (nuclease-deficient) recD double mutant was performed. The authors show that conjugational recombination and

DNA repair after UV and gamma irradiation in this mutant are highly dependent on recJ, partially dependent on recFOR, and independent of recQ. These results suggest that the recombination pathway operating in a nuclease-deficient recB recD double mutant is also a hybrid. The authors propose that the helicase and RecA loading activities belong to the RecBCD recombination machinery, while the RecJ-mediated 5'→3' exonuclease is an element of the RecF recombination machinery.

Peričić D, Lazić J, Švob Štrac D. Anticonvulsant effects of acute and repeated fluoxetine treatment in unstressed and stressed mice. Brain Res. 2005;1033:90-5.

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The authors tested the effects of the antidepressant drug fluoxetine on the seizure threshold for picrotoxin in unstressed and swim-stressed mice. The mice were, prior to exposure to swim stress and the intravenous infusion of picrotoxin (a non-competitive GABA(A) receptor antagonist), pretreated with fluoxetine (a selective serotonin reuptake inhibitor), either acutely or repeatedly (5 days), and the latency to the onset of two convulsant signs and death was registered. The convulsant signs were running/bouncing clonus and tonic hindlimb extension. As expected, swim stress enhanced the seizure threshold for picrotoxin. Fluoxetine (20 mg/kg ip) given acutely increased in unstressed and swim-stressed mice the dose of picrotoxin producing tonic hindlimb extension and in unstressed mice the dose of picrotoxin producing death. Neither 10 nor 20 mg/kg of fluoxetine affected doses of picrotoxin needed to produce running bouncing/clonus. Repeated treatment with fluoxetine (20 mg/kg ip) enhanced significantly in unstressed and swim-stressed mice doses of picrotoxin needed to produce tonic hindlimb extension and death, and in stressed mice also the dose of picrotoxin producing running/bouncing clonus. The results demonstrate that the antidepressant drug fluoxetine, given acutely or repeatedly, shows anticonvulsant properties against convulsions induced in unstressed and swim-stressed mice by antagonist of GABA(A) receptors, picrotoxin. Swim stress failed to modify the anticonvulsant properties of fluoxetine.