

Gulan G, Ravlić-Gulan J, Štrbo N, Sotošek V, Nemec B, Matovinović D, et al. Systemic and local expression of perforin in lymphocyte subsets in acute and chronic rheumatoid arthritis. *J Rheumatol* 2003;30:660-70.

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In order to elucidate the role of the cytolytic action mediated by perforin in the course of rheumatoid arthritis (RA), the authors studied the immunophenotypic characteristics of lymphocytes containing perforin in peripheral blood (systemic level), in synovial fluid (SF), and in the synovial membrane (local level) in patients during the acute or chronic phase of RA. Cells from patients with osteoarthritis were used as controls. Flow cytometry was used for simultaneous detection of intracellular (perforin) and cell surface antigens. Mean fluorescence intensity (MFI) was a measure of the mean perforin content per cell. Immunocytochemical staining was used to visualize perforin in the cytoplasmic compartment of cells. In acute RA, highly significant changes in perforin expression were found in all compartments (peripheral blood, SF, and synovial membrane): 1) increase of percentage of total perforin positive cells; 2) increase of both subsets of cytolytic cells, T (CD8⁺P⁺) and NK (CD56⁺P⁺) cells; 3) increase in the frequency of perforin positive cells in CD8⁺ and CD56⁺ cell populations; and 4) the highest content of perforin/cell (MFI values) in all compartments, except in the synovial membrane. In conclusion, perforin positive cells may participate in the acute phase of RA by maintaining and perpetuating inflammation and contributing to tissue destruction.

Tarle M, Kraus O, Trnski D, Reljić A, Ružić B, Katušić J, et al. Early diagnosis of prostate cancer in finasteride treated BPH patients. *Anticancer Res* 2003;23:693-6.

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A total of 37 patients with well-documented benign prostatic hypertrophy (BPH) were referred to finasteride. In all subjects the prostate volume was > 60 cc. Serum total PSA (TPSA) and free/total PSA (%FPSA) values were recorded at 3-month intervals. After 6 months of treatment, the patients were divided into two groups in accordance with the numerical values of these two parameters. In the first group (25 patients), a drop in TPSA approached 50% reduction while the %FPSA level remained at the initial level. No malignancy was detected in these patients after 9 months of finasteride treatment and in 4-18 months additional follow-up. The second group (12 patients), consisted of subjects with a less pronounced decrease in TPSA concentration (ca. 28%) and a significant reduction in %FPSA mostly to values <18% (cut-off point dividing BPH from cancer) during a 6-month monitoring period. During the extended part of the investigation, prostate cancer was diagnosed in 7 out of 11 of these latter patients (63.6%), or overall in 7 out of 30 (23.3%) patients who reached the end-point of the study. Accordingly, serial assessments of total and free PSA

are necessary and sufficient clinical means to detect early prostate cancer in patients with a large benign prostate referred to finasteride.

Kovačić V, Roguljić L, Kovačić V. Metabolic acidosis of chronically hemodialyzed patients. *Am J Nephrol* 2003;23:158-64.

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Metabolic acidosis of end-stage renal patients could be successfully corrected with bicarbonate hemodialysis and with peroral bicarbonate-containing phosphate binders, i.e. calcium carbonate. Bicarbonate powder compared with bicarbonate solutions has some advantages and enables a stable composition of electrolytes. "High" dialysate bicarbonate (40-42 mmol/L) is a safe, well-tolerated and useful tool for better correction of the metabolic acidosis and must become a standard of hemodialysis treatment. Measured postdialysis blood bicarbonate concentration should be obtained at least every month and correction of metabolic acidosis by maintaining serum bicarbonate ≥ 22 mmol/L should be a goal of the management of patients undergoing chronic hemodialysis.

Gotovac K, Sabioncello A, Rabatić S, Berki T, Dekaris D. Flow cytometric determination of glucocorticoid receptor (GCR) expression in lymphocyte subpopulations: lower quantity of GCR in patients with post-traumatic stress disorder (PTSD). *Clin Exp Immunol* 2003;131:335-9.

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Assessment of the intracellular glucocorticoid receptor (GCR) level may be useful in monitoring functional disturbances of the hypothalamic-pituitary-adrenocortical axis or effects of prolonged steroid therapy. Cytosolic ligand binding assays have recently been supplemented by flow cytometric determination of receptor expression in individual cells. A method based on multiparametric analysis of whole blood by simultaneous labelling of intracellular GCRs and surface markers of lymphocyte subsets is described. The authors examined 25 healthy male volunteers and 35 age- and sex-matched post-traumatic stress disorder (PTSD) patients within 8 years from traumatic event. PTSD patients had a lower relative quantity of GCR in all lymphocyte populations tested as compared with healthy volunteers. NK cells of both groups showed higher expression of GCR than other lymphocyte subsets. In PTSD patients, the expression of GCR in B-cells was also higher than in T cell. Although serum cortisol level was lower in PTSD patients, there was no correlation between cortisol level and GCR expression. Multiparameter flow cytometric determination of GCR expression in lymphocyte subpopulations may provide a useful tool for monitoring immunoregulatory action of glucocorticoids.

Bobinac D, Španjol J, Zoričić S, Marić I. Changes in articular cartilage and subchondral bone histomorphometry in osteoarthritic knee joints in humans. Bone 2003;32:284-90.

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The aim of this study was to elucidate patterns of bone parameter changes within different depths of subchondral bone in the joints with macroscopically normal cartilage and in joints with osteoarthritis (OA). Ten tibial plateaus were taken from patients during total knee replacement surgery due to severe OA. They were compared with 10 sets of tibial condyles obtained from autopsy subjects with no history of bone or joint disease. The cylindrical cartilage-bone samples were taken out from the anterior, posterior, external, and internal areas of the condyles for cartilage assessment (Mankin score) and subchondral bone histomorphometry. The study showed that subchondral bone from the OA group had significantly higher bone volume ($54.1 \pm 10.6\%$) than control group ($37.8 \pm 8.1\%$) ($p < 0.01$). In addition, trabecular parameters from the OA subchondral bone showed a smaller number of sparsely distributed and thicker trabeculae than in control group ($p < 0.05$). Medial and lateral condyle from the control group did not differ significantly, while medial condyle from OA group showed a high increase of bone volume (62.8 ± 13.3) and consecutively different trabecular parameters when compared with the lateral condyle from the same group. Also, it was shown that there are regional differences in bone parameters between both condyles within both, control and OA groups. Comparison of bone parameters from three different stage of articular cartilage degeneration (Mankin score) showed that higher degree of cartilage degeneration is followed by significant changes in subchondral bone architecture. Furthermore, it was found that progression of cartilage degeneration led to changes in bone parameters which affected deeper levels of subchondral bone. According to these results, it can be suggested that changes in histomorphometric parameters of subchondral bone are secondary to cartilage damage and proceed deeper into subchondral bone with increasing cartilage degeneration.

Vučičević-Boras V, Brozović S, Cekić-Arambašin A, Zadro R, Devčić T, Begovac J, et al. Salivary peroxidase levels in patients with AIDS. Eur J Med Res 2003;21:81-4.

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The main consequences of human immunodeficiency virus (HIV) infection and AIDS are frequent and persistent opportunistic infections at mucosal surfaces, but data upon impaired oral mucosal response in AIDS patients are still lacking. The aim of this study was to determine salivary flow rates and peroxidase levels in unstimulated whole saliva in AIDS patients together with comparison to the healthy controls. Salivary peroxidase levels were determined according to Putter and Becker in 20 AIDS patients and 18 HIV-seronegative healthy controls. Statistical analysis was performed using Student t-test. Salivary peroxidase levels were significantly increased in the AIDS group (9.41 ± 8.50 kU/L; $p < 0.009$) when compared to the healthy controls (3.1 ± 2.0 kU/L). Salivary flow rates were significantly decreased in AIDS patients (0.17 ± 0.11 mL/min, $p < 0.009$) when compared with healthy controls

(0.58 ± 0.19 mL/min). Elevated salivary peroxidase levels indicate increased salivary antimicrobial activity in AIDS patients.

Matanić D, Beg-Zec Z, Stojanović D, Matakorić N, Flego V, Milevoj-Ribić F. Cytokines in patients with lung cancer. Scand J Immunol 2003;57:173-8.

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The aim of the study was to evaluate the cytokines', tumour necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta) and IL-6, releasing capacity in patients with lung carcinoma and benign lung disease. A group of 41 patients were tested for the production of TNF-alpha, IL-1beta and IL-6 in bronchoalveolar lavage (BAL) and blood. The levels of cytokines in the lung cancer patients were as follows: in BAL – IL-6, 173 ± 85 pg/mL; TNF-alpha, 170 ± 116 pg/mL; and IL-1beta, 473 ± 440 pg/mL; in the blood – IL-6, 197 ± 53 pg/mL; TNF-alpha, 311 ± 202 pg/mL; and IL-1beta, 915 ± 239 pg/mL. Alveolar macrophages of the patients with a lung cancer secreted significantly more cytokines, IL-6 ($p = 0.0004$) and IL-1beta ($p = 0.0047$), than alveolar macrophages of the patients with a nonmalignant lung cancer. However, significantly lower levels of cytokine production by the BAL cells were found in patients with small cell lung cancer. This production decreased further in phase IV of nonsmall cell lung cancer.

Kalogjera L, Vagić D, Baudoin T. Effect of endosinusal treatment on cellular markers in mild and moderate asthmatics. Acta Otolaryngol 2003;123:310-3.

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The aim of the study was to determine the efficacy of topical endosinusal treatment in terms of reduction in activation of inflammatory cells and asthma/ rhinosinusitis symptoms in patients with asthma and chronic rhinosinusitis (CRS). Eighteen mild-to-moderate asthmatics with CRS were subjected to antral sinuscopy and endosinusal treatment with 2 mg of dexamethasone and 40 mg of gentamicin per maxillary sinus for 7 days. Sinus lavage and serum samples were taken before and after the treatment and bacteriological swabs from the sinuses were taken at the time of inclusion in the study. Subjective scores for CRS symptoms and forced expiratory volume in 1 s (FEV1) were tested at inclusion and after 30 days. Levels of eosinophil cationic protein (ECP), tryptase and myeloperoxidase (MPO) were analyzed in serum and sinus fluid before and after the treatment. ECP and tryptase levels were significantly reduced in both serum and sinus fluid, but serum MPO did not show significant changes after the treatment. MPO in sinus lavage was reduced only in moderate asthmatics. Subjective scores for CRS and FEV1 were significantly improved for the whole group. ECP, usually used as a parameter for asthma staging, was mostly affected at the systemic level, whilst tryptase was more markedly reduced at the local level. In conclusion, the topical endosinusal treatment used in this clinical study significantly reduced activation of eosinophils and mastocytes, improved FEV1 and reduced symptoms of CRS in mild-to-moderate asthmatics.