

## REVIEWS

### **S. Marincheva, R. Rashkov and ZI. Kolarov.** AUTOINFLAMMATORY SYNDROMES. PART I. DEFINITION, GENERAL CONCEPTS AND CLASSIFICATION

**Summary.** Autoinflammatory syndromes are a group of diseases, which typically present with recurrent episodes of systemic inflammation, without evidences for infectious agent, specific autoantibodies or antigen-specific T-cells. In the strict sense, the term autoinflammatory syndromes comprises monogenic diseases of innate immune system. In a broad sense, autoinflammatory syndromes include both polygenic innate immune system disorders and mixed origin syndromes – syndromes with dysfunction of the innate and adaptive immune systems. Up to date, there is no generally acknowledged classification of autoinflammatory syndromes. The most quoted classification systematizes diseases with onset in childhood. Upon our understanding we put forward a modified classification based on the proposed classification in Immunologic disease continuum by D. McGonagle et al.

**Key words:** autoinflammatory syndromes, innate immune system, adaptive immune system, classification

### **ZI. Kolarov.** COMMONLY ACCEPTED CONCEPTS ON THE USE OF ANTI-TNF BIOLOGICAL AGENTS IN RHEUMATOLOGY PRACTICE BASED ON NATIONAL AND INTERNATIONAL CONSENSUSES AND INSTRUCTIONS

**Summary.** Reviewed are the main principles of the use of biological agents in rheumatologic practice based on recent recommendations of consensuses and guidelines of the American College of Rheumatology, the British Society for Rheumatology, the National Institutes of Health of USA etc. Presented are the basic biological preparations with their indications, contraindications, adverse reactions and potential benefits and risks. Considered are the possibility to replace a given anti-TNF preparation by another one and to perform a combined therapy with conventional disease activity-modifying antirheumatic drugs and other agents as well. Stressed is the significance of creation of National Register of patients treated with biological agents.

**Key words:** anti-TNF biological agents, indications, contraindications, adverse reactions

### **R. P. Nikolov.** ADVERSE REACTIONS ASSOCIATED WITH ADMINISTRATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND NONOPIOID ANALGESICS

**Summary.** Nonsteroidal anti-inflammatory drugs (NSAIDs) and nonopioid analgesics (paracetamol, propacetamol, metamizole) are some of the most used drugs in the clinical practice. NSAIDs are used for the treatment of inflammation, pain, and fever. Paracetamol and metamizole exert analgesic and antipyretic action. The principal mechanism of action of the NSAIDs and analgesics with antipyretic effect stems from their ability to inhibit activity of cyclooxygenase. The purpose of this review is to discuss and prevent the risk of adverse reactions with the use of NSAIDs, paracetamol and metamizole. The main adverse reactions associated with administration of NSAIDs and nonopioid analgesics are gastrointestinal effects, renal effects, cardiovascular effects, hematologic effects, hypersensitivity reactions, Reye's syndrome, and hepatotoxicity (after paracetamol overdose).

**Key words:** adverse reactions, nonsteroidal anti-inflammatory drugs, nonopioid analgesics, gastrointestinal effects, renal effects, cardiovascular effects, hematologic effects, hypersensitivity reactions, Reye's syndrome, hepatotoxicity

## ORIGINAL ARTICLES

### **R. Stoilov and M. Ivanova.** COSTS OF THE TREATMENT OF RHEUMATOID ARTHRITIS WITH DISEASE MODIFYING ANTIRHEUMATIC DRUGS THROUGHOUT 2009 IN BULGARIA

**Summary.** Early diagnose and aggressive treatment of rheumatoid arthritis are the key factors for the prevention and delay of bone and cartilage destructions and disability. Disease modifying antirheumatic drugs (DMARDs) and especially biological agents show great promise to gain these points. The aim of this study is to ascertain the consumption of the conventional and biological DMARDs in Bulgaria throughout 2009. 17% of the patients with rheumatoid arthritis were treated with DMARDs during 2009. 76 patients (0,25% of rheumatoid population) received treatment with biological agents. The mean percent for the

countries from EU is 12. It suggests that this expensive and very efficacious treatment with DMARDs is with a limited access in our country. 5017 patients were treated with conventional DMARDs, 60% of them were on Methotrexate treatment, about 27% received Sulphasalazine, about 8% – Hydroxychloroquine and approximately 4% – Leflunomide (Arava). Reimbursement politics of Health insurance authority is the key for amelioration of access to biological treatment. Reimbursement of 75% of the cost of this treatment is beyond affordability of the patients. The percent of the patients treated with conventional DMARDs is too insufficient. The reimbursement is of importance, but it is not so crucial compared to situation with biological agents. The opinion of the rheumatologist and consent of the patient are of great importance.

**Key words:** rheumatoid arthritis, treatment access, affordability

**K. Ikonomova, A. Toncheva, P. Dimitrova, V. Gyrkovska and N. Ivanovska. CHANGES IN sRANKL, TLR2 AND TNF $\alpha$  IN PATIENTS WITH OSTEOARTHRITIS**

**Summary.** Joint destruction and excessive bone loss in osteoarthritis (OA) and rheumatoid arthritis are associated with changes in expression of some cell receptors and molecules as well as in sera levels of some cytokines. Aim of the study was to examine the level of soluble receptor activator of nuclear factor  $\kappa$ B ligand (sRANKL) in sera and its expression on neutrophil leukocytes in patients with active and non active osteoarthritis. In the same patients, TLR2 expression on neutrophil leukocytes and TNF $\alpha$  secretion in nonstimulated and stimulated neutrophils were analyzed. Blood neutrophils were obtained by gradient centrifugation on Histopaque 1083 after dextran sedimentation. Concentrations of sRANKL and TNF $\alpha$  in sera were determined by enzyme-linked immunosorbent assay (ELISA). RANKL and TLR2 expression by neutrophils were analyzed by flowcytometry. The percentage of RANKL and TLR2 positive blood neutrophils was higher in patients with OA than in healthy donors. The neutrophil leukocytes in patients with osteoarthritis release greater amount of TNF $\alpha$  compared with healthy controls. The results of this study prove that higher levels of sRANKL might be used as a marker of osteoarthritis. Neutrophils can participate in inflammatory processes mediated by RANKL, TLR2 and TNF $\alpha$ .

**Key words:** osteoarthritis, RANKL, TLR2, TNF $\alpha$

## CASE REPORTS

**Ts. Petranova, I. Sheytanov, S. Monov, A. Batalov and R. Nestorova. MUSCULOSKELETAL ULTRASONOGRAPHY IN PATIENTS WITH PERIARTHRITIS OF THE SHOULDER JOINT**

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