B. Varbanova. CONTEMPORARY IMMUNOSUPPRESSIVE AND TARGETED THERAPIES IN RHEUMATOLOGY – QUO VADIS?
Summary. Autoimmune diseases predispose to a greater degree of malignancy, compared with the normal population. Immunosuppressive and targeted treatments allow successful control of connective tissue diseases and improve the quality of life of patients but pose a risk of immediate or distant serious side effects, such as neoplasia and other autoimmune diseases that are considered in this article. These issues are particularly important in childhood because of the greater expected duration of treatment in the life of this category of patients.
Key words: targeted immunosuppressive treatment, malignancy, autoimmunity

M. Kazakova, V. Sarafian and A. Batalov. YKL-40 IN RHEUMATOLOGY
Summary. YKL-40 is an extracellular matrix glycoprotein with highly conserved amino acid sequence, similar to the chitinase proteins but without any enzymatic activity. The aim of the present review was to examine the clinical significance, to outline the advantages and limitations of YKL-40 application as a new inflammation biomarker in rheumatoid arthritis and osteoarthritis. YKL-40 is expressed and secreted by macrophages, neutrophils, fibroblast-like synovial cells, chondrocytes and vascular smooth muscle cells. The expression of the protein in healthy subjects is feeble, while elevated serum levels are associated with pathologic processes like inflammation, extracellular tissue remodeling, fibrosis, rheumatoid arthritis, osteoarthritis, giant cell arthritis. There are few techniques available for YKL-40 detection and it is not investigated in Bulgaria yet. It is assumed that YKL-40 may provide new information about the pathogenesis, activity, prognosis, monitoring and therapy of inflammatory joint diseases.
Key words: YKL-40, inflammation biomarker, rheumatoid arthritis, osteoarthritis

M. Ivanova, R. Stoilov and I. Manolova. OSTEOARTHROSIS – PATHOPHYSIOLOGY AND PHARMACOLOGICAL THERAPY
Summary. Osteoarthritis (OA) is a chronic disease characterized by the slow degradation of cartilage, pain, and increasing disability. The disease can have an impact on several aspects of patient’s life, including functional and social activities, socioeconomic status, body image, and emotional wellbeing. Intraarticular treatment with hyaluronic acid (HA) has recently become more widely accepted in the armamentarium of therapies for OA pain. In normal cartilage, a delicate balance exists between matrix synthesis and degradation. In OA, cartilage degradation exceeds synthesis. In this review we look at the role of proinflammatory cytokines, MMP and NO in the pathogenesis of OA, as well as at the effects of HA on the nociception, the extracellular matrix, inflammatory mediators and immune cells.
Key words: osteoarthritis, pathophysiology, proinflammatory cytokines, cartilage, hyaluronic acid

Zl. Kolarov and R. Nestorova. OSTEOARTHROSIS AND QUALITY OF THE CARTILAGE – ACHIEVEMENTS, NEW TECHNOLOGIES, NEWLY ARISEN QUESTIONS AND UNSOLVED PROBLEMS
Summary. Presented are the main clinical and pathomorphologic features of osteoarthritis (OA). It is emphasized that the pathologic process affects not only the hyaline cartilage, but also all intra- and periarticular structures. Analysed are the cardinal achievements in diagnosis and treatment of the disease: identifying the structure and function of hyaline cartilage and the chondrocytes, mechanisms of cartilage turnover, main pathogenetic mechanisms and changes, introduction of new imaging and endoscopic diagnostic methods – NMR, joint sonography, arthroscopy, creation of manuals for treatment of OA, broadening the options for surgical treatment. Newly introduced technologies in diagnosing, evaluation and treatment of OA are: therapy with chondroprotectors, lubricants, Diacerin etc, treatment with stem cells (chondrocyte cultures) – at a stage of laboratory exploration and single clinical trials, experiments for biomarker introduction in diagnosis and monitoring of the disease. Recent knowledge poses questions about association between “hypertrophic” and “atrophic” forms of OA, about possibility for biologic treatment of OA, and the connection of OA and subchondral osteoporosis. Unsolved are the problems associated with clarifying the role of genetic factors in OA, diagnosis of early disease forms, defining the diagnostic value of biomarkers of cartilage turnover, establishment of prognostic markers of course, rate of development and outcome of the disease, improvement of disease modifying drugs in OA, treatment of early forms and of patients with concomitant diseases, possibility for primary disease prophylaxis.
Key words: osteoarthritis, quality of the cartilage, new technologies, problems
R. Rashkov and Zl. Kolarov. CORTICOSTEROIDS FOR LOCAL APPLICATION IN OSTEOARTHRITIS
Summary. Presented are the main indications, contraindications and complications of the local corticosteroid application in patients with osteoarthritis. Compared are the therapeutic concentrations and dose regimens of the most commonly used corticosteroid preparations for local application.
Key words: osteoarthritis, corticosteroids

D. Tanev, R. Robeva, F. Kumanov, R. Rashkov and Zl. Kolarov. SYSTEMIC LUPUS ERYTHEMATOSUS AND ESTROGENS
Summary. Systemic lupus erythematosus (СЛЕ) is a rare autoimmune disease that affects mainly women in their reproductive age. The overt sex dimorphism leads to the suggestion that female sex hormones are an important risk factor for the development of the disease. However, the interrelations between the estrogens and the clinical signs of SLE are not clarified. Higher, similar and even lower estrogen levels in patients with lupus in comparison to healthy women were described. According to some authors, the exogeneous estrogens aggravate the clinical manifestation of the disease, while others did not found such results. In pregnancy, flares of SLE occur often, but the estrogen levels in lupus patients were found to be lower than in a normal pregnancy. The present review aims to summarize the most important data about the relations between the estrogens and SLE as well as to accent on the questions that need to be clarified in the future larger studies.
Key words: systemic lupus erythematosus, estrogens, immunity

D. Dimov. ACTUAL POSSIBILITIES AND PERSPECTIVES OF BIOLOGICAL AGENTS IN SJÖGREN'S SYNDROME
Summary. The article reviews the results from the biologic agents use in the treatment of Sjögren’s syndrome, published in the literature from 2000 to 2010. The encouraging preliminary conclusions with TNF-α-blockers (infliximab, etanercept) could not be proven in the later controlled studies. B-cell directed agents – anti-CD20 (rituximab) and anti-CD22 (epratuzumab) – seem to be more effective, above all on systemic features, extraglandular involvement, associated lymphomas, however, on sicca-phenomena – only in cases with residual gland functions. The agents directed against cytokines BAFF/BLys (belimumab, atacicept), IL-6 (tocilizumab) and IFNs or against T-cells (efalizumab, abatacept, alefacept) are possible future options. The biological agents broaden the former restricted therapeutic armoury in Sjögren's syndrome, however, the conclusion on their definite place needs bigger randomized controlled studies and balanced assessment of the benefits and adverse events of their use.
Key words: Sjögren's syndrome, biological agents, treatment

ORIGINAL ARTICLES

V. Reshkova, R. Rashkov, Zl. Kolarov. EVALUATION OF TENDER POINTS ON PATIENTS WITH FIBROMYALGIA TREATED WITH DIFFERENT GROUPS OF MEDICAMENTS
Summary. In 1990 a new group of criteria was published under the ACR guidelines. Fibromyalgia is characterized by generalized pain, widespread pain in 11 of 18 tender point sites on digital palpation with presion 4 kg/cm². The association of generalized pain and at least 11 tender points sensitive to digital pressure out of 18 possible location was found to be conclusive in identifying fibromyalgic patients with sensitivity of 88,4%, and specificity of 88,1%. The scope of the present clinical study is to evaluate and compare the groups of trigger points of 3, 5, 7, 9, 11 on the patients of fibromyalgia treated with different medicaments versus control group. In the Clinic of Rheumatology a 3-months clinical study with 4 groups of medicaments, 1 group of patients with FM without treatment, and 1 control group took place. From 18 pain trigger points the ones with highest dynamical results in 4 therapeutic groups are the epicondil D+L, greater trochanter D+L, and gluteal D+L points. We evaluate the effect of the treatment by that dynamics.
Key words: fibromyalgia, dynamics of pain triggers point
CASE REPORTS

Zdr. Kamenov, E. Zaharieva, R. Stoilov, V. Karamfilova, V. Hristov. LERI-WEILL SYNDROME – A CASE REPORT AND LITERATURE REVIEW

Summary. Leri-Weil dyschondrosteosis (LWD) is a skeletal dysplasia characterized by mesomelic short stature in combination with Madelung’s wrist deformity. The latter is a result of a disturbed growth of the distal radial epiphysis, its premature fusion leading to curvature of the radius, dorsal subluxation of the ulna, and carpal wedging. All that causes restricted range of motion, deformity and pain in the wrist that usually presents after the seventh year, 50% of cases bilaterally. LWD, first described in 1929, is caused by mutations in the SHOX (short-stature homebox-containing) gene localized in the pseudoautosomal regions of the sex chromosomes. It is inherited in pseudoautosomal mode and due to variable expression phenotype varies in different members of the family. The gene encodes a factor engaged in bone growth and development; it is highly expressed in osteoblasts and is isolated from embryonic osteogenic tissue. We present a case of a 28-year-old woman who was diagnosed with Madelung’s wrist deformity 16 years ago with short stature, change in extremities’ length and progressive muscle weakness since she was 8 years old. Three surgical interventions were performed on her left arm. Genealogic analysis and laboratory test are presented.

Key words: Leri–Weill dyschondrosteosis, Madelung’s wrist deformity, SHOX gene, short stature

D. Kalinova, M. Ivanova, R. Stoilov and R. Rashkov. CALCINOSIS: A RARE FEATURE OF ADULT DERMATOMYOSITIS

Summary. Dermatomyositis is an idiopathic inflammatory myopathy with characteristic cutaneous manifestations – heliotrope rash and Gottron papules. Calcinosis in soft tissues is rare in adult with dermatomyositis. Calcinosis occurs three times more commonly in juvenile dermatomyositis, observed between 40-70 percent of patients. Calcinosis results from hydroxyapatite calcium deposits in soft tissues, but pathophysiology is not clear. It wasn’t found sufficiently effective treatments to reduce calcium deposits. We present a case of adult calcinosis associated with idiopathic dermatomyositis.

Key words: dermatomyositis, calcinosis

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