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REVIEWS

THE ROLE OF AUTOANTIBODIES, ENDOTHELIAL DYSFUNCTION AND HEMATOPOIETIC STEM CELLS IN THE PATHOGENESIS OF DIFFERENT VASCULITIS SYNDROMES
D. Kalinova¹, V. Reshkova¹, E. Ivanova², D. Kyurkchiev² and R. Rashkov¹
¹Clinic of Rheumatology, UMHAT “Sv. Iv. Rilski” – Sofia
²MDL of Clinical Laboratory and Immunology, UMHAT “Sv. Iv. Rilski” – Sofia

Summary. The vasculitides are a heterogeneous group of diseases, characterized by inflammation of blood vessel wall, with subsequent tissue destruction and/or organ failure. The aim of the current review was to analyze the pathogenetic mechanisms in different vasculitis syndromes, especially the role of autoantibodies, endothelial dysfunction and regenerative processes taking place in the vascular wall, one sign of which being hematopoietic stem cells.

Key words: vasculitis, pathogenesis, endothelial dysfunction, hematopoietic stem cells

NON-LYMPHOID IMMUNOREGULATORY CELLS
K. Tumangelova-Yuzeir, E. Ivanova-Todorova and D. Kyurkchiev
Laboratory of Clinical Immunology, UMHAT “Sv. Iv. Rilski” – Sofia
Department of Clinical Laboratory and Clinical Immunology, MU – Sofia

Summary. The regulation of the immune response is a process with huge significance for the prevention of autoimmune disorders. Together with the central immune tolerance, a peripheral tolerance is provided and the immunoregulatory cells are those which are responsible for it. Different types of lymphocytes are the most popular cells with immunomodulatory functions, but there are cells from non-lymphoid origin which are also engaged in the modulation of the immune response. The description of some of the most important types of cells from non-lymphoid origin (mesenchymal stem cells, dendritic cells and myeloid-derived suppressor cells), which are involved in the immunoregulatory process, was the aim of the present review. No one of these cells act independently, but their action is a part of a complicated mechanism, which ensures the immune homeostasis of the organism. The immunomodulatory cells are a new and promising tool for the future therapy of autoimmune disorders.

Key words: immunoregulation, mesenchymal stem cells, dendritic cells, myeloid suppressors

ANTIPHOSPHOLIPID SYNDROME – ANTIBODIES AND CLINICO-IMMUNOLOGICAL CORRELATIONS
N. Stoilov, Ya. Zdravkova and R. Rashkov
Clinic of Rheumatology, UMHAT “Sv. Iv. Rilski”, Medical University – Sofia

Summary. Antiphospholipid syndrome (APS) is a systemic autoimmune disease of unknown etiology and complex pathogenesis. It may appear as a separate nosological unit or in the context of other systemic connective tissue diseases, most commonly systemic lupus erythematosus (SLE). Its main clinical manifestations are vascular thrombosis and pathological pregnancies. Various pathogenetic mechanisms are involved in the thrombotic process in APS, with natural anticoagulants being affected and procoagulant phenotype stimulated. Antiphospholipid antibodies (aPL) act directly on the natural anticoagulants by interfering with their physiological role in platelets-dependent phase of the coagulation cascade. aPL also attack endothelial cells which express β2GPI on the outer cell membrane, stimulating endothelial apoptosis and proinflammatory cytokines secretion. In this way, aPL cause endothelial dysfunction, which is one of the main factors for atherosclerosis process. Mechanisms of thrombogenesis also ensue in placental vessels, which is one of the leading factors in the pathogenesis of placental thrombosis and infarction with subsequent fetal death. aPL exhibit direct damaging effect on the trophoblast and decidua. aPL can influence the implantation of the fertilized egg in the uterine wall. The diagnosis of API is made according to a set of clinical and immunological manifestations. Antibodies play an important role in the pathogenesis of the disease. It is therefore necessary to use a standardized methodology for their laboratory examination.

Key words: antiphospholipid syndrome, clinical manifestations

THE ROLE OF TUMOR MARKERS
N. Chilingirova
Medical Oncology Clinic, Specialized Hospital for Active Treatment in Oncology – Sofia

Summary. The aim of this article was to review the role of tumor markers and their application in the clinical practice. The classic tumor marker is a protein that can be found in the blood in higher than normal amounts when a certain type of cancer is present. Some tumor markers are specific for certain tumor types, others
could be found in most oncologic conditions. The ideal tumor marker would be one that could be used as a cancer screening blood test for the whole population, but would only be found in people with cancer. It would correlate with stage of the disease and response to therapy and could be measured safely and accurately. At this time there are no tumor marker tests that work like this. The possible role of tumor markers is in screening for certain cancer types in the healthy and high-risk population; for determining the risk of recurrence and prognosis of the patient; for monitoring the response to treatment; for differential diagnosis; for follow-up, or used with a predictive value. Tumor markers could not be usually used alone to diagnose oncologic diseases, but could help in the diagnostic process. Recently, while looking for a better tumor marker, even bigger attention is paid to genomics and proteomics.

**Key words:** tumor markers, monitoring, screening, sensitivity, specificity, measurement

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**CURRENT PATHOGENETIC CONCEPTS OF GOUT – A METABOLIC OR AUTOINFLAMMATORY DISEASE?**

R. Gancheva and Zl. Kolarov  
Clinic of Rheumatology, MU – Sofia  

**Summary.** Gout is a disease known since antiquity. The incidence of gout varies among populations, with an overall prevalence ranging from 1% to 15.3%. The upper limit appears to be increasing. There is a significant increase in complicated gout associated with cardiovascular disease, metabolic disorders and renal failure. In the review, the current concepts of the pathogenesis of the disease were pointed out. Studies from recent years that indicate the primary role of the innate immune system in the development of gout flares were discussed. The role of inflammasome and cytokines IL1β and IL-18 synthesized after its activation has been considered.

**Key words:** gout, innate immunity, IL-1β, IL-18

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**THE USE OF CHONDROITIN SULFATE FOR THE TREATMENT OF OSTEOARTHRITIS IN CLINICAL PRACTICE**

I. Parvova and Zl. Kolarov  
Clinic of Rheumatology, Department of Internal Medicine, Medical University – Sofia  

**Summary.** Osteoarthritis (OA) affects over 10% of the world population over 60 years. The disease is a consequence of morphological, molecular, biochemical and biophysical changes in chondrocytes and extracellular matrix. One of the modern trends in the pharmacotherapeutic behavior in OA is associated with administration of chondroitin sulfate (HS). The latter refers to a group of symptomatic slow-acting drugs in OA (SYSADOAs). Its wide use in clinical practice in recent years suggests that further investigation of the mechanism of action of HS and the clinical benefits of its application are needed.

**Key words:** chondroitin sulfate, osteoarthritis, articular cartilage, chondrocytes, proteoglycans

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**PANNICULITIS WITHOUT VASCULITIS – CLINICO-MORPHOLOGICAL ASPECTS OF ERYTHEMA NODOSUM AND LIPODERMATOSCLEROSIS**

S. Radenska-Lopovok, B. Belov and O. Egorova  
Federal State Budget Institution “Scientific Research Institute of Rheumatology”, Russian Academy of Medical Sciences, Moscow, Russia  

**Summary.** Panniculitis (Pann) refers to a broad term meaning a group of heterogeneous inflammatory diseases of adipose tissue. The precise diagnosis is made by histological examination in conjunction with clinical symptoms. There are no diagnostic laboratory tests and symptoms are non-specific which often leads to over- or under-diagnosis of the disease. New nosological entities with common manifestations have been described and new treatment approaches are now of particular interest. The paper discusses the classification of Pann based on the localization of the key morphological changes and the presence or absence of vasculitis. The clinical and morphological features of the two most common forms of Pann, lobular and septal Pann without vasculitis – Erythema nodosum, and lipodermatosclerosis, have been reviewed. An algorithm for the clinical diagnosis of these two conditions was also presented.

**Key words:** panniculitis, inflammatory diseases, diagnostics
STRUCTURE OF HEALTH-CARE VISITS IN RHEUMATOLOGY OUTPATIENT PRACTICE IN BULGARIA FOR THE PERIOD 2006-2011 YEAR

N. Nikolov¹, M. Panchovska² and Zl. Kolarov³

¹Rheumatology Unit, Medical University – Pleven
²Department “Propedeutics of Internal Medicine”, Medical University – Plovdiv
³Clinic of Rheumatology, UMHAT “Sv. Ivan Rilski” – Sofia

Summary. The term “musculoskeletal disorders” includes all diseases affecting bones, joints, periarticular structures and muscles, all types of arthritis, systemic connective tissue diseases, back pain, bone diseases such as osteoporosis, soft tissue rheumatism, and any rheumatic pain. There are many other possible causes such as mechanical problems, injuries, age-related changes or inflammatory diseases. Some of these diseases are sporadic, but many of them have relapsing or chronic course and can be life-threatening. They are the most common causes of disability. Although many of these diseases are limited to the musculoskeletal system, many of them also affect other organs and systems and their management is complex. The structure of rheumatic diseases in primary care and in hospital practice, gives important information on the incidence of various rheumatic diseases. This is important for better planning of resources – personnel, facilities and finances, but also for adequate professional relationships in the interest of the patient. There have been many studies looking for a correlation between the different components affecting the prevalence of rheumatic diseases, age, gender, ethnicity, economic status of the individual and others. This review presents the structure of morbidity in rheumatology practice in Bulgaria and compares it with data from other countries.

Key words: rheumatic diseases, morbidity, structure

RESULTS FROM A SURVEY AMONG 350 PATIENTS WITH RHEUMATIC DISEASES FROM BULGARIA

N. Nikolov¹, M. Panchovska² and Zl. Kolarov³

¹Rheumatology Unit, Medical University – Pleven
²Department “Propedeutics of Internal Medicine”, Medical University – Plovdiv
³Clinic of Rheumatology, UMHAT “Sv. Ivan Rilski” – Sofia

Summary. From the occurrence of the first symptoms of rheumatic diseases to the first examination by a GP and the referral to a specialist in rheumatology, different period of time passes, sometimes long and hard enough. An analysis of the path that a rheumatology patient walks in primary care gives us information why correct diagnosis and adequate treatment are often delayed. Extensive analysis of the patient’s experience in primary care is essential in order to find the reasons for the delay of the correct diagnosis and proper treatment, as well as identify and implement the necessary mechanisms for its optimization. The article represents an analysis of a survey conducted among 350 patients with rheumatic diseases in five outpatient rheumatology centers in Bulgaria. Patients’ attitudes about medication, occurrence of side effects, and the reasons for the delayed diagnosis have been discussed.

Key words: rheumatic diseases, survey, adverse drug events

VASCUITIS AS EXTRAPULMONARY MANIFESTATION OF TUBERCULOSIS

D. Kalinova¹, Tsv. Yoneva¹, V. Stoyanova², P. Kratunkov² and R. Rashkov¹

¹Clinic of Rheumatology, UMHAT “Sv. Iv. Rilski” – Sofia
²SHATCVD “Sv. Ekaterina” – Sofia

Summary. The vasculitides are a heterogeneous group of diseases, characterized by inflammation of blood vessel walls, with subsequent tissue destruction and/or organ failure. A relationship between tuberculosis infection and different types of vasculitis – hypersensitivity vasculitis, Takayasu’s arteritis, central nervous system vasculitis, erythema nodosum, erythema induratum, retinal vasculitis, etc. have been described in the literature. The objective of this study was to analyse a form of vasculitis in six patients with tuberculosis – active or latent.

Key words: vasculitis, tuberculosis, pathogenesis
COMPARISON OF THE EFFECTIVENESS OF LOCAL LONG-ACTING CORTICOSTEROID INJECTION, ADMINISTERED IN THE SUBACROMIAL-SUBDELTOID BURSA UNDER SONOGRAPHIC GUIDANCE VERSUS “BLIND” INJECTION IN PATIENTS WITH BURSITIS

R. Nestorova¹, E. Naredo², R. Rashkov³, Zl. Kolarov³, R. Stoilov³, Tsv. Petranova³, I. Sheytanov³, S. Monov³, M. Panchovska⁴ and A. Batalov⁵

¹Rheumatology Center “Sv. Irina”, Sofia, Bulgaria
²Hospital General Universitario Gregorio Marañón, Madrid, Spain
³Clinic of Rheumatology, Medical University – Sofia
⁴Department of Propedeutics of Internal Medicine, Medical University – Plovdiv
⁵Clinic of Rheumatology, Medical University – Plovdiv

Summary. The objective of the study was to compare the effectiveness of local long-acting corticosteroid injection (betamethasone) 7 mg/1 ml, injected in the subacromial-subdeltoid bursa (SASDB) under sonographic guidance versus “blind” injection in the SASDB in patients with bursitis. Thirty-five patients with bursitis were divided into two groups. Patients with previous trauma or arthritis were excluded from the study. Patients in Group 1 (G1) received blind corticosteroid application in the SASDB (n = 17) and patients in Group 2 (G2) received sonographically guided injection in the SASDB (n = 18). Each patient was clinically and sonographically assessed 6 weeks after the procedure. Clinical evaluation included demographic and clinical data, the visual analogue scale (VAS) for pain (0-100 mm) and the Shoulder Function Assessment (SFA) scale (0-70). Six weeks after the injection, the VAS and the SFA scores showed a significantly greater improvement in G2 compared to G1 (mean change in VAS 35.7 for G2 versus 17.5 for G1, p < 0.001. The mean change in SFA score was 18 for G2 versus 6 for G1, p < 0.001. There were no ultrasonographic features of bursitis in 65% of G2 patients versus 48% of G1. In conclusion, the use of local corticosteroid injection in the SASDB under sonographic guidance is more efficient. We recommend it in patients with insufficient response to blind corticosteroid injection.

Key words: sonographic guidance, corticosteroid injections, subacromial-subdeltoid bursitis

DRUG INFORMATION

ABBOTT’ S HUMIRA® (ADALIMUMAB) – THE FIRST BIOLOGICAL AGENT IN THE EUROPEAN UNION WITH DATA PROVING ITS 10-YEAR CLINICAL EFFICACY IN RHEUMATOID ARTHRITIS