D. Dimov. GOUT IN WOMEN. I. THE OCCURRENCE AND RISK FACTORS

**Summary.** On the background of the progressively increasing occurrence of gout over the last half a century, the rate of its multiplying among females is ahead to that among males. Within the Europeid race the women's part amidst all gouty patients grows up from the classic 2-5% to 15-24%, and with respect to the feminine population the incidence of gout gets to 0.2% and the prevalence – to 0.23%. The risk factors of gout in women are still not sufficiently purposefully investigated and about them it is judged by analogy with those in men or on the basis of comparative observations. Only the role of menopause is indisputable. In comparison with men, the alcohol intake participates more rarely and weakly, the obesity has somewhat smaller significance, how ever, the bigger role of arterial hypertension, chronic renal failure and systematic diuretic use is accepted. Dietary factors, uninvestigated in women, probably have the same share as in men. The link with diabetes mellitus, some endocrinic disorders and mini-dose aspirin remains unspecified. The acquaintance and conforming with the risk factors of female gout is a prerequisite for a bigger success of its prevention and management.

**Key words:** gout, women, incidence, prevalence, risk factors

R. Nestorova, S. Zheleva and S. Monov. BISPHOSPHONATES AND OSTEONECROSIS OF THE JAW

**Summary.** The objective of the presented study is to examine the epidemiologic, pathogenetic and clinical features as well as the treatment possibilities for osteonecrosis of the jaw. The pathogenetic mechanism of the osteonecrosis of the jaw following bisphosphonate administration is still unknown. High dose or long-term bisphosphonate treatment, invasive dental/surgical therapeutic procedures, periodontitis, and others, are suggested as possible risk factors for the development of osteonecrosis of the jaw. Clinically, the disease is manifested by maxillary/mandibular bone exposure persisting for at least 8 weeks and in the absence of preceding radiotherapy of the jaw. The disease course may exclude pain regard less of the bone damage and teeth loss observed. No effective treatment is still known.

**Key words:** osteonecrosis of the jaws, bisphosphonates, osteoporosis, treatment

M. Baleva and F. Martinova. ANTIPHOSPHOLIPID SYNDROME AND HLA

**Summary.** The etiology and pathogenesis of the antiphospholipid syndrome (APS) are complicated and basically unknown. There is some scarce data for the correlation between APS with a certain haplotype. According to the literature, there is higher prevalence of HLA DR4, DR8, DQA1, DR53, DQ8, as well as lower prevalence of DRB1, DQB1, HLA DQB1. The main obstacles and limitations for the genetic studies in patients with APS are due to the selection of the patients, the influence of the concomitant medications, the activity of the disease, the geographic and racial differences. From that point of view, the multicentric, multinational studies are of great significance and will elucidate the problems in antiphospholipid syndrome.

**Key words:** antiphospholipid syndrome, HLA

S. Lambova. THE ROLE OF CAPILLAROSCOPY IN RHEUMATOLOGY

**Summary.** Aim of the author was to study and systematize current knowledge about the role of capillaroscopy in rheumatology and the necessity to evaluate microcirculation in patients with rheumatic diseases. Capillaroscopy is a non-invasive, inexpensive, easy to repeat method which is of great importance in evaluation of microcirculation in vivo. Capillaroscopy is unique for assessment of morphology of nutritive capillaries of nail-fold. It is of crucial value for diagnosis and differentiation of primary and secondary Raynaud’s phenomenon (RP) in rheumatic diseases. Capillaroscopic pattern of a digit is surprisingly constant in healthy subjects for long periods of time, while appearance of abnormal capillaroscopic picture possesses high positive predictive value for development of systemic rheumatic disease. The most specific finding is found in scleroderma – so called scleroderma pattern which is characterized by presence of dilated capillaries, haemorrhages, avascular areas and angiogenesis. Scleroderma pattern is found in more than 90% of patients with overt scleroderma. Similar changes are found in patients with dermatomyositis, mixed connective tissue disease,
undifferentiated corrective tissue diseases, overlap syndromes, and are called scleroderma-like pattern. Interesting is the correlation between capillaroscopic pattern and clinical picture, laboratory analysis and activity of the disease. Capillaroscopy may be used for control of therapeutic response. The position of capillaroscopy in rheumatology has to be strengthened. It should be performed and interpreted by rheumatologist.

**Key words:** capillaroscopy, Raynaud’s phenomenon

**ORIGINAL ARTICLES**

**St. Andreev, A. Batalov, E. Kamberov, Yul. Nikolova, F. Nikolov and B. Trifonov.** SYNTHETIC PEPTIDES OF ENTEROCYTE GROWTH FACTORS (ISOLATED FROM ENTEROCYTE STEM CELLS IN ADULTS) STIMULATE PROTEOGLYCAN BIOSYNTHESIS IN RAT ARTICULAR CARTILAGE (IN VITRO)

**Summary.** The aim of the study was to determine the effects of synthetic enterocyte growth factors, stimulating and inhibiting, [ECGF(s), ESGF(i)] on the synthesis of articular cartilage proteoglycans (PGs) in young, sexually mature, and adult rats of both sexes in vitro. Cartilage explants from knee and hip joints of BD-6 adult rats were incubated in serum-free medium for 4 days. The cultures were supplemented with ECGFs or ESGFi during the last two days. Synthesis of PGs and peptides was measured by the incorporation of $^{35}$S-sulfate and $^{3}$H-serine. The size, sulfate level and serine/sulfate ratio of the newly synthesized glycosaminoglycans (GAGs) were determined by gel-chromatography, high performance liquid chromatography (HPLC) and ion-exchange chromatography. ECGF(s) and ECGF(i) stimulated articular PGs synthesis in the rats of all three age groups in both sexes. The newly synthesized GAGs were identical in size and content with these of the control tissues. Their serine/sulfate ratio remained unchanged. These results suggest a role of ECGFs as distant and exogenous regulators of articular cartilage matrix macromolecules in maintaining the matrix integrity of joint cartilage.

**Key words:** growth factors, proteoglycans, cartilage explant, enterocyte growth factors (ECGFs)

**S. Lambova, St. Kuzmanova, Yul. Nikolova, R. Ivanova, T. Tsvetkova, T. Deneva and N. Petrova.** PLASMA ENDOTHELIN-1 LEVELS IN SYSTEMIC SCLEROSIS: CORRELATION WITH CLINICAL MANIFESTATION AND NAILFOLD CAPILLAROSCOPIC FINDINGS

**Summary.** Objective of the study was to evaluate the association of capillary microscopic findings with clinical manifestation, severity of Raynaud’s phenomenon (RP), and plasma level of endothelin-1 (ET-1) in systemic sclerosis patients. 20 women with systemic sclerosis (mean age 52 ± 6,23 years) were included in the study. 17 patients with primary RP were used as a comparative group (mean age 43 ± 8,55 years). Nailfold capillaroscopy was performed; and following parameters were evaluated: shape of capillaries; arrangement; capillary width, presence of dilated and giant capillaries; number of capillaries and presence of avascular areae; hemorrhages, bushy capillaries and angiogenesis. The severity of RP was evaluated by the physician and the patient with VAS (100 mm). Plasma level of ET-1 was measured by ELISA kit, Biomedica. For statistics, correlation analysis, analysis of empiric distribution with nonparametric test of H0 hypothesis, Student-t test were used. Abnormal capillaroscopic pattern was found in all the patients with systemic sclerosis (100%) – dilated and giant capillaries, avascular areae and hemorrhagic spots. Among the patients with primary RP, capillaroscopy was abnormal in 2 patients (12%). It was found statistically significant difference of plasma levels of ET-1 between patients with scleroderma and comparative group with primary RP (p < 0,05). It was found that elevated plasma levels of ET-1 correlate with presence of avascular areae and severity of RP. Nailfold capillaroscopy is a useful, non-invasive and low-cost method for evaluation of the microcirculation in patients with systemic sclerosis. It was found that elevated plasma levels of ET-1 correlate with presence of avascular areae and severity of RP.

**Key words:** systemic sclerosis, capillary findings, endothelin-1

**CASE REPORTS**
Summary. Vitamin D (VD) is a hormone, traditionally included in the group of the fat-soluble vitamins. It has two sources – alimentary VD$_2$ (ergocalciferol) and VD$_3$ (cholecalciferol) derived during a photobiochemical process in the skin with the contribution of ultraviolet-B radiation and skin temperature, and, in a lesser amount, from dietary origin. Further, they both undergo analogous activation by two consecutive hydroxylations to 25(OH)D in the liver and to 1α,25(OH)$_2$D (calcitriol) in the kidney. The renal 1α-hydroxylation carried out by 25(OH)D-1α-hydroxylase in the proximal tubules is crucial for the synthesis of the active metabolite and the implementation of the biological effect of VD. Calcitriol is a steroid hormone, playing an important role in calcium/phosphorus (Ca/P) regulation, bone modeling and metabolism, but also in the cell proliferation and differentiation of many other tissues. It binds selectively to the VD receptor (VDR) – a phosphoprotein member of the nuclear receptor family, followed by transcription activation of specific genes, which products determine the biological effect. VD deficiency can cause rickets, osteomalacia, and other disturbances of Ca/P homeostasis. The syndromes of VD-resistance represent a group of diseases, caused by impaired metabolic activation of calcitriol or by its dysfunction in the target tissues. Mutations of the 1α-hydroxylase gene cause vitamin D-dependent rickets type I (VDDR I), also known as pseudovitamin D$_2$-deficient rickets (PDDR). Some mutations in the VDR result in vitamin D-dependent rickets type II (VDDR II), also known as hypocalcemic vitamin D-resistant rickets (HVDRR). X-linked hypophosphatemic rickets also participates to the group of VD-resistant rickets. Tree clinical cases of familial, sporadic and hypophosphatemic rickets are presented.

Key words: Vitamin D, rickets, osteomalacia, hypophosphatemia