Comment

This issue of "Postępy Nauk Medycznych" focuses on various aspects of osteoarthritis (OA), osteoporosis (OP) and pleiotropic influence of Vitamin D. We present conceptual papers and empirical studies with the aim of passing knowledge to doctors, who in their daily practice deal with results of bone and joints dysfunction due to OP, OA, and general deficiency of Vitamin D.

In the article on genetically determined and acquired factors predisposing to osteoarthritis or osteoporosis, the authors present new arguments for the genetic influences on OA or OP as well as show various factors that predispose for the development of OA or OP. Those arguments arise from the epidemiological studies of OA and osteoporotic fractures, studies on the bone and articular cartilage metabolism, the role of kind and location of adipose tissue, the role of muscle tissue, especially the role of subchondral bone in pathogenesis of OA and the results of antiresporption treatment in OA. It is important to remember that even with the differences in bone characteristic in patients with OA and OP, antiresorption treatment is beneficial. In case of OP it is related to the imbalance of making and resorption (more resorption), and the anticatabolic influence on articular cartilage (shown in the publication "Antiosteoarthritic effect of estrogen β-receptor modulator in postmenopausal women with knee osteoarthritis and osteopenia") begins a new understanding of the role of bone in pathology of articular cartilage.

Epidemiology of osteoporotic fractures in Europe and in Poland is discussed, pointing attention of the readers to the fact that difference in prevalence of osteoporotic fractures in various populations may be related to age, gender, region of the world and socioeconomic conditions. The authors stress the fact of increased fractures of proximal femur in majority of countries, which is related to the process of aging of population across the world. It is important to know the epidemiological data because those data show the necessity of effective prophylactics of osteoporotic fractures.

In one of the articles, an important issue of glucocorticoid-induced osteoporosis was raised. The authors stress the fact that glucocirticosteroid (GS) intake is the main cause of secondary osteoporosis and write that the prevalence of chronic GS use is over 0,5% in general population, but only 15% of these patients are receiving treatment of osteoporosis. These data show that glucocorticoid-induced osteoporosis (GIOP) is an underestimated and undertreated condition. The authors present a systemic literature review on pathophysiology, clinical picture and treatment of GIOP, and describe recent guidelines for GIOP management. The article can be a good source of guidelines for doctors dealing on every day basis with patients on corticoid therapy.

In another article, the authors point out that bone complications, including periarticular erosions as well as local and generalized osteoporosis, are typical symptoms of chronic inflammatory joint diseases and can lead to increased fracture risk. Recent findings show that good control of generalized inflammatory process is the main target for management of osteoporosis.

The issue of falls has also been raised. In 2007 WHO recognized falls to be one of the most important health and social issues of the aging populations. Falls are one of the main causes of disability and the fifth most frequent causes of death above the age of 75. The authors write that reports regarding a protective influence of vitamin D on falls and fractures are diverse. They conclude that, in case of severe vitamin D deficiency, calcium and vitamin D supplementation reduces fall risk and the frequency of fractures, whereas in case of normal vitamin D levels in serum these effects are insignificant.

In the articles regarding Vitamin D, the authors present a review of literature which led them to write that Vitamin D is necessary not only for maintaining appropriate metabolism of calcium and phosphorous, function of bone in the organism, but also for appropriate functioning of various tissues and organs not related to mineral metabolism.

In the first paper the authors focused on Vitamin D as a factor responsible for appropriate functioning of bone. They discuss the influence of $1,25(OH)_2D$ which is a steroid hormone encouraging the metabolism of calcium and phosphorous. Numerous direct and indirect effects of $1,25(OH)_2D$ have been demonstrated on a range of critical bone proteins and $1,25(OH)_2D$ appears to be involved in their regulation at all stages of osteoblast differentiation and, indeed, bone remodeling. $1,25(OH)_2D$ uses VDR to regulate calcium absorption leading to increased capacity of the intestine to absorb calcium and acts on the PTH gene to decrease its transcription. This information is important for understanding why for individuals with low bone mass, when diagnosing its etiology, one should pay attention to vitamin D deficiency.

The immunomodulating effects of vitamin D were discussed with respect to rheumatoid arthritis (RA) showing that in patients with RA are related to a decrease in the number of Th1 and Th17 lymphocytes, to an increase in the number of Th2 and T-reg cells as well as to diminishing the production of proinflamma-

tory cytokines together with increasing the secretion of antyinflammatory cytokines. An inverse relationship between serum level of 25-OH vitamin D and early onset polyarthritis, severity of the disease as well as a degree of disability of the patients with RA were reported and this is a reason for Vitamin D supplementation for this pathology.

The role of Vitamin D in the modulation of innate immune system function and the body's response to microorganisms was described in the article "Vitamin D and respiratory tract." It takes an active part in the production of natural antibiotics which are also called natural antimicrob al antibiotics (PAD) using Toll-like receptor pathway (TRL) present on monocytes and macrophages. The scientific results sound promising, but there is still a long way to draw conclusions about doses and use of vitamin D in diseases of the respiratory system.

The empirical paper "A C-159T polymorphism of CD14 receptor and polymorphism of TLR4 gene in patients with alcoholic fatty liver and alcoholic cirrhosis" describes the role of receptors CD14 and TLR4 in increased immunological reaction.

Calcitriol impact on cell cycle, the induction of apoptosis and the regulation of expression of different proinflammatory cytokines and growth factors shows the anticancer activity of vitamin D in the digestive tract. Both excess and deficiency of vitamin D have impact on the immune system, and may interfere with cellular immune response. It is associated with the development of e.g. inflammatory bowel disease.

In the article "The role of vitamin D in the diseases of cardiovascular system" the authors explain the mechanisms of direct and indirect influence of Vitamin D on the cardiovascular system. Findings suggest profitable influence of vitamin D on the cardiovascular system. The majority of studies, however, are animal, epidemiological and observational studies which are less reliable than interventional, randomized ones. The studies performed as yet are not sufficient to recommend general vitamin D supplementation in the prevention of cardiovascular disorders.

The paper "Obesity – the condition predisposing to vitamin D deficiency" shows that obesity is related to deficiency of Vitamin D, which is more common than in patients with proper body mass. Obesity is associated with various co-morbidities such as cardiovascular diseases, diabetes, cancer (prostate, breast and colon cancer). Thus, it is necessary to supplement Vitamin D deficiency in the obese. The relationship between low circulating 25-hydroxyvitamin D concentration and obesity and between adipose tissue as an endocrine system and Vitamin D metabolism show the complexities of the problem.

The authors of article "Vitamin D provision and supplementation standards" stress that the problem of vitamin D deficiency seems rather as an endocrine than nutritional issue. 1α,25-dihydroxyvitamin D [1α,25(OH)$_2$D], an active form of vitamin D, is a member of genome operated hormone superfamily, but the only one , which synthesis is permanently limited by substrate shortage 25(OH)D. Therefore, proper serum 25(OH)D concentration is the primary target, and achievement and maintenance of proper vitamin D status is crucial for vitamin D effectiveness and health benefits. A target range of 30-80 ng/ml serum 25(OH)D concentration is recommended as effective and safe which was evidenced by various studies. However, lack of RTC trials which would provide enough evidence for the thesis of improvement of the biochemical and clinical indicators in cardiovascular disease, auto immunological diseases, including diabetes Type 1, complications in insufficiency of renum stage II-III, muscle-scheletal diseases and the organism's immunity when the optimal concentration of 25(OH)D in serum (30-80 ng/ml) makes is more difficult to state clear guidelines for supplementation.

Deciding what is appropriate supplementation of Vitamin D may be easier when using VITAL study (a 5-year RTC observation of 20 000 individuals older than 65 years of life). The study will measure the effects of daily supplementation of Vitamin D (2000 IU/day) and fatty acids Omega 3 (1 g/day) on the risk of cardio-vascular disease and cancer.

It is important to state that nowadays the basis for recommendations for supplementation of Vitamin D and calcium for postmenopausal women and men after 65 years of age is based on the meta analysis done by Tang et al. (RTC trials). In this study it was shown that calcium intake of 1200 mg/day by itself or combined with Vitamin D (800 IU/day) decreases the risk of osteoporotic fractures. Those issues are discussed in detail in the paper on calcium and Vitamin D in prevention of osteoporotic fractures.

Research on the possibility of forming urinary tract stones during Vitamin D supplementation, especially with calcium supplementation, is presented in the paper "Prevention and treatment osteoporosis and urolithiasis." Based on published research the authors state that appropriate intake of calcium and Vitamin D may limit the danger of crystalline calcium oxalate and apatite in the urinary tract.

In the paper "Comparison of two automated serum 25(OH)D assays – the experience of pediatric hospital laboratory participating in DEQAS proficiency testing" the performance of two recently developed automated 25(OH)D Total assays (LIAISON and ELECSYS) was compared using pediatrician samples and results of DEQAS (The International External Quality Assessment Scheme for Vitamin D Metabolities). Automated 25(OH)D Total

assays, LIAISON and ELECSYS demonstrated good intra- and inter-assay precision. Both methods showed good accuracy according to HPLC and LC-MS in DEQAS system. Precision of automated 25(OH)D Total assays by LIAISON and ELECSYS are very high and comparable which is important to know for doctors who have to interpret the results of 25(OH)D tests, which are often recommended, especially for patients from risk groups for Vitamin D deficiency.

Prof. dr hab. med. Ewa Marcinowska-Suchowierska
Head of the Department of Family Medicine,
Internal and Metabolic Bone Diseases
Medical Centre of Postgraduated Education