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**Congress Report: The II
International Symposium "Bone and
Joint Diseases and Age": The Review
of Basic Topics**

Kuprinenko N

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Congress Report

The II International Symposium “Bone and Joint Diseases and Age”: The Review of Basic Topics*

N. Kuprinenko

For scientists and practical physicians who are interested in problems of osteoporosis and other bone and joint diseases spring 2016 has begun with a significant scientific event. On March 9–11th the II International Symposium “Bone and Joint Diseases and Age” was held in Lviv (Ukraine). The organization of this symposium can be called a continuation of tradition that was started a year ago by the Ukrainian Association of Osteoporosis, the Austrian Society of Bone and Mineral Research, and the Slovak Society for Osteoporosis and Metabolic Bone Diseases under the aegis of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases. Then this International Symposium was held for the first time and had a great interest not only among Ukrainian scientists and physicians, but among lectures from abroad. And the II International Symposium, that was organized this year, had greater scope because of more lecturers from abroad, over a wide range of topics, and the larger number of participants. As venue of the II International Symposium “Bone and Joint Diseases and Age” was chosen the Lviv House of Scientists. It was built in 1897 by the famous Austrian architects Fellner & Helmer. Rich noble interior in classic style inspired all the participants for serious productive work. Comfortable lecture halls provided the opportunity to all necessary technical support for the conference. Also the simultaneous translation of lectures, presentations and discussions was provided, so all the participants of the symposium could focus on new professional useful information.

Seven scientific sessions and three round tables were held and more than 70 lectures and reports were presented during three days of productive work. It was very honorable that this year scientists from 17 different countries of Europe and from the USA attended the Symposium and presented their lectures. Among them were leaders of the two major international foundations in the study of osteoporosis in the world – Professor John A. Kanis, President of the International Osteoporosis Foundation (IOF), and Professor Jean-Yves Reginster, Presi-



dent of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). The II International Symposium “Bone and Joint Diseases and Age” was their first time of being in Ukraine as well as their first time of attending the scientific medical event in this country. That’s why before the Opening Ceremony we asked them about their impressions, their plans and hopes for the next three scientific days.

Professor John A. Kanis: *“I am looking for discussion with Ukrainian physicians about fracture risk in Ukraine, about the extension of using FRAX for evaluation of risk of osteoporosis. Also the management and treatment of osteoporosis had followed up during last years, and I believe to pay attention to these topics here. It is my first time of visiting Ukraine and I believe to learn something about this country, at least to see the beautiful Lviv.”*

Professor Jean-Yves Reginster: *“This conference is mostly important in sense of clarifying of critical issues of aging process of bone, joints and muscles. Today the population is aging all around the world and particularly in Eastern Europe because of the increasing of life expectancy. This means that we have more patients suffering from osteoporosis, osteoarthritis and sarcopenia. The conference is able to gather scientists from 17 countries and to cover most important clinical aspects of bone and muscular diseases and aging medicine.”*

The Opening Ceremony started with the welcoming speech of Professor Vladyslav Povoroznyuk, President of the Ukrainian Association of Osteoporosis. On behalf of the members of the organization committee, Professor V. Povoroznyuk thanked all participants and all lecturers for their attendance in this scientific event and expressed the gratitude to the National Academy of Medical Sciences of Ukraine, National Society of Gerontology and Geriatrics of Ukraine, Institute of Gerontology named after D.F. Chebotarev NAMS of Ukraine, Lviv National Medical University named after Danylo Halytsky, Lviv City Council and to the Ukrainian Medical Association in Lviv for their assistance in organizing the International Symposium.

The scientific program of the symposium started with the lecture “FRAX in clinical practice”, that was presented by **Prof. John A. Kanis, the IOF President (United Kingdom)**. Prof. J. A. Kanis reminded the definition of osteoporosis (a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent

increase in bone fragility and susceptibility to fracture), common sites of osteoporotic fractures (spine, hip, wrist) and risk factors of osteoporosis in population. He emphasized that the prevalence of hip fracture in most countries worldwide was in the range between 200 and 600 incidences per 100,000/year. And FRAX was the main tool for assessment of the 10-year probability of major fracture and hip fracture. The using of the FRAX algorithm let us predict fractures with higher accuracy than just using of bone mineral density (BMD). Nowadays

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FRAX is available in 58 countries and lets cover about 70 % of world population. This method of fracture risk prediction was incorporated into more than 80 assessment guidelines. There was no own model of FRAX in Ukraine, but we would work on it.

Prof. Jean-Yves Reginster, the ESCEO President (Liege, Belgium) presented two lectures – about vitamin D and calcium and about sarcopenia. The fact that calcium supplements with vitamin D are an important therapy to prevent bone loss and reduce the risk of fractures, especially in the elderly, was well-known and evidenced in numerous studies. But there were a lot of discussions about the influence of calcium supplements on cardiovascular risk. Prof. Jean-Yves Reginster presented the review of some large studies and meta-analysis where the role of calcium supplementations, vitamin D and both calcium and vitamin D supplements on risk of cardiovascular events, including myocardial infarction (MI), cardiovascular death and stroke, in various cohorts of people was investigated. The basic conclusions were: no effects of calcium supplements on stroke or mortality, coronary artery calcification were accelerated. In some trials calcium supplements (without vitamin D) in doses above 1400 mg/day, in women, were associated with higher death rates from all causes and cardiovascular diseases but not stroke. And none of the trials had cardiovascular outcomes as the primary endpoints, none of the trials had adjudicated cardiovascular outcomes in standardized manner, inconsistent data in individual studies, findings did not apply to combined use of calcium and vitamin D, all-cause mortality reduced in patients given calcium and vitamin D. In the conclusion of the lecture, Prof. Jean-Yves Reginster paid attention to the mandatory adjunction of vitamin D and calcium supplements in addition to anti-osteoporosis drugs. Calcium supplement in a dose of 500 mg/day is mandatory to use in patients who get risedronate; vitamin D in a dose of 400 IU and more is mandatory in case of using strontium; both calcium (in dose from 500 to 1200 mg/day) and vitamin D (in dose of 400 IU) are mandatory with raloxifene, teriparatide, ibandronate, zoledronate, PTH, bazedoxifene, lasofoxifene. Only in case of using alendronate the prescription of calcium supplement and vitamin D is not mandatory; these supplements are recommended in cases of low calcium and vitamin D plasma levels.

The second lecture of Prof. Jean-Yves Reginster was focused on the “pitfalls” in the problem of sarcopenia. Sarcopenia was characterized by progressive and generalized loss of skeletal muscle mass and strength which is associated with increased risk of negative outcomes, including mobility disability, falls, hospitalization, poor quality of life and death and it was a major pathway that led to physical frailty. Sarcopenia had a high prevalence in older population. Diagnostic criteria of sarcopenia were a decrease in muscle mass and strength and/or speed. The European Working Group on Sarcopenia in Older People (EWGSOP) recommended using the presence of both low muscle mass and low muscle function for diagnosis of sarcopenia. According to EWGSOP criteria, sarcopenia in older patients (> 65 y.o.) was diagnosed in cases of gait speed ≤ 0.8 m/sec, grip strength < 30 kg for men and < 20 kg for women, muscle mass < 7.25 kg/m² for men and < 5.5 kg/m² for women. FNIH (Foundation for the National Institutes of Health) criteria of sarcopenia included grip strength < 30 kg

for men and < 20 kg for women, appendicular lean mass (ALM) < 0.789 for men and < 0.512 for women. Nevertheless both Consensus have included objective measure of muscle/lean mass and both have incorporated muscle weakness or reduced physical functioning into the definition. In addition to the grip strength some other tests can be used for evaluation of muscle strength and function (4-meter walking speed, 6-min. walking test, 400-meter walking test, 5-time chair stand, lower and upper limb press, stair climbing, Short Physical Performance Battery [SPPB]). The SarQol questionnaire was recommended for patient self-assessment of quality of life. Potential treatments of sarcopenia were under development, but there were no guidelines to support regulatory studies for new chemical entities. In the conclusion Prof. Jean-Yves Reginster outlined the key issues of sarcopenia investigations that required the focusing of attention. They included the presence of numerous gaps in knowledge, particularly in risk assessment and the necessity to build the risk model similar to FRAX for osteoporosis. Also the value of indexing threshold values for sarcopenia measures and outcomes needs to be further investigated, using risk-based analysis for one of the strong clinical endpoints. The consensus core outcome set would bring standardization and comparability to research in sarcopenia and therefore would help improve the evidence base.

The lecture of **Prof. Heinrich Resch (Austrian Society of Bone and Mineral Research, Wien, Austria)** has proved that medicine is an art, and art can help physicians, patients and investigators. During the lecture all participants could forget about modern serious scientific topics and fly away in their thoughts to the world of art legacy. Professor Heinrich Resch demonstrated some well-known pictures of famous artists of last centuries and noticed that if we look at their characters not only watching on story, dresses and background, but paying attention to details, such as the skin colour, skin condition, joints, limbs, nails, we'll see symptoms of some diseases. For example, there were a lot of cases of rheumatoid arthritis, gout, osteoporosis and osteoarthritis in characters of pictures of Sandro Botticelli, Pierre Renoir, Jacob Jordaens, Marc Hodler, Diego Velázquez, Pinturicchio Bernardino di Betto, El Greco, Vincent van Gogh etc. This let us conclude that these diseases were widespread in last century and were the cause of short life expectancy.

Prof. Juraj Payer, President of the Slovak Society for Osteoporosis and Metabolic Bone Diseases (Bratislava, Slovakia), presented the lecture about effects of growth hormone (GH) on bone. GH had an anabolic effect on bone *in vitro* and *in vivo*. Effects were mediated by insulin-like growth factor 1 (IGF-1) which was produced mostly by the liver. The impact of GH on bone in various periods of life included the stimulation of longitudinal bone growth in childhood, stimulation of bone maturation to achieve “peak bone mass” (main predictor of fracture) in adolescence and maintenance of bone mass through bone regulation in adulthood. Data about bone quality in patients with growth hormone deficiency (GHD) were scarce as well as the effect of GH on trabecular bone score (TBS) was not well documented yet. Professor Juraj Payer presented results of a study that was made by his colleges and him. The objective was to compare effect of recombinant GH (rhGH) on BMD and TBS, to assess risk factors of rhGH effect on bone and to

assess the impact of rhGH on bone with regard to vitamin D status. The investigators have concluded that GH replacement in adults with growth hormone deficiency (GHD) led to BMD increase, preferentially in males and patients with childhood onset GHD (CO-GHD). GH-induced trabecular bone score (TBS) increase was greater in females and CO-GHD. In adult patients with GHD (AO-GHD) the improvement of TBS was observed only in patients with higher 25(OH)D levels. GH replacement of GHD adults positively affected on bone tissue after growth plate closure, and decreased future fracture risk. Maybe that optimal effect of GH treatment to improve bone quality, represented by TBS, in GHD adults was achieved only in those with sufficient 25(OH)D levels.

Prof. Vladyslav Povoroznyuk, President of the Ukrainian Association of Osteoporosis (Kyiv, Ukraine), told about the situation with osteoporosis and musculoskeletal diseases in Ukraine and presented activities and achievements of the Ukrainian Association of Osteoporosis. The average life expectancy in men in Ukraine was 65.2 years, in women – 75.3 years. As in other countries, the aging of population in Ukraine progressively increased and in 2013 about 15.7 % of people were in age 65 and over. The prognosis was that to 2050 about 21 % of the population in Ukraine would be in age 60 and over. The Ukrainian Scientific Medical Centre of Osteoporosis started working in Kyiv in 1998. Later Regional Medical Centers of Osteoporosis were opened in large cities of the country. Osteoporosis, vitamin D status and calcium intake levels in Ukrainian population have been studied a lot during the last decade. Recently in the limelight of medical attention in Ukraine were sarcopenia, the usage of the trabecular bone score (TBS) method in fracture risk assessment, hyperuricemia and neuropathic pain component in patients with knee osteoarthritis. Results of those studies were presented in different scientific meetings in Europe and in the USA and were published in scientific medical journals in Ukraine and abroad.

● Sarcopenia and Dismobility Syndrome

Some reports were devoted to sarcopenia – a topic that has been widely discussed in recent years.

In his report **Prof. Edward Czerwinski (Krakow, Poland)** noticed that sarcopenia incidence increased with age, ranging from 15 % after 60 to as much as 50 % over 85, and aging was one of the main causes of sarcopenia. The development of sarcopenia was also affected by hormonal factors (testosterone, estrogen, growth hormone/IGF-1), humoral factors (subliminal chronic inflammation) and environmental factors (diet, sedentary lifestyle). The only effective methods for both prevention and treatment of sarcopenia were regular physical activity and proper diet. The most effective exercises were resistance exercises, particularly progressive resistance training, affecting both the increase in strength and muscle mass. In turn, the lack of physical activity triggers muscle atrophy. Diet recommendations were focused on proper protein and vitamin D₃ intake. The recommended consumption equaled 0.8–1.2 g of protein per kg of body weight per day. Proteins provided the appropriate course of post-exercise regeneration processes and were an important anabolic stimulus for skeletal muscle. Vitamin D₃ stimulated the synthesis of

myocytes and their differentiation, inhibited apoptosis, affected the conductivity and muscle contraction. Sarcopenia was a fall risk factor. Due to such aging factors as depleting biologic reserves, slow reflexes and osteopenia or osteoporosis, a seemingly harmless fall from own height could have serious consequences and the most serious are fractures. In the elderly people fractures could cause not only pain and temporary immobilisation, but also a permanent impairment of mobility, functional deterioration, increasing morbidity and mortality. Various forms of physical activity were recommended for fall prevention. Regular exercise of moderate intensity was recommended at least 3 times a week: Nordic Walking, Tai-Chi, dancing, brisk walking.

Results of studying sarcopenia in Ukrainian women were presented by **Natalia Dzerovych (D. F. Chebotarev Institute of Gerontology NAMS of Ukraine, Kyiv, Ukraine)**. 311 healthy women-volunteers aged 20–87 years (mean age – 57.3 ± 0.9 yrs; mean height – 1.62 ± 0.004 m; mean weight – 63.5 ± 0.5 kg, BMI – 24.2 ± 0.2 kg/m²) were examined. No subject had any systemic disorders or took medications known to affect the skeletal and muscle metabolism. Appendicular lean mass (ALM) was measured at all four limbs with DXA. The appendicular lean mass index (ALMI) was also calculated according to the formula: ALM/height (kg/m²). The frequency of sarcopenia increased with age and was the highest in women aged over 80 years (30.8 %). The frequency of sarcopenia in women aged over 65 years was 21.3 %. Also it was determined that dietary protein intake significantly decreases in women with age. In women with lower appendicular lean mass, lower dietary protein was observed. Results confirmed the literature data on the association between dietary protein, amino acids intake and lean (skeletal muscle) mass in older people. In another Ukrainian study (38 postmenopausal women aged 53–82 years) it was determined that using individually targeted vitamin D therapy and OTAGO Exercise Programme during 12 months significantly improves daily activity, muscle strength, quality of life and reduces fall frequency in postmenopausal women.

Prof. Neil Binkley (University of Wisconsin Osteoporosis Clinical Research Program, Madison, Wisconsin, USA) presented the report about dysmobility syndrome. Prof. N. Binkley mentioned that osteoporosis and sarcopenia contributed to falls and fractures risk, but we must remember obesity as a risk factor especially in postmenopausal women. Also the combination of low muscle mass and function (sarcopenia) and high fat mass (obesity) had poor prognosis. It was termed “sarcopenic obesity”. However, rather than focusing on each condition individually, an opportunity existed to combine clinical factors to potentially improve identification of older adults at risk for falls and fractures. Such combination was termed “dysmobility syndrome”. Dysmobility defined as 3 or more symptoms such as high body fat, osteoporosis, low muscle mass, low muscle strength, slow gait or falling risk. To reduce falls and fractures in patients with dysmobility syndrome, all components of it, especially obesity, must be corrected. 2000 IU of vitamin D daily would be a reasonable place to start for optimizing the vitamin D status. Using existing osteoporosis medications to treat the bones were recommended.

● Healthy Aging and Focus on Patients

Prof. Vidmantas Alekna (Vilnius, Lithuania) discussed problems of healthy aging and interface between lifestyle and geriatric syndromes. First of all Prof. V. Alekna mentioned some interesting historical and statistical points about aging. It was known that from the Bronze Age to 1900 (the 6000-year period), the average human life expectancy has risen by only 13 years, from 1900 to 2005 (during 105 years), the average life expectancy has risen by 35 years, life expectancy worldwide has risen on average by 4 months each year since 1970, and in early 2016, the average life expectancy at birth was 68.7 years. In humans, aging represents the accumulation of changes in a human being over time, encompassing significant physical, psychological and social change, and at a biological level, aging is associated with the gradual accumulation of a wide variety of molecular and cellular damage. Physical health is of key importance in healthy aging. Poor health is a characteristic of older people – they have many chronic diseases. But nowadays geriatrics deals with so-called geriatric syndromes. Common multifactorial geriatric syndromes such as dementia, malnutrition, gait and balance problems, sarcopenia, falls, frailty, urinary incontinence and chronic inflammation/increased frequency of infection have shared the risk factors and pathophysiologic mechanisms with multiple chronic diseases. This calls for a unified approach to treatment and prevention of these syndromes, in order to improve health care systems so that the needs of our rapidly aging population can be addressed adequately. In the conclusion Prof. V. Alekna noticed that a change towards a healthy lifestyle made early in life and continued to older ages increases the chance of survival, is most effective for the prevention of diseases and delays the onset of deterioration of health. As healthy lifestyle behaviors are related to survival and health at the age of 70–75 years, and are likely to contribute to healthy aging. Nevertheless, healthy lifestyle does not eliminate all risk factors, that is why a number of older people will anyway suffer from geriatric syndromes.

The report of the **President of the Romanian Association for Osteoporosis Prevention (ASPOR), Prof. Andrea Ildiko Gasparik (Romania)**, was focused on patients with chronic diseases and the role of physicians. The main stream of the report was the hypothesis “the doctor is the drug”. Prof. Gasparik noticed that the interaction “doctor – patient” was affected by the technological progress, the economical, social changes. Physicians played an active role in regulating the quantity of information elicited at the beginning of the clinical encounter. The consequence of this controlled style was the premature interruption of patients, resulting in the potential loss of relevant information. It was estimated that in 69 % of the visits the physician interrupted the patient’s statement, in average after the first 18 seconds, and 54 % basic informations are not transmitted. On the other hand, patients forget 80 % of what clinicians tell them as soon as they leave and almost 50 % of the remembered data is recalled incorrectly. To reduce these factors the “patient-centered” care was provided. It would be help to support active involvement of the patients in the design of new care models, to enhance quality of life and control over the disease, to increase concordance between patient and doctor, to reduce overutilization of diagnostic and therapeutic procedures and to reduce costs and burden of disease.

● TBS in Fracture Risk Assessment

Prof. Didier Hans (Lausanne, Switzerland) is the world expert of using the Trabecular Bone Score method (TBS). In his report he reminded that TBS was a DXA software program that estimated bone texture information and provided fracture risk information that was additive to BMD and clinical risk factors. A higher TBS correlated with better bone microstructure, a lower TBS correlated with a worse one. TBS was officially recognised worldwide as an independent fracture risk prediction tool. TBS was associated with fracture, in women and men, predicted fracture independently from BMD, CRF and FRAX™, including cases of fracture in secondary osteoporosis context (type-2 diabetes, hyperparathyreosis, glucocorticoid-induced osteoporosis). But TBS should not be used alone to determine treatment recommendations in clinical practice. In the second part of the report Prof. D. Hans presented series of clinical cases where the TBS estimating of fracture risk was used.

Prof. Vladyslav Povoroznyuk (Kyiv, Ukraine) presented the results of evaluating TBS changes with age and the role of TBS in fracture risk assessment according to recent literature and Ukrainian studies. In studies of correlation of TBS and age, the significant decrease in TBS values (14.5 % in Dufour R et al. [2013] study; 16.0 % in Simonelli C et al. [2013] study) was obtained for all lumbar vertebral combinations between 45 and 85 years of age. Age-related declines in lumbar spine BMD and TBS were also observed in a large cross-sectional study of 29,407 women ≥ 50 years from the province of Manitoba, Canada [Leslie WD et al., 2013]. Similarly, a negative correlation between L2–L4 TBS and age ($r = -0.39$, $p < 0.001$) was observed in 4907 Lebanese women from 20 to 90 years of age [El Hage R et al., 2013]. In cross-sectional analysis from two facilities in Ukraine and Spain, TBS values were obtained for all lumbar vertebral combinations (L1, L2, L3, L4) [Povoroznyuk V, Del Rio L, Di Gregorio S et al., 2014]. There was a linear decline of 13.5 % (~ -1.75 T-score) in TBS at L1–L4 between 40 and 90 years of age in men whereas a decline of 16.7 % (~ -2.58 T-score) was observed in women. Conversely to women, it seems that there is no modification of TBS decline rate after 65 years in men. The retrospective case-control study by Pothuaud L et al. (2009) evaluated 135 postmenopausal women (45 women had radiographically confirmed osteoporotic fractures). Women with any fracture had significantly lower TBS values than controls (0.784 ± 0.176 versus 0.899 ± 0.177 ; $p = 0.0005$).

TBS in contrast to spine bone mineral density could predict vertebral fractures in men. TBS value ≤ 0.987 was a cut-off point related to over 5× higher risk of vertebral fracture. TBS is significantly lower in fractured men and no significant difference was found for bone mineral density [Lorenc R, 2012].

To evaluate the TBS values (L1–L4) in Ukrainian men depending on vertebral fractures presence, 197 men aged 45–89 years were examined [Povoroznyuk V et al.]. The basic group consisted of 52 men with osteoporotic vertebral fractures in the anamnesis and the control group – of 145 men without fractures. In all age groups (45–59 yrs [$n = 83$], 60–74 yrs [$n = 86$], 75–89 yrs [$n = 28$]) of men with osteoporotic vertebral frac-

tures the TBS values were significantly lower than in men of the control group and were decreased with age.

Thus, it would be concluded that TBS significantly decreased with age; TBS results were lower in women who had sustained a fragility fracture but in whom DXA did not indicate osteoporosis or even osteopenia; TBS predicted fracture risk as well as lumbar spine BMD measurements in postmenopausal women; the combination of any BMD measurement with TBS significantly improved fracture prediction compared with BMD or TBS alone.

● Secondary Osteoporosis

The section of secondary osteoporosis was started with the report of **Prof. Heinrich Resch (Wien, Austria)** about diabetes and bone, in which molecular and clinical findings of diabetic bone disease were introduced. Prof. H. Resch reminded that the anabolic effect of insulin on bone provided the strong association of type-1 diabetes with osteoporosis. Insulin deficiency associated with low BMD altered bone architecture that resulted in increased propensity to fall and higher fracture risk. In the same time during many years type-2 diabetic (T2DM) patients were considered to be protected from fragility fractures. Nevertheless, data of some recent studies have improved the increased risks of fractures in T2DM patients. Specific risk factors were more prevalent in T2DM in cases of poor glycemic control, long-time duration of the diseases, as well as some of the diabetic medications may exacerbate fracture risk. For example, oral glitazones (more in females), thiazolidinediones doubled the fracture risk. Fragility fractures in T2DM may result from diabetes-related alterations in skeletal properties not captured by DXA. In such cases TBS could be an alternative assessment tool. Furthermore, in cases of prescribing medications for the T2DM patients we must remember that even some of the new oral antidiabetic drugs also can harm bone metabolism.

The association of male hypogonadism and bone mass was discussed in the report of **Prof. Mario Rui Mascarenhas (Lisboa, Portugal)**. Normal testosterone levels provided proper protein formation, muscle strength and volume, and bone density. Androgens contributed to osteoblast growth, differentiation, proliferation, increased protein synthesis of bone matrix (osteocalcin, type-I collagen, osteopontin), caused calcium retention and optimized peak bone mass. Hypogonadism is one of the major causes of osteoporosis and osteoporotic fractures in adult men. It was detected a significant low BMD at several skeletal sites in men with postpubertal onset of hypogonadism, as compared with a group with normal gonadal function. Low BMD was in 26.0 % of hypogonadal men vs 9.6 % of men from the control group; osteoporosis was in 39.8 % of hypogonadal men vs 1.4 % of men from the control group. The BMD in men with late onset hypogonadism was reduced at the hip, as compared with the normal gonadal function group. In the same time BMD at L1–L4, at the distal radius and at the whole body was similar between the groups. In hypogonadal elderly men, vitamin D deficiency modified bone and muscle masses. Testosterone therapy (injectable testosterone 200 mg 2–4 weeks, transdermal patch 5 mg nightly and transdermal gel 5 mg daily) inhibited osteoclast activity and increased bone formation. After a mean 3 years of therapy 31 % of the hypogonadal men



Prof. Heinrich Resch (Austrian Society of Bone and Mineral Research, Wien, Austria)

had a normal BMD (7 % more than before treatment). But no reduction in fracture risk was shown in men under androgen therapy and with osteoporosis.

Prof. Ana Paula Barbosa (Lisboa, Portugal) paid attention to the topic of the influence of hypopituitarism on bone structure. Pituitary disorders made different influence on bone and fractures. For example, acromegalia, hypogonadism, hyperprolactinemia increased bone turnover, but hypopituitarism, Cushing's disease, growth hormone (GH) deficiency decreased it. In cases of all these disorders BMD and fracture risk were increased. GH deficiency was the major determinant of bone loss in hypopituitarism. The mechanisms underlying other hormonal deficiencies (ACTH/TSH) were not clarified. Fragility fractures are frequent complications in patients with hypopituitarism, and relatively underestimated and not strictly dependent on BMD (may occur with normal BMD). Higher prevalence of vertebral fractures was in hypopituitary adult patients treated with hydrocortisone in dose > 28 mg/day, thyroxine in dose > 1.35 mcg/kg/day. The negative effects of glucocorticoid overtreatment are more evident in patients with untreated GH deficiency. The negative effects of thyroxine overtreatment are more evident in patients with treated GH deficiency.

Prof. Nenad Prodanovic (Bosnia and Herzegovina) in his report focused on bone changes in cases of chronic diseases. It was noticed that patients suffering from chronic neuromuscular, inflammatory rheumatic and bowel diseases had a tendency to bone mineral density loss. People living with Parkinson disease had the highest incidence of accidental falling down, but osteoporotic bone fracture occurred more frequently among patients suffering Crohn's disease and ulcerative colitis. Deficiency of vitamin D and calcium are common in patients with multiple sclerosis, inflammatory bowel diseases, rheumatoid arthritis and ankylosing spondylitis.

Prof. Sekib Sokolovic (Bosnia and Herzegovina) mentioned about the impact of nutrition on osteoporosis and cardiovascular diseases. He noted that common factors for osteoporosis, atherosclerosis and cardiovascular diseases were lipid abnormalities, smoking, aging, underlying disorders and using

of corticosteroids. Bone metabolism directly correlated to dietary acid/base balance. In disbalance the bones released calcium to keep normal levels of hydrogen and $\text{pH} = 7.35\text{--}7.45$. Excess of acid in the body for a long time could result in loss of calcium and bone and muscle breakdown. Vitamin D inadequacy with low BMD increased fracture risk, secondary hyperparathyroidism, calcified coronary arteries and cardiovascular events. Correlation of atherosclerosis and osteoporosis indicated the parallel progression of two tissue destruction processes with increased fatal and non-fatal coronary events and higher fracture risk.

● Innovations in Pain Management in Osteoarthritis

Prof. Laszlo Hodinka (Budapest, Hungary) focused on questions of innovative pain management in patients with osteoarthritis. He noticed that the perception of chronic pain was projected in well defined areas of the brain where pain experience, emotions and behavioral patterns were coupled to the nociceptive input (insula, amygdala, hypothalamus and prefrontal cortex) and this complex resulted in chronic central pain. Descending modification was generated mostly in the anterior cingulate cortex and in the midbrain (cuneiform nucleus, periaqueductal grey material, dorsolateral pontine tegment and rostroventromedial medulla) and resulted in pain behaviour. In osteoarthritis tissue injury evoked the nociceptive input for the central sensitization and antidromic neurogenic inflammation. Among small molecular neurotransmitters, Nerve Growth Factor (NGF) and Calcitonin-Gene-Related Peptide (CGRP) neuropeptides played a crucial role in the maintenance of central pain. They were evaluated as therapeutic targets in pain management of osteoarthritis. In recent

studies possibilities of modulation of pain perception by biological response modifying bioproteins, as monoclonal antibodies to NGF and CGRP, were evaluated.

Of course it would be difficult to overview all the lectures and reports that were presented during three working days of international symposium. Vitamin D status and gout also were among discussed topics.

All the time the lecture hall was full of participants, and all presentations continued with discussions. That suggested that the problem of musculoskeletal diseases is constantly being studied, and specialists in this field of medicine always have something new to discuss, especially when so many scientists from various countries meet together.

To be concluded, it must be said, that besides hard work the participants of the symposium had an opportunity to discover the City of Lviv for themselves, to walk by its ancient streets, to admire old buildings, chapels and cathedrals, to visit the famous Lviv Opera.

And let's continue this fantastic tradition to meet in Lviv at the next International Symposium of Bone and Joint Diseases and Age again and again!

Correspondence to:

*Nataliia Kuprinenko
Journal "Pain. Joints. Spine"
Publishing House Zaslavsky
PO Box 74
Kyiv, 04107, Ukraine
E-Mail: medredactor@i.ua*

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