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Rats’ meniscus thickness in norm and after intrafetal antigen injection

Background. In recent years diseases of the musculoskeletal system are among the leading pathologies and problems of modern medicine. Undifferentiated connective tissue dysplasia (UCTD) holds a special position among them. Previous researches showed that intrafetal antigen injection can be used for modeling this condition. The meniscus of the knee joint of rats is a structure of interest in terms of reactivity to the modeled condition, because it is of great importance for the knee joint, preventing damage and degenerative processes including osteoarthritis.

Objective. To study the features of the menisci thickness dynamics in the knee joint of rats in norm and after the intrafetal antigen injection.

Materials and methods. 160 white laboratory rats from the 1st till the 90th day of life were studied. The first group included 60 intact rats. 60 rats of the second group underwent transuterine, transmembranous, intrafetal injection of liquid purified staphylococcal anatoxin (10–14 binding units in 1 ml, 10-fold diluted, 0.05 ml) on the 18th day of prenatal period according to the method of M.A. Voloshyn (1981). 40 rats of the third group after injection of saline solution served as control. The progeny was born on the 22nd–24th day of prenatal period. Euthanasia was performed on the 1st, 5th, 7th, 11th, 14th, 21st, 30th, 45th, 60th and 90th days after birth. When working with experimental animals we were guided by the «European Convention for the protection of vertebrate animals...» (Strasbourg, 18.03.86) and the Law of Ukraine «About protection of animals from cruel treatment» (№ 3447-IV).

For the research left knee joint was taken, fixed in 10 % neutral formalin. Decalcification was carried out using Trilon B, dehydration — in ethanol of rising concentration. Paraffin sections were made and stained with hematoxylin and eosin. Thickness of medial meniscus (MM) and lateral meniscus (LM) in the peripheral portion was measured using ocular-micrometer. The obtained data were processed using methods of variation statistics. Results were considered significant at p ≤ 0.05.

Results. On the 1st day both medial and lateral menisci are thicker in the experimental group in the peripheral zone as compared to intact rats (MM: 184.23 ± 16.70 μm in intact group and 240.28 ± 7.78 μm in experimental group; LM: 241.27 ± 24.69 μm and 362.85 ± 10.10 μm, respectively). On the 5th day of life this regularity persists and there is a slight meniscus thickening in the intact group along with significant one in experimental rats (MM: 196.00 ± 6.26 μm and 359.98 ± 13.17 μm; LM: 261.37 ± 0.89 and 362.48 ± 30.12 μm, respectively). Considerable thickening of the meniscus in the animals of intact group starts from the 7th day, while in antigen-injected group statistically significant decrease of thickness is observed in the lateral meniscus (399.44 ± 26.94 μm in norm and 269.50 ± 3.38 μm in experiment). Between 11th and 21st days analyzed indicator is less in the experiment as compared to the intact group. On the 21st day in the group of rats subjected to intrafetal injection of staphylococcal anatoxin rapid growth of the studied parameters occurs, they become significantly higher than those in norm (MM: 407.44 ± 27.55 μm in intact rats and 518.80 ± 39.99 μm in experiment; LM: 400.79 ± 25.83 μm and 506.00 ± 23.38 μm, respectively).

On the 30th day studied parameters are almost equalized in both groups. Subsequently, from the 45th till the 90th day of postnatal life there is a gradual increase in the thickness indicators of the meniscus in intact group rats. Against this background, there is retard of these indicators in antigen-injected animals statistically significant for the 45th day — MM: 539.0 ± 6.76 μm and 462.83 ± 33.22 μm, LM 450.00 ± 46.75 and 318.00 ± 13.54 μm; 60th day — MM: 606.67 ± 21.08 μm and 450.33 ± 25.09 μm; 90th day — LM: 595.87 ± 33.31 μm and 441.09 ± 29.63 μm.

Conclusions. It has been established that the intrafetal antigen injection results in the change of rates and terms of the morphogenesis of the knee joint menisci in rats, which manifests in their peripheral portion thickening as compared to intact group during the first and the third weeks of postnatal life and thinning during the second and third months. This can be considered the expression of UCTD syndrome and become the basis for subsequent disorders of joints including osteoarthritis.
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Status of bone metabolism in postmenopausal women with type 2 diabetes mellitus

Relevance. The problem of osteoporosis has become particularly important in recent years due to aging population and a significant increase of postmenopausal women number. Mortality due to complications caused by osteoporotic fractures in the population of Caucasian women aged of 50 years and older is 2.8 % corresponding to mortality rates from malignant breast tumors. On the other hand, there is present focus on osteoporetic changes caused by endocrine disorders, including diabetes mellitus (DM) in which is associated with a variety of bone lesions (diabetic osteoarthropathy). It is clear that the combination of these two pathologies is very important as is an additional burden on quality of life and its duration.

Study purpose. Study of osteodestructive immunological markers and bone formation in women with T2DM.

Material and methods. We examined 101 persons (women of reproductive aged of 31–50 years: 14 — without menstrual dysfunction; 56 —postmenopausal women and 31 —postmenopausal women with T2DM). Additionally postmenopausal women were divided into groups according to age, duration of menopause, compensation of carbohydrate metabolism or type of species hypoglycemic therapy The study of bone metabolism was evaluated by content of bone remodeling factor (C-telopeptide of collagen type I β-CrossLaps) and marker of osteocalcin osteosynthesis in blood serum.

Results. It was found that concentration of β-CrossLaps in blood serum of postmenopausal women with T2DM is significantly lower compared with postmenopausal women without T2DM. It is shown that the content of osteocalcin in serum of women with T2DM is also significantly lower compared with women without T2DM suggesting the negative dynamics of change of osteosynthesis markers with T2DM. The study showed that concentrations of both markers of bone metabolism status in postmenopausal women with T2DM were significantly lower compared with the corresponding age group of women without T2DM. It is shown that age-related changes of content of in biochemical indicators of osteogenesis/osteoporosis in patients with T2DM and without it are duplicated with unidirectional changes of content of markers of bone metabolism in women with different duration of menopause. We did not find any significant differences in blood markers of bone remodeling/osteosynthesis in different types of therapy, but there is only a tendency of β-CrossLaps content increase in the blood of patients receiving insulin therapy.

Conclusions. Received data of bone markers of bone remodeling in women with T2DM can be a valuable prognostic factor for the rate of loss of boneorganic portion. We should take into account identified reduction of bone remodeling and bone formation with DM which may be potential cause of increased risk of fractures with disease and increased duration of menopause regardless of insulin therapy.
Fat layer is observed even in the 60–70 year old people enabling muscular hypertrophy and reducing the thickness of the articular cartilage. Determined that the morphological, biochemical and physiological systems of human organism are significantly limited by the frequency of side effects, so the use of physical factors for the low incidence of these adverse events has more opportunities, especially at the sanatorium stage of rehabilitation. Preformed physical factors affecting the deep structure in the joint were included in our rehabilitation program to ensure multifactor therapeutic effect on the pathological process in patients with PGA with low bone mineral density. It was considered literature data that alternating electric current of low frequency affects deep tissue and pulsed electric current is the best stimulus for bone receptors, therefore the stimulation of bone receptors in the affected bone and fibrous structures accompanied by marked neurotrophic effect.

Objective — investigate the efficacy of physical therapy influences in rehabilitation programs in patients with primary gonarthrosis with reduced BMD at the sanatorium stage of rehabilitation.

Materials and Methods. 34 patients age of 52–74 years (62.14 ± 0.88) with PGA and low BMD without comorbidities that could affect the metabolism of bone tissue included in the study using differentiated physical therapy methods. By the results of densitometric examination osteopenia revealed in 22 patients and osteoporosis — in 12. There were 6 (17.6 %) men and 28 (82.4 %) women. Duration of the disease is from 4 to 18 years (62.14 ± 0.88) with PGA and low BMD without comorbidities that could affect the metabolism of bone tissue included in our rehabilitation program to ensure multifactor therapeutic effect on the pathological process in patients with PGA with low bone mineral density.

Results. The application in the medical complex IFT and OPES reduce the degree of expression of clinical manifestations of pain syndrome, improve physical activity and physical working capacity in patients with PGA and low BMD. However, application of the OPES technique has more pronounced analgesic effect in patients with pain for VAS over 60 mm, contributing significantly (p < 0.05) reduction of (64.80 ± 1.39) to (36.40 ± 1.18) and significantly (p < 0.05) impact on quality of life by the index of the HAQ (16.0 ± 1.3) to (13.6 ± 0.2), while the application IFT method in patients with pain on VAS more than 60 mm analgesic effect was less expression: from (67.40 ± 0.24) to (45.20 ± 0.56), and quality of life by the HAQ index improved slightly: of (15.6 ± 0.5) to (14.8 ± 0.7). The application in the medical complex IFT has a pronounced analgesic effect in patients with pain by VAS at least 60 mm: before treatment (51.40 ± 0.52), after (36.20 ± 1.19). Changes HAQ index are also significant (p < 0.05): before (15.1 ± 0.4), after (13.1 ± 0.6).

Conclusions. Investigations have shown that exposure of pulse low-frequency and alternating current using methods IFT and OPES has analgesic effect, relieves spasms of periarticular structures and makes it possible to carry out rehabilitation more efficiently. But these methods should be applied differently, depending on the arthological status of patients with PGA with decreased BMD.

Using of physical restoration treatment methods in patients with primary gonarthrosis with low bone mineral density at sanatorium stage of rehabilitation

Strength exercises have a positive effect on the changes of morphological, biochemical and physiological systems of human organism. Determined that the muscular hypertrophy and reducing the thickness of the fat layer is observed even in the 60–70 year old people engaged in strength exercise, and the strength of leg muscles in old age affects the ability to self-service. Generally, the programs of rehabilitation of patients with osteoarthritis include various exercises: aerobic exercise cyclic direction (increase endurance and physical working capacity), special power exercises performed in different modes with varying intensity — from moderate to high (to strengthen the muscles located around joints, to develop compensatory functions (especially at instability). Mechanical stress is the main regulator of bone mass and bone geometry. Physical activity has a positive effect on bone tissue, but mechanical load on the bone helps to prevent bone loss during muscle stretching or pressure. The main objective of the mechanical loading is to reduce resorption and in-
crease bone formation in places where strength is the most necessary to resist the load. Thus, the use of mechanical force may be the most physiological way to increase bone strength and prevention or treatment of osteoporosis and osteoarthritis.

**Objective.** To study the clinical efficacy of strength exercises techniques in patients with primary gonarthrosis (PGA) with decreased bone mineral density.

**Materials and Methods.** The study included 43 patients with PGA with low bone mineral density (according densitometry). Osteopathy was diagnosed in 36 (83.7 %), osteoporosis — in 7 (16.3 %) patients. Men were 6 (13.9 %), women — 37 (86.1 %), patient age — 52–74 years, the average (61.41 ± 0.74) years, disease duration 4–18 years (9.04 ± 0.68) years. The patients did not have comorbidities that could affect the metabolism of bone. 1st radiological stage of PGA was found in 30 (69.7 %) patients, and the IInd stage in 13 (30.3 %) patients (according to classification Kellgren J.N. and Lawrence J.S.) By the method of randomization, patients were divided into 2 groups. All patients with PGA received basic medical complex, which included the using of sulfurated hydrogen sulfide baths with inhalation of sulfurated hydrogen water, applique on the joints low temperature pelotherapy, method interferential therapy, massage. The difference between the medical complex is next. Patients in the control group (20 people) received traditional physical rehabilitation scheme in accordance with the clinical protocol of sanatorium treatment, approved by the Ministry of Health of Ukraine. For 23 patients in the experimental group physical rehabilitation program included the using of strength exercise for the knee joints with elastic bands 20 minutes day duration.

**Results.** It was marked statistically significant (p < 0.05) positive dynamics of arthrological status (the amount of motion in the joints, joint pain by VAS, WOMAC and Leken indexs, and Lovett test) in patients with PGA after applying the medical complex with the inclusion of strength exercises. Compared with the control group the amount of movement in the joints has increased by 18 %, muscle tone by 29 %, pain by 14 %, joint function has improved by 21 %.

**Conclusions.** In patients with osteoarthritis with low bone density inclusion of the strength exercises to medical complex has not only analgesic effect but helps to stabilize and unloading the knee joints by strengthening muscle groups and ligaments. Moreover static tension of skeletal muscle leads to intensive development of muscle strength and increase hypotrophic muscle mass, with minimum strain on the affected joint during exercises.

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**Hypopituitarism and bone**

The pituitary gland is responsible for the production of several hormones that control peripheral target organs like thyroid, adrenals, gonads, breast and uterus and also blood vessels and kidneys.

Bone is also under the influence of the pituitary gland, which has both direct and indirect important effects on it, some of them not yet completely clarified. Growth hormone (GH) and FSH/LH and the gonadal steroid hormones (testosterone and estradiol) are responsible for the linear growth and affect the peak bone mass. Through life, the most important pituitary hormones influencing bone metabolism are ACTH, TSH, GH, FSH/LH and also Prolactin. GH (through IGF-1), TSH (through T3 and T4) and ACTH induce bone formation; FSH/LH (through gonadal steroids) and TSH affect positively the bone turnover because they inhibit bone reabsorption. On the opposite, Prolactin, TSH (through T3 and T4), ACTH (through cortisol) and GH (through IGF-1) induce bone reabsorption. Hypopituitarism can be due to one or to several pituitary hormones deficiency. GH deficiency suppresses bone turnover, while FSH/LH deficiency (and subsequent hypogonadism) increases it. Vertebal fractures can occur, even with normal BMD.
Dysmobility syndrome: the future of fracture risk reduction

Falls and fractures increase with age, and adversely impact independence and well-being of older adults. Both sarcopenia and osteoporosis contribute to falls/fracture risk; because of this, the term osteosarcopenia has been suggested. However, other factors, e.g., obesity, is also a risk factor for falls and fractures. As such, even osteosarcopenia is not adequately inclusive of a term. Indeed, rather than focusing on each condition individually, an opportunity exists to combine clinical factors to potentially improve identification of older adults at risk for falls and fractures. Our group has termed such a combination «dysmobility syndrome». Within such a conceptual framework, dysmobility syndrome becomes analogous to metabolic syndrome, i.e., a group of conditions that lead to increased risk for adverse health outcomes; vascular disease for metabolic syndrome, falls/fractures for dysmobility syndrome. To summarize, «osteoporosis-related» fractures are not solely due to osteoporosis, but rather the result of a complex geriatric syndrome with multiple inputs (e.g., sarcopenia, osteoporosis, obesity, diabetes, etc.) Whether this syndrome ultimately comes to be called dysmobility syndrome is irrelevant; it is the concept that is important. Reducing fracture risk, and thereby maintaining independence and quality of life for older adults, requires focus on the entire individual, not simply the parts. Such an approach is certainly the future of «osteoporosis» care. There is no reason that today's knowledge cannot or should not be applied now.

Assessing vitamin D status: what/when to measure and how to interpret the result

What constitutes «vitamin D inadequacy» is unclear. Huge numbers of people either do, or do not, have this condition which may, or may not, cause multiple diseases. This chaos ensues from deficient understanding of what constitutes «inadequacy». Currently, an individual’s vitamin D status is assessed by measurement of circulating 25(OH)D; whether this is the correct approach remains to be determined. Efforts to define vitamin D inadequacy to this point have used serum 25(OH)D, but have failed to standardize measurement thereby confounding attempts to develop cut-points to define vitamin D status. The Vitamin D Standardization Program (VDSP) has developed methodology standardize current and future research by use of 25(OH)D assays traceable to these standards. Importantly, VDSP also developed methodology for standardizing prior research; past studies can obtain calibrated 25(OH)D values by re-measuring a statistically defined subset of stored serum samples. Using retrospective calibration alters the prevalence of vitamin D inadequacy; examples will be presented. Failure to utilize standardized 25(OH)D data is destined to maintain the current (chaotic) status quo. Additionally, virtually all vitamin D supplementation clinical trials have inadequacies, importantly inclusion of subjects who do not have low vitamin D status and failure to recognize individuals at 25(OH)D response to vitamin D supplementation.

These issues highlight the changes to conducting meta-analyses with unstandardized 25(OH)D data and inclusion of subjects who could not have a positive response to additional vitamin D. As such, it is suggested that additional vitamin D-related meta-analyses not be published at this time. These examples underscore the challenges (perhaps impossibility) of developing rationale vitamin D guidelines at this time. Given this uncertainty, it is suggested that highly sun exposed individuals be used to guide determination of the target 25(OH)D level. Taking this approach identifies «normal» vitamin D status as a 25(OH)D of ~ 100 nmol/L; supplementation to achieve this level is reasonable.

Antenatal prevention of phosphorus-calcium metabolism disorders in children: realities and prospects

The role of vitamin D in calcium-phosphorus metabolism is indisputable. Organs and systems development of the fetus, its rapid prenatal growth require not only adequate intake of calcium in the mother’s body, but vitamin D too.

According to the Protocol for the treatment and prevention of rickets is vitamin D intake at a dose of 500 IU in healthy pregnant women and 1000–2000 IU in the case of risk presence, ranging from 28–32 weeks with-in 6–8 weeks.

The aim of our study was to establish awareness of pregnant women and obstetricians about methods of antenatal prevention of rickets in children and based on an analysis of the literature data to determine its feasibility.

Materials and methods. The survey of 120 pregnant women was done. It included a questionnaire containing a block of questions related to the supplance of vitamin D (according to the Protocol), as well as questions about the awareness of women recently confined about the role of the vitamin D. The survey of 25 obstetrician-gynecologists was conducted to measure and how to interpret the result
Sarcopenia falls and fractures

Bone is a highly mineralized static organ while muscle is a dynamic organ, built mostly of protein. The main function of the muscles from a mechanical point of view is to transform chemical energy into mechanical Energy and, consequently, to generate power required to move and maintain posture. Muscle cells are formed by the differentiation of mesenchymal stem cells, which are initially converted into myoblasts and then merging and extending to form myotubes. In the process of maturation within myotubes actin and myozin filaments are formed. The key phase for the emergence of the muscle cells is the attachment of the neuromuscular junction. Muscle contraction is based on myofibrils containing actin and myosin myofilaments. For one thick filaments of myozin and two halves of thin filaments of actin. Muscle contraction is the result of inserting the filaments of actin filaments on myosin.

According to the clinical definition developed by the European Working Group on Sarcopenia in Older People, sarcopenia is a syndrome characterized by a progressive and generalized loss of muscle mass and strength with the consequential risk of disability, poor quality of life and death. A decrease in muscle mass and strength and/or speed is a diagnostic criterion of sarcopenia. For the measurement of muscle mass the following are used: magnetic resonance imaging, computed tomography, densitometry and bioimpedance. Magnetic resonance imaging is by far the most accurate method, however costly and time-consuming. Computed tomography is also an accurate measurement method, yet, exposes a patient to high radiation dose. The optimal measurement is the so-called Body Composition performed by means of a densitometer. It distinguishes fat mass and lean body mass. It is basically used to measure the ASM — Appendicular Skeletal Muscle Mass (the norm for women equals 5.5 kg/m², men 7.23 kg/m²). Bioimpedance is an non-invasive and inexpensive method, however, it exhibits a poor sensitivity (standard according to BIA — women 6.2 kg/m², men 8.6 kg/m²). Muscle strength is assessed by means of a dynamometer with patient clenching the hand on a handle (the norm for women > 20 kg, men > 30 kg), while the speed is measured by gait speed (> 0.8 m/s) or timed up and go.

The aging is one of the main causes of sarcopenia (similarly as in the case of osteoporosis). Sarcopenia incidence increases with age, ranging from 15 % after 60 to as much as 50 % over 85. The main causes of aging are: the loss of energy production ability in mitochondria, telomere shortening, metabolic waste (free radicals, toxins). The development of sarcopenia is also affected by hormonal factors (testoste-
rhone, estrogen, growth hormone/IGF-1), humoral factors (subliminal chronic inflammation) and environmental factors (diet, sedentary lifestyle).

Regular physical activity and proper diet are the only effective methods for both the prevention and treatment of sarcopenia, as per the EBM criteria. The most effective exercises are resistance exercises, particularly progressive resistance training, affecting both the increase in strength and muscle mass. In turn, the lack of physical activity — whatever the reason — triggers muscle atrophy. The second key element in treating sarcopenia is a diet modification: a proper protein and vitamin D3 intake. The recommended consumption equals 0.8—1.2 g of protein per kg of body weight per day. Proteins provide the appropriate course of post-exercise regeneration processes and are an important anabolic stimulus for skeletal muscle. Vitamin D3 stimulates the synthesis of myocytes, their differentiation, inhibits apoptosis, affects the conductivity and muscle contraction.

According to the EBM muscle weakness is considered as particularly predisposing to falls — for this reason sarcopenia is a fall risk factor. Other important fall risk factors are: balance disorders, vision disorders, cognitive function conditions, insufficient physical activity, age above 80. Due to such aging factors as depleting biologic reserves, slow reflexes and osteopenia or osteoporosis a seemingly harmless fall from own height can have serious consequences and the most serious are fractures, which in the elderly can cause not only pain and temporary immobilisation, but also a permanent impairment of mobility, functional deterioration, increasing morbidity and mortality.

In falls prevention the main Focus must be placed on improving the efficiency of gait, balance and coordination and efficiency of the cardio-respiratory system. A special attention should be paid on various forms of physical activity. Regular exercise of moderate intensity is recommended at least 3 times a week: Nordic Walking, Tai-Chi, dancing, brisk walking. The most effective exercise plans are those under the guidance of instructors in fall prevention centers (e.g. The Falls Prevention Service of Shropshire Community Health NHS Trust, Falls Prevention Team of Berkshire Healthcare NHS Foundation Trust) and individually tailored home exercise programs.
Conclusions. The surface of the articular cartilage is covered by synovial layer. Pronounced glycoconjugates expression in the synovial layer, in the middle zone and covered by synovial layer. Pronounced glycoconjugates in the patients with diabetes mellitus.

Results from monitoring studies of students bone tissue structure and function at Kharkiv region

Currently, the prevalence rate of the musculo-skeletal system pathology takes one of the leading places in the structure of morbidity among children in Ukraine. The purpose of the study was to analyze the results of osteopenia prevalence rates monitoring among children of school age of the large industrial region.

The monitoring of the structural and functional state of bone tissues among students of Kharkiv region was conducted in 2005–2015. 4200 children aged 9 to 18 were comprehensively examined. The study of structural and functional state of the bone tissues was performed on the heel bone using ultrasound densitometer «Sonost-2000». The evaluation of densitometry results was performed in full compliance with WHO guidelines.

Selective methods of mathematical statistics, together with the substantiation of representative number of observations, as well as methods of variation statistics leaning upon mean values and the error absolute (M ± m) and relative (P ± m) values, standard deviation (σ) with the assessment of authenticity following Student’s test (not less than p < 0.05), were employed during the analysis of the study findings.

In 2005 the prevalence rate of osteopenia among children in the region accounted for 29.5 ± 3.1 %, on the average, wherein I degree of osteopenia was found among (43.3 ± 5.1) %, II — (36.7 ± 2.8) %, III — (20.0 ± 2.5) % of children. It should be noted that the OP prevalence among prepubertal aged children turned out to be higher than among children of pubertal age ((24.8 ± 1.8) % and (18.2 ± 2.0) %, respectively; p < 0.05). No significant gender differences in diagnosed OP identified. Though, it should be mentioned that the incidence increased only slightly among girls ((26.1 ± 2.5) %, compared with boys (24.3 ± 2.7) %, p > 0.005.

Over a span of the decade the negative dynamics in the structural and functional state of bone tissue was observed. Thus, in 2015, (41.2 ± 3.6) % of children were diagnosed with OP. It should be mentioned that the OP structure severity has changed: I degree osteopenia incidence constituted (32.8 ± 3.8) %, II — (46.1 ± 4.1) %, III — (21.1 ± 2.5) % of cases.

Thus, what is being observed is the increase in the incidence of moderate OP, while there is the decrease in mild OP, while the III degree of OP prevalence remains at the same level as in 2005. Attention is also attracted by the fact of the significant increase in cases of OP among children of pubertal age, as opposed to prepubertal aged children ((35.6 ± 4.7) % and (23.9 ± 2.3) %, respectively; p < 0.05). In addition, almost 68 % of all the OP cases among students who live in the Kharkiv region constitute II degree of OP.

In 2015, no significant differences in the incidence of OP depending on the gender of the child have been noted. However, still there is a slightly increased incidence of OP among girls against boys ((27.3 ± 2.9) % and (25.1 ± 2.5) %, respectively, p > 0.005).

As for the OP distribution, in 2005 there prevailed II degree of osteopenia, which is associated with chronic diseases of the gastrointestinal tract and kidneys. While in 2015 the share of I and II degree of OP was almost on the same level. As for the I degree of OP risk factors, in 2015 the key factor contributing to the development of OP turned out to be malnutrition with excessive consumption of sweet carbonated beverages, snacks and fast food; deterioration of the ecological environment and sedentary lifestyle.

Thus, the analysis of OP prevalence monitoring among school children showed a significant increase in the incidence of I degree of OP, which clearly shows the deterioration in the quality of nutrition and lifestyle among modern students, i.e. those factors that are subject to correction requiring minimum costs incurred by families themselves, as well as the state on the whole.

Osteoarthritis of large joints in the patients with diabetes mellitus

Introduction. Osteoarthritis has a great medical, social and economic influence on the society, and the most pressing problem is considered to be knee and hip joint diseases, as gonarthrosis (GA) and coxarthrosis (CA) are the most disabling localizations of the pathological process. Diabetes mellitus (DM) is one of the independent risk factors for the development of osteoarthritis.

The objectives of this research were the comparative evaluation of clinical, radiological and sonographic signs of GA and CA in the patients with different types of DN and in
the patients without it, the study of the links of the bone-destructive characteristics with the disturbances of carbohydrate metabolism including physical, chemical integral indices, the determination of the effect of DM on the rates of the progression of the changes in the knee and hip joints.

**Material and methods.** There were 153 patients with osteoarthritis who were divided into two groups. The 1st (main) group consisted of 47 people (16 men and 31 women aged 25 to 72 years) with DM, and the 2nd (control) group included 106 patients without DM (83 men and 23 women aged 32 to 73 years). The average age in the 1st and the 2nd groups was 54 years old and 49 years old (the differences were authentic), respectively. Type 1 DM (DM1) and type 2 DM (DM2) were diagnosed in 24 % and 76 % of the cases, respectively. Type 1 DM (DM1) and type 2 DM (DM2) were diagnosed in 24 % and 76 % of the cases, respectively. The indices of the severity and progression of GA and CA have been calculated. The patients were underwent the X-ray and ultrasound examination of the knee and hip joints, as well as dual—energy X-ray osteodensitometry of the proximal femur. The concentrations of glucose, glycosylated hemoglobin and insulin have been studied in the blood, the surface tension of blood serum, its viscoelasticity module, the slope and the phase slope of tensiograms with the calculation of the indices of insulin resistance, glucose ratio of interfacial activity, adsorptive and glycose integral ratio have been determined.

**Results.** In the patients with OA and with DM the hip joints in 3.7 times are likely to be involved in the process and in 1.2 times more — the knee joints. Diabetes affects the severity of GA and CA. Polyarthrosis has been revealed in 98 % of the patients with DM and in 63 % among the rest ones. The cases of tendovaginitis have been detected in 55 % of the cases of diabetes and the cases of enthesopathy have been revealed in 21 %, whereas these cases have been diagnosed only in 2 % and 3 % in the control group. The incidence of reactive synovitis in both groups showed no significant difference (45 and 54 %). Heberden’s nodules occurred in 10 % of the cases, Bouchard’s nodules — in 4 %, the signs of spondylarthrosis and osteochondrosis of the cervical spine were detected in 37 % of the cases, thoracic osteochondrosis — in 41 %, lumbar osteochondrosis — in 63 %. The analysis of variances shows the dependence of the development of osteoarthritis, subchondral sclerosis, epiphysial osteoporosis, intraarticular calcifications, ligamentosis and cartilage flaps in GA from DM, but it doesn’t demonstrate the dependence of the amount of narrowing of articular fissure, the formation of Baker’s cysts, Hoff and Pella-Shiatai bodies from DM. In general, shown statistically significant components of GA were detected in 30, 55, 64, 38, 18, 16, 13 % of the number of the surveyed, respectively. DM in the patients with OA determines the number of affected joints in the form of polyarthrosis, not only starting, but also morning stiffness, the increase of the frequency of some roentgenosonographic signs of the articular syndrome, the severity of the involvement of the spine, knee and hip joints in the process that depend on the rates of insulinemia and glycosylated hemoglobin in the blood. The development of GA and CA is often observed in the patients with DM of type 2, which is more aggressive factor as for the hip joint disease, while DM of type 1 in the patients with GA causes mainly the cases of tendosynovitis and enthesopathy. In such cases the intensity of synovitis is associated with diabetic macro- and microangiopathy. The presence of DM in the patients with GA affects the formation of osteoarthritis, subchondral sclerosis, osteoporosis, intraarticular calcifications and cartilage flaps, ligamentosis.

**Conclusion.** DM affects the course of the GA and CA, and the detection of the disturbances of carbohydrate metabolism in such joint pathology can have a practical significance as a risk factor of some structural changes of articular and periarticular tissues.
In men with intra-articular hip fractures the indices of the length of hip axis, length of femoral neck, intertrochanteric distance, basis of the head and head diameter were significant lower in comparison with indices of patients without fractures. In men with extra-articular hip fractures the indices of length of hip axis, intertrochanteric distance, basis of the head and head diameter were also significant lower in comparison with indices of patients with fractures. We did not find the significant differences of hip geometry parameters in women depending on the hip fractures.

**Conclusion.** Femoral geometry and FRAX indices are independent risk factors for hip fractures in Ukrainian patients. Identified differences should be considered for both planning surgery after hip fracture and for predicting the risk of hip fracture in older age patients.

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**Epidemiology of lower limb fractures in Ukrainian population**

Lower limb fractures (LLF) account for approximately one third of all fractures and may result in substantial mortality and morbidity. Age, osteoporosis, road collision, obesity and different diseases (osteoarthritis, Parkinsonism, cataract, dementia etc.) are the risk factors of LLF. Fractures are a considerable public health burden but information on their epidemiology in Ukraine is limited.

**Material and methods.** We identified 665 subjects from 76,765 citizens, living in Vinnitsa region, who had a first time (incident) diagnosis of LLF recorded in the Regional Hospital database from 1.01.2011 to 31.12.2011.

**Results.** Frequency of the LLF of was 42.4 % from the total fractures in all patients and 44.4 % from the total fractures in patient aged 50 years and older. The most common anatomical site of LLF was the tibia and/or fibula (48.9 % of all incident lower limb fractures), followed by the hip (29.5 %), and the tarsal/metatarsal bones (21.6 %). Incidence of fracture in patient 50 years and old was 519.8 per 10,000 patient for all LLF, 212.3 per 10,000 patient for tibia and/or fibula fractures and 226.9 per 10,000 patient for hip fracture.

Lower limb fractures were more common among males than among females in the younger age groups (up to 39 years old). Among subjects 50 years and older the incidence of LLF was higher in women than in men, and the difference increased with increasing age.

Incidence of the tibia and/or fibula fractures was 340.7 per 10,000 patient in the age group 60–69 years old, 44.9 per 10,000 patient in age group 70–79 years old, and 102.4 per 10,000 patient in age group 80–89 years old.

**Conclusion.** Our study provided the new information about the epidemiology of lower limb fractures in Ukrainian population according the age. This information is important for planning of the prevention and treatment strategy in patients of different ages.

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**Vitamin D deficiency among children 10–16 years of the western Ukraine**

Recently the deficiency of vitamin D is a generally recognized public health problem in the world. The role of vitamin D in the body has been significantly revised, it not only regulates mineral metabolism, but also has a wide range of extra-skeletal action. It has been proved that the effect of vitamin D largely depends on its relationship with the human genome. Specifically, it interacts with a nuclear receptor that determines the expression of over 900 genes.

In humans, most of circulating vitamin D is synthesized from cholesterol under influence of ultraviolet radiation in sunlight. Proceeds of vitamin D from food defines only 10–20 % of the content of 25(OH)D, but becomes significant at low insolation. Recently recommendations for preventive doses of vitamin D for children and adults were revised and increased. However, the need for studies of vitamin D among children of Ukraine remains relevant because there are certain differences in the level of insolation and consumption of foods containing vitamin D among groups living in different territories.

**Objective:** to find out the prevalence of vitamin D deficiency among 10–16 years old children who live in the Ternopil region, Western Ukraine.

**Materials and methods.** 118 children were examined in one of the secondary schools of Ternopil region. The average age of children was 12.8 ± 2.5 years, average height — 1.56 ± 0.14 m, the average weight — 45.9 ± 10.9 kg. The study was conducted from mid-October to the end of December 2011 to reverse the impact of seasonal factors on the level of 25(OH)D.

After general clinical examination and interviewing, the level of 25(OH)D was determined using the electro-chemiluminescence method on the analyzer Elecsys 2010 and serum Ca content.

Evaluation of vitamin D-status was performed according to the latest current classification, according to which vitamin D deficiency is established at the level of 25(OH)D serum below 50 nmol/l, insufficiency of vitamin D is diagnosed when levels of 25(OH)D 75–50 nmol/l. The concentration of 25(OH)D from 75 to 150 nmol/l is considered as being in the normal range.

**Results.** Vitamin D deficiency was found in 107 (90.7 %) children surveyed, insufficiency — in 9 (7.6 %). The average content of 25 (OH) D in the boys 10–13 years was 34.7 ± 11.4 nmol/l, 14–16 years 30.3 ± 10.0 nmol/l; girls 10–13 years — 31.1 ± 11.1 nmol/l, 14–16 years 28.3 ±


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**Innovative pain management in osteoarthritis**

Mechanisms of nociception, central sensitization and central elaboration of chronic pain and the projection of pain in the central nervous system are reviewed. Mediators of pain perception with special respect to neuropeptides as Nerve Growth Factor (NGF) and Calcitonin–Gene-Related Peptide (CGRP) are evaluated as therapeutic targets and development of innovative interventions in pain management are discussed. Possibilities of modulation of pain perception by biological response modifying bioproteins, as monoclonal antibodies to NGF and CGRP and recent studies are presented.

Perception of chronic pain is projected in well defined areas of the brain where pain experience, emotions and behavioral patterns are coupled to the nociceptive input (insula, amygdala, hypothalamus and prefrontal cortex) and this complex result in chronic central pain. Descending modification is generated mostly in the anterior cingulate cortex and in the midbrain (cuneiform nucleus, periaqueductal grey material, dorsolateral pontine tegment and rostroventromedial medulla and results in pain behaviour.

In osteoarthritis tissue injury evokes the nociceptive input for the central sensitization and antidromic neurogenic inflammation. Among small molecular neurotransmitters, NGF and CGRP neuropeptides play a crucial role in the maintenance of central pain. Painful effects of joint load and therapeutic interventions to modify pain sensation may be followed by functional MRI.

Blocking antibodies against neuropeptides specifically inhibit their neurological functions, mainly pain induction. However effective in pain management, NGF may accelerate necrotic processes in the target OA joints.

**Patients and methods.** A cross-sectional trial in 56 women patients with T2DM and 30 controls without DM. Mean age of the patients was 51.2 ± 6.1 years. The mean duration of diabetes was 10.3 ± 5.8 yrs. All patients were treated only by oral antidiabetic drugs (metformin and DPP-4), not by insulin. The BMD at lumbar spine (LS), femoral neck (FN) were measured at baseline and after 1 year of treatment by dual energy X-ray absorptiometry (DXA, Hologic). TBS was performed by TBS Insight software (Medimaps, France) from LS DXA scans.

**Results.** Diabetes was associated with higher BMD than the control group (1.008 ± 0.175 g/cm² vs 0.961 ± 0.176 g/cm², p = 0.05). The LS-TBS was lower in T2DM than in control group (1.172 ± 0.120 vs 1.304 ± 0.018, p < 0.001). HbA1c was an important determinant effecting BMD (r = −0.30, p < 0.05) and TBS (r = −0.35, p = 0.01). But the cut-off was 8.5 % for BMD and 7.9 % respectively.

**Conclusion.** Our datas confirm, that poor glycemic control based on an HbA1c is an important determinant for BMD as a marker of bone quantity and also TBS, a marker of bone

**Bone quality in diabetic patients**

**Introduction.** Patients with both types of diabetes are known to have an increased risk of fractures. While in type 1 diabetes the major reason is low bone mass, patients with type 2 diabetes are at an increased risk despite increased bone mineral density (BMD) and this is caused by inferior quality of bone. The association between glycemic compensation and diabetic complications or comorbidities is well known. Various trials observed that poor glycemic control is associated with higher all types of fracture risk.

**Objective.** To determine the role of metabolic compensation measured by A1c haemoglobin (HbA1c) on bone quality measured by trabecular bone score (TBS) and also on BMD in T2DM patients.

**Patients and methods.** A cross-sectional trial in 56 women patients with T2DM and 30 controls without DM. Mean age of the patients was 51.2 ± 6.1 years. The mean duration of diabetes was 10.3 ± 5.8 yrs. All patients were treated only by oral antidiabetic drugs (metformin and DPP-4), not by insulin. The BMD at lumbar spine (LS), femoral neck (FN) were measured at baseline and after 1 year of treatment by dual energy X-ray absorptiometry (DXA, Hologic). TBS was performed by TBS Insight software (Medimaps, France) from LS DXA scans.

**Results.** Diabetes was associated with higher BMD than the control group (1.008 ± 0.175 g/cm² vs 0.961 ± 0.176 g/cm², p = 0.05). The LS-TBS was lower in T2DM than in control group (1.172 ± 0.120 vs 1.304 ± 0.018, p < 0.001). HbA1c was an important determinant effecting BMD (r = −0.30, p < 0.05) and TBS (r = −0.35, p = 0.01). But the cut-off was 8.5 % for BMD and 7.9 % respectively.

**Conclusion.** Our datas confirm, that poor glycemic control based on an HbA1c is an important determinant for BMD as a marker of bone quantity and also TBS, a marker of bone
Efficacy of correcting vitamin D deficiency/insufficiency in women with arterial hypertension in premenopausal and early postmenopausal periods

Background. Vitamin D deficiency/insufficiency and its correcting is an actual problem of today. It is due to both high incidence of vitamin D deficiency in the general population varying from 70 % to 96.8 % and its relationship with cardiovascular pathology, particularly arterial hypertension (AH) in postmenopausal women [1, 2].

Aim. To assess the serum level of 25(OH)D in women with AH in premenopausal and early postmenopausal periods as well as to evaluate the efficacy of its correction.

Materials and methods. We investigated 102 women with AH stage II risk 3 aged 50 (48, 53) years: of these 50 females in premenopausal period — group I and 52 females in early postmenopausal period — group II. Using the immunoenzymatic assay we determined the serum level of 25(OH)D total including 25(OH)D2 and 25(OH)D3. According to the serum level of 25(OH)D in female patients in groups I and II we identified the subgroups with its deficiency/insufficiency: subgroup IB (n = 25) and subgroup IIB (n = 21) respectively. In these subgroups the algorithm of antihypertensive therapy (ramipril and indapamide) was supplemented with cholecalciferol (Aquadetrim, Poland) at a daily dose of 2.000 IU for 3 months. In subgroups IA (n = 25) and IIA (n = 31) without vitamin D deficiency cholecalciferol was not administered. Statistical analysis was performed using STATISTICA 10.0 software package.

Results. At baseline the serum level of 25(OH)D was lower (p < 0.05) in subgroups IB (19.3 ± 8.5 ng/ml) and IIB (18.2 ± 9.5 ng/ml) than in the comparable subgroups IA (26.7 ± 11.5 ng/ml) and IIA (27.4 ± 10.5 ng/ml). In subgroup IB 60 % of women had vitamin D deficiency, and 40 % demonstrated vitamin D insufficiency. In subgroup IIB 61.9 % of women had vitamin D deficiency, 38.1 % showed insufficiency. After 3 months of cholecalciferol therapy in subgroup IB the serum level of 25(OH)D increased significantly (p = 0.0001) and it became higher (p = 0.001) than in subgroup IA. In subgroup IIB the serum level of 25(OH)D increased (p = 0.004) as well and made 36.4 ± 10.0 ng/ml; it also became higher (p = 0.007) than in subgroup IIA. Optimal level of serum 25(OH)D was achieved in 80 % of women in subgroup IB and 76.2 % women in subgroup IIB. The level of serum 25(OH)D deficiency was observed in 8 and 9.5 % of patients respectively.

Conclusion. Women with AH stage II in premenopausal and early postmenopausal periods demonstrated high incidence of vitamin D deficiency/insufficiency — 76.5 %. Cholecalciferol therapy at a daily dose of 2.000 IU lasting for three months efficiently corrects serum vitamin D deficiency/insufficiency and allows to obtain its optimal level in 80 % of women with AH in premenopausal period and 76.2 % of women in early postmenopausal period.

References
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Structural and functional state of bone and fracture risk in patients with atherosclerosis of coronary vessels

Introduction. According to WHO experts, osteoporosis and coronary heart disease occupies a leading place in the structure of morbidity and mortality. Results of studies in recent years indicate the presence of common pathogenetic mechanisms that lead to the development of osteoporosis and atherosclerosis. So, the study of the factors that may influence the increase of risk of fractures in patients with established atherosclerosis, their prompt correction is important in our modern medicine.

The aim is to study changes in the structural and functional state of the bone tissue in patients with diagnosed coronary atherosclerosis and to analyze risk factors of bone fractures.

Materials and methods. The study was conducted in terms of student scientific society of the Department of Internal Medicine № 2 Bogomolets National Medical University. The survey of 21 patients with coronary atherosclerosis which was diagnosed according to coronaroventriculography was conducted coronary atherosclerosis. In order to identify risk factors for fracture technique FRAX (fracture risk assessment tool) was determed. General laboratory methods included the determination of lipid metabolism. Study of structural and functional state of the bone was conducted with the help of an ultrasonic densytometer «Achilles» + «Lunar» (USA).

Results. The positive correlation between the index of FRAX-1 and the level of total cholesterol and FRAX-2 and total cholesterol levels was revealed.

Conclusions. The investigations indicate the need for early densitometry of surveys and questionnaires in patients with established coronary atherosclerosis, hypercholesterolemia, for the prevention of bone fractures.

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Dynamic of bone mineral density and pain syndrome in patients with rheumatoid arthritis during the standard treatment

Background. In patients with rheumatoid arthritis (RA) develop both local and systemic osteoporosis due to inflammation and medications that are used in treatment of RA. Severe clinical presentation with a high level of activity, glucocorticoid treatment, low body weight, menopause peri-

In the study in depth osteopenic syndrome surveyed a direct correlation between the values of BMD (\(r = 0.75\)), \(Z\) (\(r = 0.63\)) and the value of BMI.

Body mass index in patients with low BMD \((15.84 ± 0.58)\) kg/m\(^2\) was authentically (\(p < 0.05\)) lower than in patients with normal bone mineralization (\(19.30 ± 0.62\)) kg/m\(^2\) and in healthy children (\(23.42 ± 0.53\)) kg/m\(^2\). It was also found authentically (\(p < 0.05\)) reduction in body mass index in patients with osteopenia \(I + II\), \(III\) degrees and OP against children of the control group and patients with normal bone mineralization. Differences of this indicator depending on sex and activity of CH is not found, but found significant (\(p < 0.05\)) differences in values of body mass index between different age groups with low BMD, \((14,21 ± 1,06)\) kg/m\(^2\) — children and 5–10 years \((18.54 ± ± 0.55)\) kg/m\(^2\) — in persons 11–15 years, respectively.

In this way, body mass index with a value \((15.84 ± ± 0.58)\) kg/m\(^2\) and below may be one of the diagnostic criteria osteopenic syndrome in children with inaparant and subclinical forms of chronic hepatitis B and/or C.
DAS28 is 2.78 ± 0.35, randomized into 2 groups. As basic therapy 20 patients (42.55 %) received methotrexate 7.5–15 mg per week, 23 patients (48.94 %) combined methotrexate with glucocorticoids 5–10 mg per day, 4 patients (8.51 %) received leflunomide 20 mg per day. Patients of the first group (n = 23) along with basic therapy were treated with osterogen, the second group (n = 24) — basic therapy and calcium with vitamin D. Pain syndrome was assessed according to visual analogue scale (VAS) before treatment and after 1, 3 and 6 months. BMD was determined by dual energy X-ray absorptiometry.

**Results.** Pain decreased by 35.4 % (p < 0.05) in the group of patients receiving osteogen and in the group receiving combination of calcium and vitamin D to 9.1 % (p < 0.05). Bone mineral density increased in the group receiving osteogen (+ 6.9 %, p < 0.001) after 6 months of treatment, in contrast to second group, in which was not observed reliable dynamic (+ 1.35 %, p > 0.05).

**Conclusions.** More significant improvement of BMD was registered in first group in comparison with a group of patients that received the combination of calcium with vitamin D at recommended doses.

**Comparison of TBS and FRAX in fracture risk assessment of postmenopausal females with osteopenia**

**Introduction.** More than half of osteopenic patients suffer from fracture (Fx), but BMD osteopenia is usually not considered for treatment initiation. To our knowledge there is no study which compares risk stratifying methods in Fx prediction of BMD non-therapy group.

**Objective.** Comparison of three methods, trabecular bone score (TBS), FRAX and FRAX adjusted for TBS in Fx risk prediction of postmenopausal (PM) females.

**Methods.** Observational cohort study of PM females with BMD osteopenia (defined as T-score −1 ≥ −2.5) during 2/2009-5/2015 was performed. Patients underwent TBS, FRAX and FRAX adjusted for TBS evaluation. Using NOF cutoff values of 20 % for major osteoporotic Fx and 3 % for hip Fx were used to consider patients at high absolute 10 years risk of Fx. With regard to TBS patients were divided to 3 groups: normal, moderate and degraded. According to temporary consensus guidelines patients with BMD osteopenia + very low (degraded) TBS (< 1,1) are at high risk of developing Fx. TBS Insight® tool was used to assess TBS derived from L-spine DXA scans. Primary endpoint during follow-up was clinical Fx/death.

**Results.** In total, 144 PM females (mean age 66.1 yrs., BMI 26.7 kg/m², T-score: neck —1, L-spine 1,4, TBS 1,24) were included. At baseline, 31.9 %; 30.5 and 34 % belonged to high Fx risk group according to TBS, FRAX and FRAX adjusted for TBS, respectively. Trend to increase Fx risk (RR 2.3; 95% CI 0.32; 12.5) was observed by degraded TBS. Fx/death probability was significantly 4.28-times higher in patients with degraded TBS value (RR 5.28, 95% CI 1.4; 19.1). Mean time to Fx/death was 4.4 yrs.

**Conclusions.** Patients with BMD osteopenia with degraded trabecular microarchitecture are at high risk of Fx. This study provides supportive results that TBS is appropriate method to assess high risk of Fx patients with BMD osteopenia.
infections background significantly (p < 0.001) exceeds its activity at healthy pregnant women (5.37 ± 0.17 vs. 6.94 ± 0.18 pg/ml).

Conclusion. In pregnant women with the verified perinatal infection rates of ultrasonographic densitometry demonstrate significant decrease of the bone mineral density assist reduction of the bone tissue mineral density.

Male hypogonadism and bone mass

Normal sex steroids hormone levels are essential for optimizing peak bone mass and their deficiencies during adulthood may modify the bone mass, as it causes bone loss by increased bone resorption and can be associated with a low BMD, osteoporosis or/and fragility fractures risk. Sex steroids hormones affect the skeleton by direct and indirect mechanisms. Androgens affect osteoblast activity and probably stimulate directly the bone formation and may exert a moderate resorption of the trabecular bone, similar to estrogens effects on bone. In male hypogonadism there is not enough sex steroid hormone synthesis by the testes, sperm or both; hypogonadism is also characterized by the lack of estrogen and unequivocally androgen: the bone disease of men with hypogonadism is associated with the absence of estrogen actions. In adult men with primary or hypogonadotropic hypogonadism due to bilateral orchietomy there is a BMD decrease detectable 1 to 3 years after orchietomy. These men had a rapid loss of vertebral bone mass (about 7% per year) progressing together with an increased osteoclast activity, which is inhibited by non-aromatisable androgens; the rapid bone mass loss and increased bone turnover are more intense in the years just after orchietomy, with a consequent diminished bone loss phase, a process menopause-like. In prepubertal secondary or hypogonadotropic hypogonadism there is a reduced BMD at the cortical and cancellous bone. GnRH analogues therapy (inhibition of the pituitary gonadotropins production and secretion originating gonadal deficiency) in adults is also related with a marked bone mass loss and osteoporotic fractures. Chronic glucocorticoid therapy may reduce substantially testosterone levels and contribute also to the bone mass loss.

Our group detected a significant low BMD at several skeletal sites in hypogonadal men, as compared with a group with normal gonadal function. Studies in chronic male hypogonadism revealed decreased rates of bone formation, increase in average of bone remodeling rates, increased levels of osteocalcin, interaction between testosterone and vitamin D metabolism and a reduction in the trabecular bone number. The BMD is correlated with free testosterone plasma levels in old men. In prepubertal hypogonadism and growth hormone deficiency, vertebral sizes are small due to short stature and vertebral fractures (compression or wedge) are frequent. Hypogonadism may contribute to severe osteoporosis in about 15% of men; androgen deficiency is associated with 30% of the osteoporotic vertebral fractures and hip fractures that occur most often in old hypogonadal men with vitamin D deficiency.

Testosterone therapy inhibits osteoclast activity and increases bone formation. Therapy of adult males with hypogonadism showed positive effects on BMD in most osteoporotic patients but the BMD may not normalize even if the testosterone levels are already normal for one year. Our group observed a significant low BMD in a group of hypogonadal men treated during 7 years. Finally, no data were published about osteoporotic fractures risk and testosterone therapy for the different types of male hypogonadism.

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Markers of bone tissue metabolism and their clinical significance in patients with chronic obstructive pulmonary disease

Introduction. Contradictions of the literature data on the relationship of vitamin D level with pulmonary functional parameters determine the aim of this research to study of vitamin D-status and markers of bone metabolism in patients with chronic obstructive pulmonary disease (COPD).

Materials and methods. 47 patients who were hospitalized because of exacerbation of COPD during the autumn-winter (September-December) period of 2012 were examined.

The average age of patients was (53.59 ± 12.83) years with the weight (78.80 ± 12.53) kg and height (170.54 ± 7.84) cm. The body mass index (BMI) was (27.17 ± 4.07). 27 (57.45%) men and 20 (42.55%) women were examined. 24 (51.06%) patients were smokers, pack/years index was 29.08 ± 16.62. All patients were divided into the groups depending on the age and sex.

All patients were determined such parameters as 1) markers of bone formation — type I procollagen propeptides (P1NP) and osteocalcin propeptide first type procollagen, osteocalcin; 2) markers of bone resorption — β-C-terminal telopeptides of type I collagen (β-CTX); 3) hormonal regulation markers — intact Parathyroid Hormone (iPTH), total vitamin D level (25-OH vitamin D3 and 25-OH vitamin D2) with the use of the electrochemiluminescence method on Eleksys 2010 analyzer.

Results. Content of P1NP decreased by 82.96 % in patients with stage IV compared to stage I COPD (p = 0.002)
Similarly, level of osteocalcin decreased to 41.00% in stage IV patients compared to the patients of stage I ($p = 0.002$). The content of $\beta$-CTx increased by 70.66% in stage IV COPD patients compared to patients with stage I ($p = 0.018$).

It was revealed that all the patients with COPD suffered from vitamin D deficiency. It should be noted that the severe form of vitamin D deficiency was in 48.94% of patients. This statistically significant changes of 25 (OH) D level were noted comparing to the stage I and IV ($p = 0.006$). The 1PH index was changed from 37.17 ± 17.91 to 41.68 ± 14.10 (pg/ml) and in I and IV stages COPD patients respectively ($p = 0.031$). PTH level was higher than normal in 4.26% of COPD patients, moreover in 97.87% of cases it was combined with vitamin D deficiency.

Conclusions. That bone metabolism impairment in COPD patients are characterized by a vitamin D deficiency, suppression of type I procollagen propeptides and osteocalcin production, increased $\beta$-C-terminal telopeptides of type I collagen and parathyroid hormone synthesis. The intensity of these changes has a direct correlation to the stage of COPD and the presence of harmful habits.
Diagnoses and treatment issues of the Ollier disease in clinical practice

Chondrogenic tumors, including chondromas and osteochondromas, are among the majority of the tumors and tumor-like conditions that affect the osseous system. Chondromatosis of the osseous tissue manifests in the evolving malformation of bones which results in falling off of the quality of life (QOL) and to the rise of the rate of patients’ disability.

One of the similar diseases is the Ollier disease. It is a congenital disorder characterized by a unilateral affection of osa, by shortening and thickening of extremities, change in the manner of walking and lameness. Besides, recurrent irregularly shaped pelvis bones and scoliosis are its frequent characteristics.

Despite the fact that a great amount of research papers with respect to the disease have been published worldwide, many medical practitioners find it difficult to detect the Ollier disease. In Ukraine there are only few occasional descriptions of the disease that report about far from all the typical aspects of the disease.

The multiple scientific literature data and clinical observations report about the complexity in diagnostics of the Ollier disease. It includes a complex diagnostic investigation involving the computer tomography, magnetic resonance imaging, scintigraphy and bone-biopsy together with the conventional methods of research.

Pharmacotherapy approaches in treatment of this symptom complex is being actively discussed, though the final patient management protocol for the Ollier disease has not been developed yet due to some conflicting data.

Therefore, the discussed above field of medical investigation is challenging and showing promise and potential, taking into consideration the low-frequency of the disease in clinical practice, the complexity of diagnostic investigation, absence of a strategy in case management, low effectiveness of conservative therapy. Besides, there is no unique specialists’ opinion as to performing of a surgical correction.

Zoledronic acid in the therapy of steroid-induced osteoporosis in patients with inflammatory joints disease

Osteoporosis is the most common bone disease in humans, representing a major public health problem as outlined in Bone Health and Osteoporosis. The disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility. The disease often does not become clinically apparent until a fracture occurs. Although glucocorticosteroids may effectively be used in the management of many inflammatory conditions, their use is associated with significant morbidity and mortality. The bone loss and increased fracture risk are a common consequence of using glucocorticosteroid drugs. The most pressing issue remains the prevention of osteoporosis in patients with prolonged therapy by glucocorticosteroid. Oral bisphosphonates increase bone mineral density and reduce frequency of vertebral fractures. The role of Zoledronic acid (ZOL) for steroid-induced osteoporosis in patients with inflammatory joints disease remains debatable.

Objectives. We aimed to evaluate the effects of Zoledronic acid for steroid-induced osteoporosis in patients with inflammatory joints disease.

Methods. 30 patients (mean age — 59.30 ± 3.76 years) with inflammatory joints disease were enrolled. All patients were women and received glucocorticoid during more than 5 years (mean duration of treatment — 3.80 ± 0.67 years). Women had osteoporosis documented by either a lumbar spine T-score ≤ −2.5 or lumbar spine T-score ≤ −1.5 with 2 mild or 1 moderate prevalent vertebral fracture. 15 (50 %) patients received the standard treatment and Zoledronic acid 5 mg infusion once a year (study group), while 15 (50 %) (control group) — received only the standard treatment for 3 years. Visual Analog Scale (VAS), bone mineral density (BMD) were performed in all patients at baseline and at the end of the study.
Results. VAS and BMD did not differ significantly between the groups. After 3 years of treatment with Zoledronic acid the incidence of symptoms, including arthralgia were significantly lower in the study in comparison of control groups (P = 0.01). The increase in BMD was greater in the study group than in the control group (P = 0.05). During 3 years among patients in the control group 33 % have compression fractures in compare with study group (P = 0.01).

Conclusion. Zoledronic acid is effective and safe for patients with glucocorticoid-induced osteoporosis in patients with inflammatory joints disease. Its administration may provide benefits for the reduction of hospitalizations and mortality in its population.

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Results of evaluation an overall well-being in children with juvenile rheumatoid arthritis

In recent years, there has been growing interest in the parent-reported and child-reported assessment of overall well-being in patients with juvenile rheumatoid arthritis (JRA). Integration of these measures in clinical evaluation is considered important as they reflect the parent’s and child’s perception of the disease course and effectiveness of therapeutic interventions. As parents and children are asked with increasing frequency to actively participate in shared decision-making, integration of their perspective in clinical assessment may facilitate concordance with physician’s choices and improve adherence to treatment.

The aim of the research was to determine overall well-being in children with JRA by the results of parents and children assessment.

The 99 children were examined — 60 sick by JRA patients and 39 healthy children. Selected groups were matched by the sex, age, and nationality. Overall well-being was evaluated by the using of visual analogue scale (VAS) in parents and their children.

It was established that overall well-being in patients with JRA was much worse than in healthy children by the results of the parent-reported assessment (3.7 ± 0.2 cm, 0.7 ± 0.2 cm; p < 0.05), and the patient-reported assessment (3.5 ± 0.3 cm, 0.5 ± 0.1 cm; p < 0.05). In general overall well-being in patients with JRA survey by the various applicants didn’t differ (p > 0.05).

The results of correlation analysis between an overall well-being, some clinical and laboratory parameters of JRA by the parent- and child-reported assessment are present in table 1.

<table>
<thead>
<tr>
<th>Parameter of JRA</th>
<th>Evaluation of overall well-being</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>parent-reported</td>
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<tr>
<td>Joint form</td>
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<tr>
<td>Stage of activity of the disease</td>
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<tr>
<td>Morning stiffness</td>
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<td>Parent-reported evaluation of pain (VAS)</td>
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<tr>
<td>Child-reported evaluation of pain (VAS)</td>
<td>0.83*</td>
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<tr>
<td>Child-reported evaluation of overall well-being</td>
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<tr>
<td>Doctor-reported evaluation of overall well-being</td>
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<td>Erythrocyte sedimentation rate</td>
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<tr>
<td>C-reactive protein</td>
<td>0.10</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>0.15</td>
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</tbody>
</table>

Note: * — pearson’s correlation coefficient was significant at the < 0.05 level.

For standardization of diagnostic approach to evaluation an overall well-being the parent and child a diagnostic value coefficient by Zemskov A.M. formula was calculated. The most informative was founded the parent-reported evaluation of overall well-being (diagnostic value coefficient equal 2.91), something less the child-reported evaluation of overall well-being (diagnostic value coefficient equal 3.15).

The results of research helps to conclude that overall well-being in children with JRA are much worse in comparing with healthy one. The results of parent-reported and child-reported evaluation an overall well-being are associated with some clinical peculiarities of JRA and didn’t depend on laboratory markers of disease activity. The parent-reported evaluation of overall well-being is more informative than child-reported and should be primary considered in physician assessment of further management of patient with JRA.
The role of vitamin D and exercises in correction of age-related skeletal muscle changes in postmenopausal women

The aim of the study was to evaluate the role of vitamin D and exercises in correction of age-related skeletal muscle changes in postmenopausal women.

Materials and methods. 38 postmenopausal women aged 53–82 years (mean age — 67.00 ± 7.08 yrs; mean height — 160.31 ± 6.83 cm; mean weight — 63.25 ± 8.59 kg, body mass index — 24.62 ± 3.09 kg/m²) were examined. All subjects were free of systemic disorders (endocrine, renal, hepatic etc.) and did not take any medications known to affect skeletal and muscle metabolism. The women were divided into the following groups: A — control group (n = 10), B — women who took an individually-targeted vitamin D therapy (n = 11), C — women who took an individually-targeted vitamin D therapy and OTAGO Exercise Programme (http://www.hfwcn.org/Tools/BroadCaster/Upload/Project13/Docs/Otago_Exercise_Programme.pdf) during 12 months. The assessment of the examined women was conducted every 3 months at the medical center. We used the following questionnaires: SARC-F, IADL—questionnaire, frailty scale, Desmond fall risk questionnaire. For evaluation of skeletal muscle function and strength, we assessed the usual gait speed and used hand dynamometry. 25(OH)D total and iPTH levels were measured by electrochemiluminescent method i.e. Elecsys 2010 analytical system (Roche Diagnostics, Germany) and test-systems cobas. The lean mass was measured by the DXA method (Prodigy, GEHC Lunar, Madison, WI, USA). Statistica 6.0 © StatSoft, Inc. was used for the data processing purposes.

Results. At the baseline, the groups of examined women did not differ in their age, anthropometric characteristics, 25(OH)D values, data of skeletal muscle mass, strength and function. In women of the control group, the mean 25(OH)D level significantly increased after 9 months of observation (9 months — p = 0.03) purportedly due to the seasonal factors. In women of 2nd and 3rd groups, the 25(OH)D level significantly increased after 3, 6, 9 and 12 months of observations (2nd group: 3 months — p = 0.009, 6 months — p = 0.007, 9 months — p = 0.005, 12 months — p = 0.003; 3rd group: 3 months — p < 0.001, 6 months — p < 0.001, 9 months — p < 0.001, 12 months — p < 0.001). The data of SARC-F, IADL—questionnaires did not change during 12 months of observation in women of 1st and 2nd groups; however, in the 3rd group the SARC-F data significantly decreased after 12 months (p = 0.02) while the IADL data — significantly increased after 9 (p = 0.04) and 12 months (p = 0.05). The data of frailty scale and Desmond fall risk questionnaire did not differ in all groups during 12 months. The muscle strength significantly increased after 9 months (p = 0.01) in women of 3rd group while in women of 1st and 2nd group this parameter did not change. The usual gait speed and lean mass assessed by DXA did not change in all groups during 12 months. The fall frequency in women of 1st group significantly increased after 12 months, in women of 2nd group it did not change while in women of 3rd group the fall frequency significantly decreased.

Conclusion. Using individually-targeted vitamin D therapy and OTAGO Exercise Programme during 12 months significantly improves daily activity, muscle strength and decreases the fall frequency in postmenopausal women.
**Chronic diseases and osteoporosis**

**Objective.** Numerous chronic neuromuscular and inflammatory rheumatic or intestinal diseases are listed as a risk factor for osteoporosis development. Above mentioned disorders are connected with increased possibility of accidental falling down, whose results are more frequent bone fractures.

**Material and methods.** During the period from Jun 2014 to October 2015 we measured bone mineral density (BMD) using Lunar Prodigy Advance device on the lumbar spine and femoral neck, to 62 patients living with rheumatoid arthritis, 36 with ankylosing spondylitis, 46 with Crohn disease, 52 with Parkinson, 21 with sclerosis multiplex; and analised impact of accidental falling down and osteoporotic fracture during the one year period.

**Results.** Out of 62 patients (37 female and 25 male) living with rheumatoid arthritis (average age 57.38+/±11.64) BMD (T-score –1.07), over the last 12 months we registered 19 (30.6 %) accidental falling down and 6 (9.67 %) new fractures. Out of 36 patients (9 female and 27 male) suffering from ankylosing spondylitis (average age 49.2+/±16.0), BMD (T-score –1.2+/±1.8) we registered 7 (19.4 %) accidental falling down and 2 (5.5 %) fractures. We registered 11 (23.91 %) accidental falling down and 6 (13.04 %) bone fractures among 46 patients (31 female, 15 male) with Crohn disease (average age 57+/±9), BMD (T-score –1.7+/±1.3). Out of 32 patients (21 female, 31 male) suffering M. Parkinson (average age 64+/±13), BMD (T-score –1.70+/±2.10), 18 (34 %) accidental falling down and 4 (7.69 %) bone fractures were registered. Among 21 patients (16 male, 5 female) with sclerosis multiplex (average age 27+/±9) BMD (T-score –0.70+/±0.97 %), 7 (33 %) accidental falling down and 2 (9.5 %) fractures were registered. In the control cohort formed of 50 people (average age 45+/±20) BMD (T-score –0.10) we registered 4 (8 %) accidental falling down and fractures 1 (2 %) bone fractures.

**Conclusion.** Patients with chronic neuromuscular and inflammatory rheumatic or intestinal diseases have decreased bone mass in comparison with healthy people. People living with Parkinson disease have highest incidence of accidental falling down, but osteoporotic bone fracture occur more frequent among patients suffering Crohn disease.

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**Calcium and vitamin D: the true story**

There is evidence that Calcium and Vitamin D, given in combination, reduce the risk of fractures in the elderly. Based on available data, almost all individuals get sufficient Vitamin D when their blood levels are at, or above 50 nmol/l. Controversial results were observed, in observational studies, regarding Calcium and ischaemic heart disease. Intakes of Calcium above 1400 mg/day, in women, were associated with higher death rates from all causes and cardiovascular diseases but not stroke. Other studies reported an increased risk of myocardial infarction in patients receiving Calcium supplementation but no increase in cardiovascular death.

In interventional studies, when appropriate reporting of cardiovascular events was used, no difference was observed between patients receiving Calcium supplements and those who did not. The conclusion of a recent meta-analysis was that, when using events verified by clinical review, hospital record or death certificate, the hypothesis that Calcium supplementation, with or without Vitamin D, increases coronary heart disease or all-cause mortality risk in elderly women, was not supported.

In summary, whereas one cannot formally exclude that Calcium supplements (without Vitamin D) may be associated with an increase in the risk of myocardial infarction, this risk remains unclear but cardiovascular mortality is unaffected, coronary artery calcification is not accelerated and the risk of stroke is not elevated.

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**Pitfalls in the Development of Drugs in Sarcopenia**

Sarcopenia is characterized by a loss of muscle mass and muscle function. Sarcopenia is frequently a precursor of frailty, mobility, disability and premature death. It has a high prevalence in older population and therefore presents a considerable social and economic burden. Potential treatments are under development but there are no guidelines to support regulatory studies for new chemical entities. There are numerous gaps in our knowledge, particularly concerning risk assessment. It would be instructive to build a risk model similar to the one for osteoporosis (FRAX). The value of indexing threshold values for sarcopenia measures and outcomes needs to be further investigated, using a risk-based analysis, for one of the strong clinical endpoints. A consensus core outcome set would bring standardization and comparability to research in sarcopenia and therefore, would help improve the evidence base for health care. A common operational definition of sarcopenia is urgently needed. It is time to address the lack of regulatory guidelines concerning the evaluation of drugs for the prevention and treatment of sarcopenia.
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**Diabetes and bone**

Osteoporosis and type 2 diabetes share several common features: their incidences are steadily rising and they are of multifactorial etiology. Initially, both diseases are asymptomatic, but in the long run may severely impair the quality of life. Due to the high life expectation of the world population, the incidence, the costs, and the complications of osteoporosis and diabetes mellitus will increase dramatically. While an association of type 1 diabetes with osteoporosis has been established since many years, traditional type 2 diabetic patients were considered to be protected from fragility fractures. Nevertheless, data accumulated over the past years indicate that also type 2 diabetic patients — even if they have an augmented bone mineral density — are at increased risks of fractures. Most advanced sophisticated analytic methods which allow high resolution assessment of bone have also added to our knowledge of diabetic caused changes in bone tissue, especially in cortical structures expressed as cortical porosity and also on material level. Furthermore there are some oft he new oral antidiabetic drugs which also can harm bone metabolism. In this review, molecular and clinical findings of diabetic bone disease will be introduced and discussed together with features of own experience.

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**Modern aspects of rachitic clinical course**

**Introduction.** The rachitic remains one of the most common diseases in early-aged children. The symptoms of rachitic are detected in more than 50% of infants [1]. Frequent use of products of a children’s food with addition of vitamin D is at the cause of change of a clinical picture of disease. The present-day course of the rachitic is characterized by slight forms of this disease without evident clinical symptoms. This is due to the increased role of perinatal and postnatal predisposing risk factors. In Belarus, the recorded incidence of rickets is extremely low — about 20–25 cases per 1000 infants [2]. Obviously, recorded moderate and severe forms of rickets. Mild forms are not detected and not treated. However, the transfer could be the cause of rickets pathology associated with the violation of calcium-phosphorus metabolism in older children and adults: scoliosis, flat feet, caries, violation of visual acuity, osteoporosis, muscle hypotonia and autonomic dysfunction [3]. Consequently, the investigation of rickets underestimated by pediatricians, and the attitude of the medical community to this pathology requires revision.

**The aim** of our work was to examine the rachitic clinical manifestation in the first-year infants at modern stage, depending on preventive vitaminization.

**Material and methods.** We have examined 175 histories of a postnatal development of infants up to one year old. 63 of them were under natural feeding and took a prophylactic dose of the vitamin D. 82 infants were fed with adapted milk formula containing vitamin D and did not take additional vitaminization. 30 infants, who were under natural feeding up to 6-month age, underwent a nonspecific rachitic prophylaxis only. The clinical anamnestic data of infants in these groups were homogenous.

**Results.** These initial clinical examination and analysis of the stories of children in the first months of life have shown that all children have the same clinical and medical history. In 28.6% of the children were factors predisposing to a breach of calcium-phosphorus metabolism (the time of birth from June to December, prematurity, morphological and functional immaturity, birth weight over 4 kg, the children of twins or from repeated birth with small intervals, particularly the antenatal period, the pathology of the liver, kidneys, skin, malabsorption syndrome, frequent respiratory and intestinal infections, receiving anticonvulsants). The signs of rachitic are revealed at 65 (37.1%) of the first-year old infants. Risk factors of development of the rachitic in the allamnesis have been revealed at 100% of children in this group. None of the infants showed severe signs of the rachitic. The frequency of was lower in the group of infants who took vitamin D (3.2%; p < 0.001). The clinical signs of the rachitic more often were diagnosed in infants under natural feeding without additional vitaminization (46.7%; p < 0.001), as well as in the group of infants who had artificially fed (46.7%; p < 0.001). The respiratory morbidity in the breast-fed infants taking vitamin D was 3 times lower and the cases of neurologic-and-behavioral maturation disorder were much rarer than in other groups (p < 0.05) in the first year.

**Conclusion.** Thus, wide circulation of the rachitic is determined now by a decisive role of prenatal and postnatal predisposing risk factors. The most effective method of the rachitic and respiratory morbidity prophylaxis is a preventive vitaminization of the breast-fed infants and the infants fed with adapted milk formula having risk factors.

**References**

The changes of bone metabolism in gonarthrosis

The topicality of the problems of osteoarthritis of the knee joints (gonarthrosis) is caused by its wide spreading and high risk of the restriction of joint function with the director disability and reduced quality of patients’ life.

The aim and the objectives of this study were to evaluate the role of the bone metabolism with different variants of the clinical course of gonarthrosis, the links with the development of osteoporosis, bone destructive changes in the knee joints according to the findings of X-ray, sonography, magnetic resonance tomography of X-ray densitometry.

Material and methods. We observed 104 patients with osteoarthritis (47 % of the men and 53% of the women) aged 32 to 76 years old. Gonarthrosis is revealed in 96% of the cases. Overt reactive synovitis is diagnosed in 62% of the cases on the results of the clinical and sonographic study, polyarthrosis — in 55%, systemic osteoporosis in 14%, osteocystosis — in 91%, spondylopathy in the form of osteochondrosis and athrosis of facet joints is detected in 72%. The patients were underwent the X-ray and ultrasound examination of the peripheral joints and the spine, dual-energy X-ray osteodensitometry of the proximal femur, and magnetic resonance imaging of the knee joints. On examination osteo deficiency indices were estimated, bone mineral density values, rates of severity and progression of osteoarthritis.

Results. In healthy people the blood levels of calcium were 9.40 ± 0.68 mg/l, magnesium — 27.20 ± 0.71 mg/l, phosphorus — 412.70 ± 9.17 mg/l, parathyroid hormone — 2.90 ± 0.94, ASDAS-ESR — 2.75 ± 0.96, BASDAI — 4.39 ± 1.86, BASFI — 2.57 ± 2.15, CRP — 15.0 ± 22.4, ESR — 22.5 ± 21.9. In axial SpA mean value were: ASDAS-CRP — 2.80 ± 0.88, ASDAS-ESR — 2.65 ± 0.91, BASDAI — 4.06 ± 1.88, BASFI — 2.55 ± 2.18, CRP — 11.7 ± 12.0, ESR — 23.1 ± 20.2. In peripheral SpA patient mean value were: ASDAS-CRP — 3.03 ± 1.02, ASDAS-ESR — 2.86 ± 1.02, BASDAI — 4.81 ± 1.78, BASFI — 2.54 ± 2.21, CRP — 18.9 ± 30.6, ESR — 21.7 ± 24.3. SPARCC score was 26.5 ± 11.9, without significant differences between axial (28.7 ± 12.3) and peripheral (23.8 ± 11.3) SpA.

SPARCC MRI SIJ score showed correlation only with ASDAS-CRP (r = 0.319, p = 0.045) in all SpA patients, and with BASFI (r = 0.566, p = 0.014) in patients with the involvement of peripheral joints.

Conclusion. For all SpA patients MRI inflammatory changes of SIJ (SPARCC score) showed significant correlation only with ASDAS-CRP but not with any others classical clinical and biological parameters. Correlation between SPARCC score and functional status (BASFI) was also determined but only in patients with peripheral SpA.
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Peculiarities of course osteoarthritis of the knee joints depending on the degree of comorbidity and damage of hepatobiliary system

Background. Osteoarthritis (OA) is age-dependent disease and more common in people over the age of 40. Important perceived influence on the course of osteoarthritis of diseases that share common pathogenic mechanisms and have co-burden effect (comorbidity).

The high frequency of the combination of OA with lesions of the hepatobiliary system has a common pathogenetic mechanism based on chronic low-level inflammation, metabolic disorders and enhances the risk of mortality from age cardiovascular pathology. The above creates difficulty in implementing a complex treatment of OA and requires a differentiated approach to it.

Aim was to study the peculiarities of OA depending on the degree of comorbidity and damage of the hepatobiliary system and levels of cardiovascular risk (CVR).

Materials and methods. The study involved 112 patients with OA, including 97 (86.6 %) women and 15 (13.4 %) men aged 43 to 77 years (58.10 ± 6.82) in exacerbation period. The diagnosis of OA established according to the diagnostic criteria by EULAR, comorbidity index by Charlson (1988).

Results. According comorbidity index, depending on the age group of patients and stage of OA revealed that I stage of OA was observed mainly in middle-aged patients (32.14 %) who had less comorbidity index (3.30 ± 0.12), and the second stage of OA detected in elderly and senile patients (67.86 %) with a comorbidity index fluctuations within 5–8 points (6.80 ± 0.16).

By clinical and instrumental verification hepatobiliary lesions in the patients revealed that in addition to patterns of growth with age, there was a tendency increases their degree of severity, progression of stage OA, comorbidity index and the degree of CVR. Thus, in patients with OA established frequency of acalculous cholecystitis in middle age 35 (31.3 %), elderly and senile patients — 60 (53.6 %), gallstone disease correspondently 6 (5.4 %) and 11 (9.8 %) and chronic steatohepatitis this background 18 (16.1 %).

The duration of treatment for patients in hospital increased with increasing of comorbidity index, degree of CVR and stage OA for 2–4 days. Due to the already mentioned inpatient treatment phase of complex prevention of cardiovascular events was carried out considering comorbidity index, pathogenetic features of comorbidity states, including damage of liver.

Conclusion. With increasing age of patients with OA increases the number and severity of comorbidity diseases (comorbidity index), the stage of the disease, including damage of the hepatobiliary system and the degree of CVR. In order to improve the results of treatment and prevention of cardiovascular events advisable to use complex application of methods, that affect the common pathogenetic links their formation and progression.
**Anent the structure of the articular surface**

**Introduction.** For a long time the structure of the articular surface attracted attention of many researchers and remains not fully understood. W. Hunter (1742–43), B. Brodie (1813), J. Toynbee (1849) believed the cartilage surface is covered by synovial membrane. Subsequently, a lot of scientists, such as V. Н. Пасюта (1980, 1988), J. M. Clark (1990), R. Teshima (2004), V. Н. Баранова (2004), І. М. Ахмедов (2006), А. J. Sofia Fox (2009), J. Rauhainen (2015) and others researchers disproved this statement, used terms «lamina splendens» and «chondral membrane», claiming the cartilage surface is acellular.

**The aim** of the study. To determine the structure of the articular surface during the postnatal period in order to solve above-mentioned contradictions.

**Materials and methods.** Hip and knee joints of white laboratory rats from the 1st to 90th days of their postnatal life were chosen as materials of the present study. Joint fragments were fixed in the Buend liquid, decalcinated in a 20 % formic acid solution, dehydrated in an ascending battery of alcohols and chloroforms, immersed in paraffin. For the overview microscopy by means of χ10, χ40, χ100 lens magnifications hematoxylin and eosin stain, stain after Laidlaw, stain according to Mallory’s method, Hart’s staining, PAS staining, alcinblau staining, lectin histochemical staining with peanut (PNA–HRP), vicia sativa (VSA–HRP), soybean (SBA–HRP), wheat germ (WGA–HRP), perca fluviatilis (PFA–HRP) agglutinins. The method of M. A. Voloshyn (1981) was used as a model of antenatal antigen injection does not change significantly, and anatomical integrity of synovial layer on articular cartilage remained steady. Obtained data indicate the leading role of the synovial layer in the protection of articular cartilage from aggressive influences of synovial fluid. Single and indivisible lining the articular cavity synovial layer is believed to be innate, protective, nonspecific, immunobiological, anatomical and physiological barrier between articular cartilage and fibrous layer of joint capsule. It indicates the different morphological and functional state of the synovial layer in all its length. The distribution of glycoproteins, glycosaminoglycans and glycoconjugates after antenatal antigenic injection does not change significantly, and anatomical integrity of synovial layer on articular cartilage remained steady.

**Results.** It has been established that all intraarticular formation of joints, including articular surface, in new-born rats are covered by morphologically different from cartilaginous tissue structure which is nothing else, but synovial lining cells which continue directly from joint capsule to articular cartilage. Synovial lining cells are clearly delimited from articular cartilage by fibrous argenophil lamina (proposed term — basal lamina). Basal lamina mainly comprises collagen and to a lesser extent elastic fibers, which distinctly separate synovial lining cells from adjacent articular cartilage. Moreover, basal lamina has a significant content of glycoproteins and glycosaminoglycans, and shows pronounced expression of all studied lectin receptors. Shape of synovial lining cells varies from cubical to prismatic. Intercellular amorphous substance is detected among synovial lining cells. Throughout the apical (luminal) surface of synovial lining cells during the whole observation period, there is a strong expression of polysaccharides and intensive deposition of lectin-binding sites without significant changes. Poor detection of basal lamina and intercellular substance, absence of polysaccharides and glycoconjugates expression on the luminal surface of synovial lining cells were observed in synovial layer which covers intraarticular ligaments and fibrous layer of joint capsule. It indicates the different morphological and functional state of the synovial layer in all its length. The distribution of glycoproteins, glycosaminoglycans and glycoconjugates after antenatal antigenic injection does not change significantly, and anatomical integrity of synovial layer on articular cartilage remained steady. Obtained data indicate the leading role of the synovial layer in the protection of articular cartilage from aggressive influences of synovial fluid. Single and indivisible lining the articular cavity synovial layer is believed to be innate, protective, nonspecific, immunobiological, anatomical and physiological barrier between articular cartilage and fibrous skeleton of joint capsule on the one hand, and synovia on the other hand. Glycoconjugates expression on the basal lamina and on the luminal surface of synovial lining cells plays the role of nonspecific lectin mediated mechanism in articular cartilage protection.

**Conclusions.** The surface of the articular cartilage in new-borns is covered by synovial layer. Any changes in the structure of covering synovial layer, its age-related involu- tion and transformation into «lamina splendens» may play a key role in articular cartilage degeneration and dystrophic processes in it with consequential predisposition to osteoarthritis development.
tion appeared to be not significant in each group. To assess the effect of age, sex and diagnosis on the level of 25(OH)D, we performed multiple linear regression analysis by forward stepwise method. Formed regresional relationship was significant ($R^2 = 0.10; F (2.42) = 19.77; p < 0.000001$), $b$ coefficient for the independent variables included in the model was significant for age and PTH and valued at $-0.18 (p = 0.001)$ and $-0.097 (p = 0.000001)$ respectively, which indicates their negative association with the level of 25(OH)D. Also another regression equation was significant ($R_i = 0.07; F (6.44) = 5.58; p < 0.000001$), $b$ coefficient for the independent variables included in the model was significant for sex and diagnosis and valued at $-0.10 (p = 0.027)$ and $-0.18 (p = 0.003)$, which also indicates their negative correlation with the level of 25(OH)D.

After separation of the entire group by the age into 5 subgroups: $3b$ — 30–39; $4b$ — 40–49; $5b$ — 50–59; $6b$ — 60–69; $7b$ — 70–79 years we found the differences ($p = 0.00002$) in the level of 25(OH)D between the group $3b$, where the level was highest ($25.3 \pm 11.3$ ng/ml) and other four groups, between $7b$ group where the level of 25(OH)D was the lowest ($14.97 \pm 9.20$ ng/ml) and group $3b$ ($p = 0.000004$), $4b$ ($p = 0.007$), $5b$ ($p = 0.006$). However, after separation of groups by diagnosis in each of them there were no differences by level of 25(OH)D between age groups. After separation into groups by diagnosis ANOVA analysis revealed that CHD group was older ($64.6 \pm 8.1$ years) than control group ($46.1 \pm 6.7$ years; $p = 0.00001$) and the AH group ($52.4 \pm 7.6$ years; $p = 0.000009$). Levels of 25(OH)D in blood plasma in CHD group was $13.2 (8.3; 21.1)$ ng/ml and was lower ($p = 0.00001$) than in AH group — $20.1 (12.4; 29.1)$ ng/ml and lower ($p = 0.00001$) than in the control group — $20.8 (11.4; 27.9)$ ng/ml. Furthermore, PTH level in CHD group was the highest — $46.16 (33.19; 71.57)$ pg/ml and was higher ($p = 0.0001$) than in AH group — $36.67 (25.22; 51.29)$ pg ml and control group ($43.12 (28.54, 55.26)$ pg/ml; $p = 0.002$). After separation of groups by sex no significant differences in 25(OH)D levels were found in a whole group and in groups separated by diagnosis, as well as in comparison of 5 subgroups comparable by age.

**Conclusions.** 25(OH)D level in blood plasma is negatively associated with age and it is dependent on cardiovascular diseases, in particular it is lower in individuals with CHD compared to individuals with AH II degree. Gender does not have a significant effect on the level of 25(OH)D in the blood plasma.