УДК 616.72:616.8-009.12]:57.088.6](045)

DOI: http://dx.doi.org/10.15674/0030-598720223-452-61

Conceptual model of the process of formation of immobilization contractures

O. A. Tyazhelov [1], A. M. Khasawneh Ayham [2], O. D. Karpinska [1], M. Yu. Karpinsky [1], M. Z. Bitsadze [1]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] National Pirogov Memorial Medical University, Vinnytsya. Ukraine

Contractures — limitation of passive movements in the joint — are a fairly frequent complication after immobilization or limitation of mobility and loading of the limb due to injuries, but the exact cause of their formation has not been clarified. Objective. Based on the meta-analysis of the results of experimental modeling and clinical studies of immobilization contractures, create a conceptual model of their formation. Methods. Literature sources from scientific bases were analyzed: Cochrane Library, Scopus, National Library of Medicine, ReLAB-HS Rehabilitation Resources Repository, Mendeley Reference Manager, The Physiological Society library, Google Scholar. Results. A conceptual model of the development of contractures was created. It is shown that immobilization of the joint of the injured limb blocks the execution of the signal of motor impulses. The lack of movement in the joint leads to a decrease in muscle strength and a slowdown in blood circulation. These processes are interrelated: hypotonia of the muscle is due to the restriction of nutrition through the blood supply, and the lack of contractile activity of the muscles leads to the rearrangement of the blood vessels. Articular cartilage is nourished through the subchondral bone and due to osmosis from the synovial fluid during movements. The lack of movement limits nutrition, protein synthesis is disrupted, the surface of the cartilage, synovial membrane and fluid begins to be rebuilt, the joint capsule, ligaments, and tendons thicken. At the same time, the structure of the muscles changes, they shorten and become denser. With long-term immobilization, degenerative processes in the tissues of the joint worsen its general condition, which can eventually lead to complete immobilization. Conclusions. The created conceptual model of the formation of immobilization contractures of joints takes into account the morphological changes of tissues as a result of immobilization. Immobilization affects all components of the joint and adjacent tissues from the first days, the changes progress over time. The use of the model will allow the development of a system of treatment measures to prevent the development of contractures.

Контрактури — обмеження пасивних рухів у суглобі — доволі часте ускладнення після іммобілізації чи обмеження рухомості та навантаження кінцівки внаслідок травм, але точна причина їхнього формування не з'ясована. Мета. На підставі метааналізу результатів експериментального моделювання та клінічних досліджень іммобілізаційних контрактур створити концептуальну модель їхнього формування. Методи. Проаналізовано джерела літератури з наукових баз: Cochrane Library, Scopus, National Library of Medicine, ReLAB-HS Rehabilitation Resources Repository, Mendeley Reference Manager, бібліотеки «The Physiological Society», Google Scholar. Результати. Створена концептуальна модель розвитку контрактур. Показано, що іммобілізація суглоба ушкодженої кінцівки блокує виконання сигналу рухових імпульсів. Відсутність рухів у суглобі призводить до зменшення сили м'язів та уповільнення кровообігу. Ці процеси взаємопов'язані: гіпотонія м'яза обумовлена обмеженням живлення через кровопостачання, а відсутність скорочувальної діяльності м'язів призводить до перебудови русла судин. Живлення суглобового хряща здійснюється через субхондральну кістку і завдяки осмосу з синовіальної рідини під час рухів. Відсутність рухів обмежує живлення, синтез білків порушується, починається перебудова поверхні хряща, синовіальної оболонки та рідини, потовщується суглобова капсула, зв'язки, сухожилки. Разом із цим змінюється структура м'язів, вони вкорочуються і стають щільнішими. За тривалої іммобілізації дегенеративні процеси в тканинах суглоба погіршують його загальний стан, що згодом може призвести до повного знерухомлення. Висновки. Створена концептуальна модель формування іммобілізаційних контрактур суглобів ураховує морфологічні зміни тканин унаслідок знерухомлення. Іммобілізація впливає на всі компоненти суглоба та прилеглі тканини з перших діб, зміни прогресують із плином часу. Використання моделі дозволить розробити систему лікувальних заходів для профілактики розвитку контрактур. Ключові слова. Іммобілізація суглоба, контрактура, структура суглоба, біосинтез, концептуальне моделювання.

Key words. Joint immobilization, contracture, joint structure, biosynthesis, conceptual modeling

Introduction

A contracture is a restriction of passive movements in a joint, i.e., a condition in which the limb cannot be fully bent or extended in one or more joints. It is a fairly frequent complication after immobilization or limitation of mobility and loading of the limb due to injuries, but the exact abnormality underlying contractures has not been clarified, and to this day there are conflicting opinions about which elements of the joint are involved in the process of contracture formation.

Depending on the etiology, joint contractures are divided into arthrogenic (changes occur in the cartilage, synovial membrane, capsule, and ligaments) and myogenic (caused by changes in muscles, tendons, and fascia). The primary factors in the formation of joint stiffness are still being discussed. In a large number of studies, the first of which date back to the 1940s, individual joint tissues were studied in animal models and were limited to a period of up to 6 weeks. Only in recent years, the results of studies on the formation of immobilization contractures in time course (from 4 days to 32 weeks) on a significant number of animals have been published, which contemplate the changes in the tissues of the joints and the muscles that surround them.

The purpose of the study: to create a conceptual model of their formation based on a meta-analysis of the results of experimental modeling of immobilization contractures and clinical studies of patients with contractures.

Material and methods

The study was performed using a meta-analysis of literature sources from scientific bases: Cochrane Library, Scopus, National Library of Medicine — National Institutes of Health, ReLAB-HS Rehabilitation Resources Repository, Mendeley Reference Manager, Physiological Society Library, and literature on physiology and biochemistry of domestic and foreign authors.

We studied the data on the effect of restriction of movements and long-term non-use of joints on their mobility and changes that occur in tissues as a result of these actions.

The study involved an assessment of 150 sources, of which 56 were selected, where the impact of immobilization on joint structures was directly considered. Other articles not used in the review dealt with genetic, immunological changes and the basis for the formation of contractures, and also covered other issues that were not the subject of our study.

Results and their discussion

General structure of joints

The knee and elbow joints are classified as synovial joints. A synovial joint consists of bony surfaces covered with cartilage, a joint cavity containing synovial fluid, and a joint capsule [1]. The joint is characterized by the presence of mandatory main elements and auxiliary (additional) apparatus.

The main elements of the joint are as follows (Fig. 1):

1. Articular surfaces of bones covered with articular (hyaline) cartilage.
2. Joint cavity with synovial fluid.
3. Joint capsule consisting of outer fibrous and inner synovial layers (synovial membrane).

Auxiliary structures of the joint include ligaments, which can be extracapsular, capsular, intracapsular; intra-articular (fibrous) cartilages located between the articular surfaces; synovial folds, i.e. connective tissue formations covered with a synovial membrane, synovial bags.

To determine the changes in the joint structures under the conditions of the formation of immobilization contractures, we will consider their functionality from a review of tissue biochemistry (Fig. 2).

From the standpoint of modern osteology, bone is studied as an organ of the locomotor system, which shape and structure (macro- and microscopic) is determined by functions [2]. The composition of the bone includes cortical (compact) and spongy substances (in the skeleton, they make up 80 and 20 % of the mass, respectively), the content of which depends on the shape of the bones. Bone tissue mainly consists of mineral substances bound by a small amount of organic matrix.

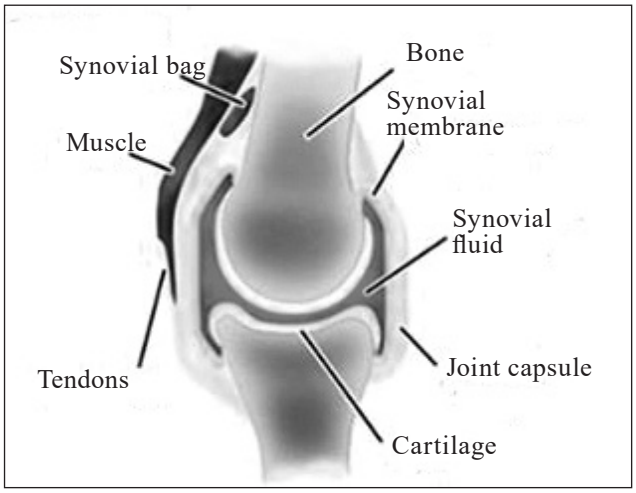

Fig. 1. Structure of a joint

Hyaline cartilage, joint capsule, synovial membrane, tendons, and ligaments are made of different types of connective tissue. Connective tissue contains from 50 to 80 % water. That is, water is the main component ensuring its normal functioning. Let us consider the role of water in the functioning of the connective tissue of the joints to understand the processes that take place under the conditions of its limitation.

Articular cartilage consists mainly of extracellular matrix (ECM), synthesized by chondrocytes [3]. In adults, they make up approximately 1 % of tissue volume [4]. Under normal physiological conditions, chondrocytes are responsible for maintaining cartilage homeostasis, balancing the synthesis and degradation of extracellular matrix components [5] and providing the tissue with nutrients [6]. Articular hyaline cartilage comprises four zones (superficial, intermediate, deep and calcification) depending on the location of collagen fibers of the extracellular matrix and the morphology of chondrocytes.

In addition to water, the matrix of hyaline cartilage contains collagens (up to 40 %), proteoglycan aggregates (mostly in the form of aggrecans), and glycoproteins.

Proteoglycans give characteristic properties to hyaline, elastic and fibrous cartilage. In particular, the critical mechanical properties of hyaline cartilage (elasticity and stiffness during compression) are due to the ability of aggrecan complexes to bind water [7]. Articular cartilage absorbs the load owing to deformation and ensures the smoothness of the articular surfaces to minimize friction during joint movements [8].

The complexity of body movements leads to various loads on cartilage tissue. In the knee joint, deformations of the articular cartilage can reach 20 % or more, depending on the movements [9–11]. In addition, movements in the joint include sliding and rotation, that is, the articular cartilage is subject to shear forces [12].

The main component of ECM of articular cartilage of an adult is water (65–80 % of the total mass), which is tightly bound inside it due to the special physical properties of cartilage tissue macromolecules that are part of collagens, proteoglycans, and non-collagenous glycoproteins [13]. The presence of water in ECM is an important component. It determines the volume of the tissue and, due to connections with proteoglycans, provides resistance to compression. In addition, water provides transport of molecules and diffusion in ECM. The biomechanical properties of cartilage depend on the interaction of collagen fibrils, proteoglycans and the fluid component of the tissue. Structural and compositional changes caused by a mismatch between the processes of synthesis and catabolism, degradation of macromolecules and physical trauma significantly affect the properties of cartilage and change its function.

During loading, there is a complex distribution of tension, shear and compression forces [14] (Fig. 3).

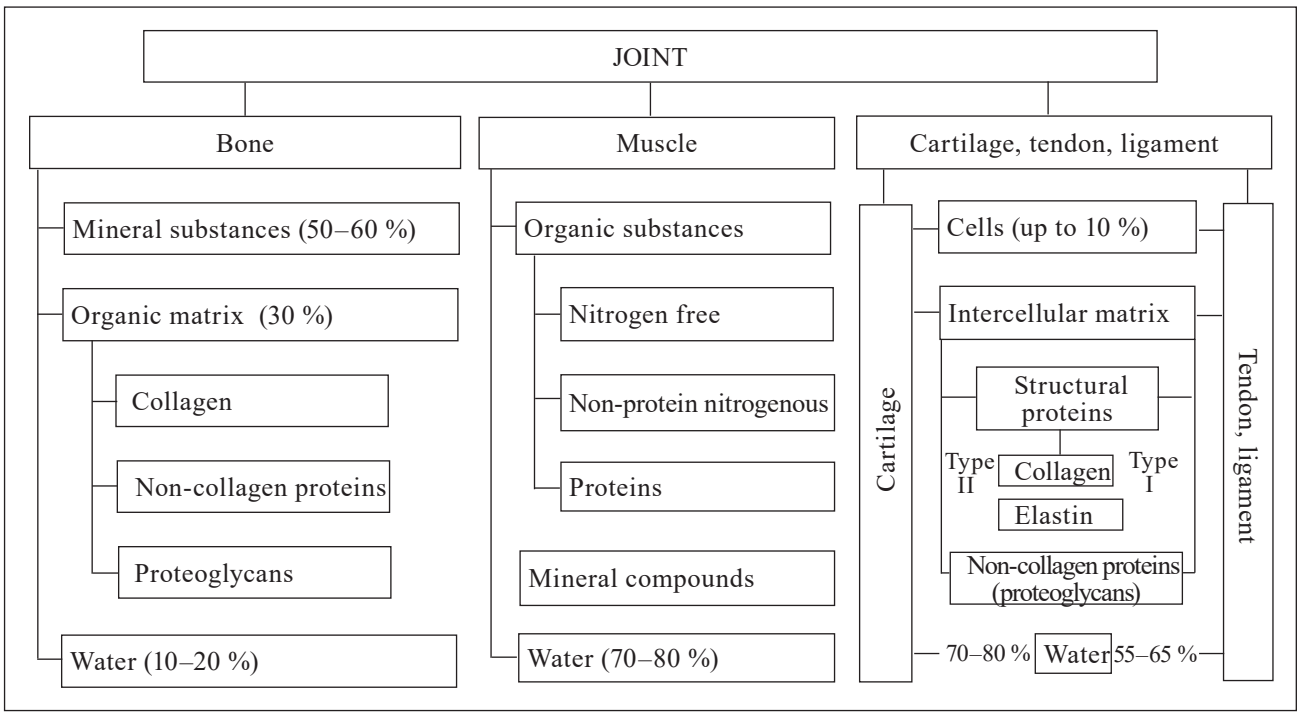

Fig. 2. Contents of substances in tissues forming a joint

The movement of water directly depends on the duration and strength of the applied load. The liquid moves towards the joint cavity under the influence of the load, taking along the products of cellular metabolism. A small amount of water remains in cartilage tissue thanks to proteoglycans, which actively bind water and increase cartilage elasticity. During deformation of the tissue, proteoglycans are more tightly pressed against each other, thus effectively increasing the density of the negative charge, and intermolecular ones, repelling the negative charge force, increase the resistance of the tissue to further deformation. Eventually, the deformation reaches equilibrium, in which the external load forces are equal to the internal resistance forces — swelling pressure (interaction of proteoglycans with ions) and mechanical stress (interaction of proteoglycans and collagens). When the load is removed, the structure of the cartilage tissue can be restored by absorption of water along with nutrients [14], and the swelling pressure of the proteoglycans is balanced by the resistance of the collagen network. Without load, most of the water in the tissue is bound to proteoglycans.

Cartilage, as a tissue without blood vessels and nerves, receives nutrition through diffusion due to movement. During movements, it absorbs synovial fluid like a sponge, only to return it back after some time. When joints are immobilized, the flow of water is limited, the synthesis of proteoglycans slows down, but the content of collagen fibers increases, which can retain calcium salts and become calcified, which again reduces the degree of hydration of proteoglycans and the elasticity of cartilage tissue [16]. That is, all types of immobilization of joints lead to dystrophic changes of cartilage tissue of varying severity [17–19]. Injuries of long bones without immobilization, but only with a restriction in the range of movements in the joint and the load on the limb, were found to result in thinning of the cartilage and dystrophic changes in the long term. Instead, an increase in dynamic load led to a moderate increase in the synthesis and content of proteoglycans [20].

In immobilization of the joint in the flexed position for more than 8 weeks, thickening of the cartilage in the loaded areas of the joint is often observed. During immobilization of the joint with subsequent axial load on the limb, no changes occur in the cartilage tissue. In a similar situation, thickening of articular cartilage was found in animal models. It is precisely such differences between animal models and the real situation in humans that must be taken into account when analyzing the results of experiments.

Under the conditions of 20-day bed rest, a rapid decrease in the mineral density of bones, mainly lumbar and metatarsal, was noted, although biochemical markers of bone resorption were not observed in the blood [21]. During prolonged bed rest or in conditions of weightlessness, the loss of bone matrix can be from 10 to 30 %, but due to bone remodeling after the beginning of adequate loading, this problem is leveled [22].

The joint is surrounded by a joint capsule, which consists of collagen fibers and is attached to the bone near the periphery of the articular cartilage, passing into the periosteum. This structure seals the joint cavity, provides passive stability due to restriction of movements and active stability with the help of proprioceptive nerve endings through reflex control

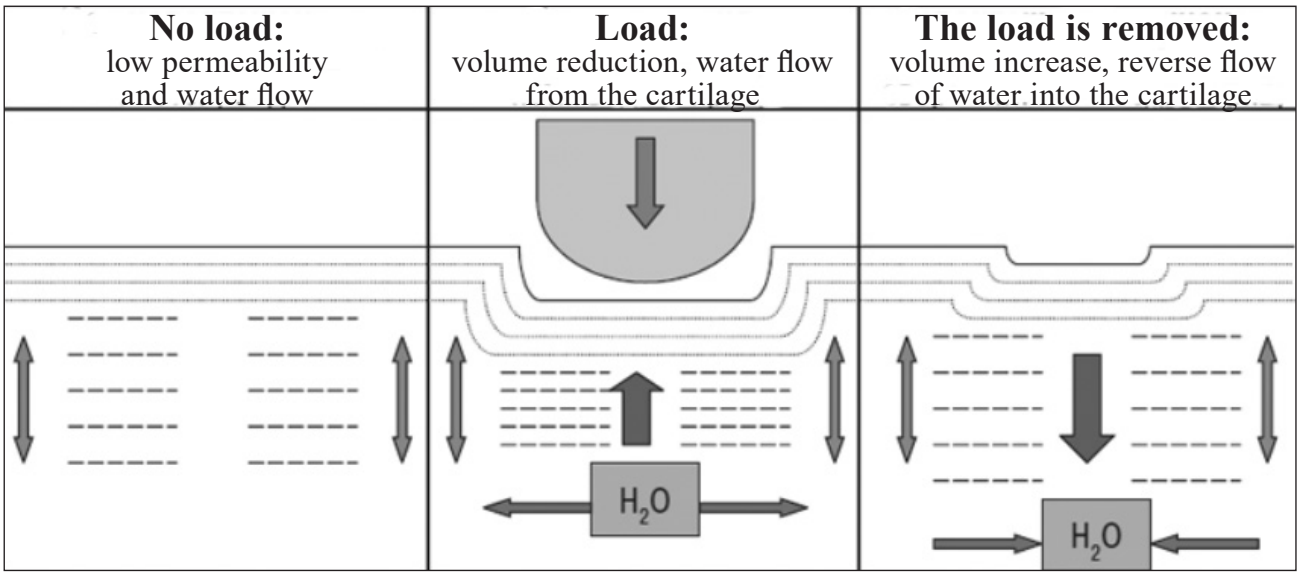

Fig. 3. Movement of water in an articular cartilage under the impact of load and without it (according to [15])

of the corresponding muscles [23, 24]. Localized thickenings of the capsule form capsular ligaments that provide strong points of bone fixation. Tendons are usually attached to the joint capsule and sometimes replace it, as in the case of the quadriceps and patellar tendons in the front of the knee. Blood vessels and nerves pass through the joint capsule.

The main material of the joint capsule is type I and III collagen, the balance of which is disturbed under conditions of immobilization: the amount of type I collagen increases [25, 26]. Some authors consider hypertrophy of the synovial membrane and fibrosis of the joint capsule to be the main cause of post-immobilization contractures [27, 28]. It has been shown that fibrosis of the joint capsule with excessive expression of type I collagen occurs and progresses within a week after immobilization, collagen density increases in 2 and 4 weeks, biochemical changes develop in the composition of periarticular fibrous connective tissue, with a noticeable decrease in the content of water and glycosaminoglycans [29].

The synovial membrane is the inner layer of the joint capsule, producing synovial fluid that lubricates the joint surfaces and provides nutrition to the cartilage [30]. It is a well-vascularized structure that consists of two layers: superficial (contains one or two layers of synovial cells) and basal (connective tissue). There are two types (A and B) of synovial cells: A — macrophage-like, B — fibroblast-like (secreting hyaluronic acid and glycoprotein molecules, which are part of synovial fluid). An extensive system of permeable capillaries allows plasma to flow out of the bloodstream and enter the joint cavity. The content of filtered plasma combines with hyaluronic acid, glycoproteins and leukocytes, forming synovial fluid [31].

Tendons and ligaments are structures made of dense connective tissue and tightly bound together. They play an important role in the mobility and stability of the musculoskeletal system [32]. Tendons connect muscles to bones and facilitate body movements by transmitting tensile forces and storing elastic energy. Ligaments stabilize joints and direct movements within the normal range [33–35]. One of the important features of tendons is the ability of their bundles to slide independently of each other. This allows them to transmit stress during movements, despite changing joint angles [36], and to change shape in case of muscle contraction. Sliding inside tendons occurs not only between bundles of collagen fibers, but also between fibers, which can account for up to 50 % of the longitudinal deformation (i.e. stretching) of the structure [37]. Any sliding of collagen fibers or their bundles relative to each other must occur within the proteoglycan-rich matrix.

The functions of tendons and ligaments depend on a strong, flexible structure of collagen fibers, which are hierarchically organized and connected by sheaths of connective tissue. Tendons and ligaments are composed of type I collagen, proteoglycans, elastin, and glycoproteins. In tendons, type I collagen fibers are located parallel to each other along the longitudinal axis, in ligaments, the fibers are multidirectional and less organized to better withstand tension loads [38].

Tendons and ligaments are attached to bones through an enthesis, which is designed to dissipate mechanical stress at the interface between hard and soft tissues [33].

Short-term immobilization leads to a violation of the mechanical properties of tendons, they lose stiffness and elasticity [39], but only long-term (more than 9 months) immobilization or bed rest causes dystrophic changes.

Muscles are not directly part of the joint, but provide its stabilization and mobility. The muscular system is a collection of muscle fibers capable of contraction, united in bundles. The mass of muscles is much greater than that of other organs, in an adult it can reach up to 40 % of the total body weight. The main functions of muscles are motor, protective (protection of the abdominal cavity), formative (muscle development to some extent determines the shape of the body and the function of other systems, for example, respiratory); energy (transformation of chemical energy into mechanical and thermal energy). 70–80 % of muscle mass is water. Most of the dry residue (20–30 %) is made up of proteins and other organic compounds and mineral salts.

The description of the structures of the joint in view of the structure and biochemistry makes it possible to understand what happens in it during immobilization or long-term restriction of mobility. Let us briefly summarize the above. As a result of immobilization or forced reduction of motor activity, signs of dystrophic changes in the form of a decrease in strength and mass begin to develop in the muscles [40]. This leads to the initiation of biochemical processes, which is manifested in a decrease in the number of myofibrillar proteins; levels of ATP and creatine phosphate, activity of sarcoplasmic enzymes, ATPase activity of myosin; an increase in the amount of stroma proteins and myoalbumin, the activity of lysosomal enzymes, the activity of creatine phosphokinase (CPK) in the blood, creatinuria [41]. Loss of muscle strength occurs at different rates and averages between 5 and 15 % per week, increasing with age [42].

In our opinion, immobilization contractures can be divided into two types, namely: developing directly as a result of immobilization; developing due to restriction of movements and load on the joint or degenerative diseases. Depending on the etiology, joint contracture is divided into arthrogenic and myogenic. Arthrogenic is caused by changes in bone, cartilage, synovial membrane, capsule and ligaments. Myogenic is caused by muscles, tendons and fascia [43, 44]. If there have been changes in the joints due to the violation of biochemical processes with the subsequent restructuring of tissues, we can talk about the process of contracture formation. But the signs of stiffness in the joints after short-term immobilization, or the presence of temporary pain due to trauma, skin irritation, etc., are often observed.

In such cases, tissue reconstruction does not occur, and mobility is restored in full after a short period of time after the elimination of limiting factors. The described conditions are classified as neurogenic reflex contractures. In the study, we do not consider neurogenic contractures caused by persistent disorders of the central nervous system, cerebral palsy, paralysis.

The specified changes in the immobilized joints occur from the beginning of the limitation of mobility, but become visible with time. We present the time course of the reconstruction of the joints in co ditions of limited mobility (Fig. 4).

The first changes occur after 72 hours of joint immobilization. In muscles, dystrophic disorders of slow and fast muscle fibers occur in 14 and 17 %,

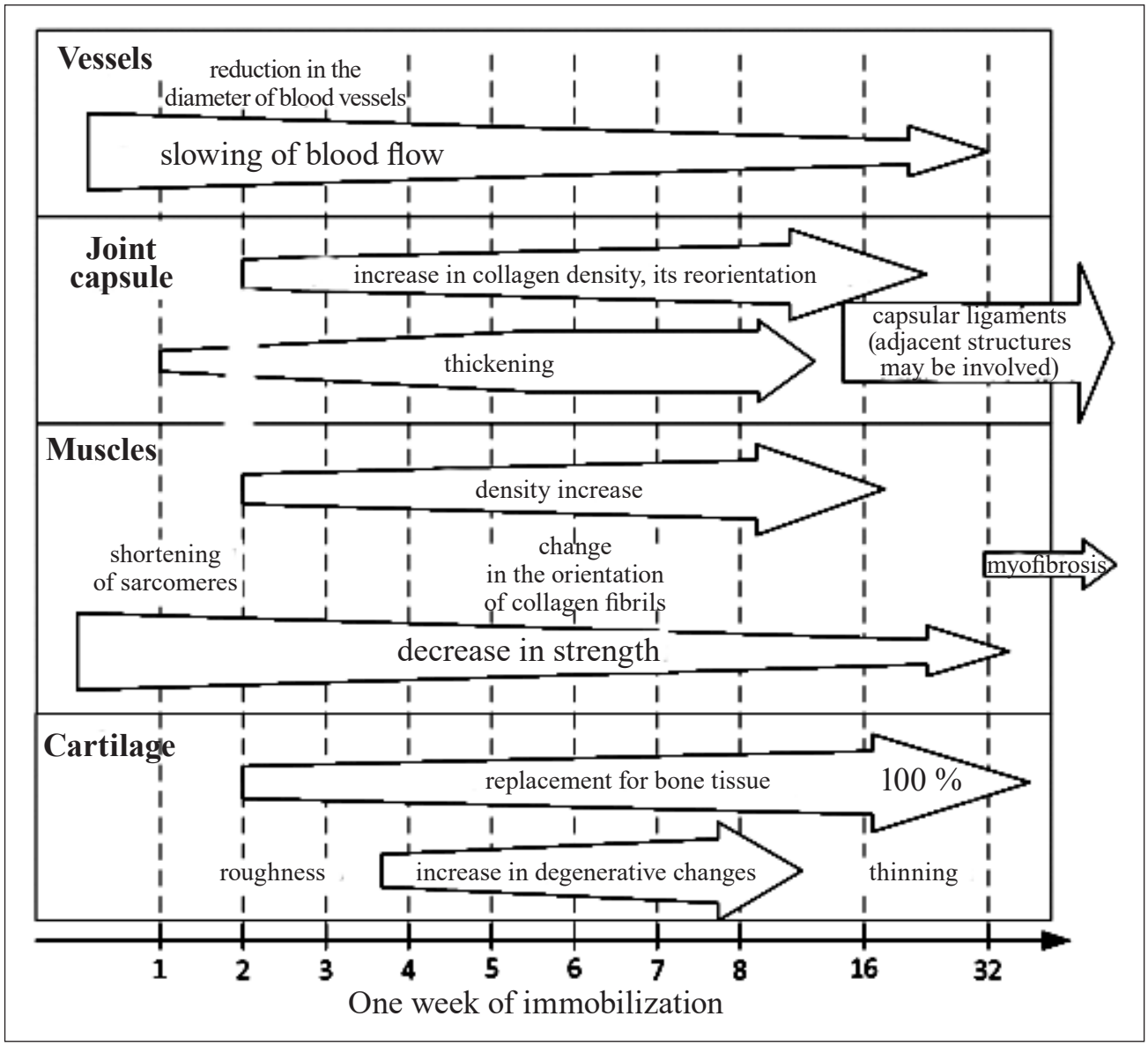

Fig. 4. Temporal changes in structural elements of a joint under conditions of limited mobility

respectively [45]. After a week of immobilization, a decrease in the length of the muscle sarcomeres [46] is noted, followed by disruptions in the collagen network. That is, in the first 2 weeks collagen fibers are located longitudinally along the axis of muscle fibers, then circularly in 4, 8 and 12 weeks. In addition, the amount of hyaluronic acid increases, resulting in tighter muscles. That is, their mechanical properties change: they become harder and lose elasticity.

The response to long-term immobilization is myofibrosis, a condition with excessive formation of connective tissue in the endomysium and perimysium of skeletal muscles [47]. In addition, the biochemical composition of muscle tissue is disturbed, which collectively makes normal muscle functioning impossible [48].

After a week of immobilization, the first changes in the joint capsule were recorded [27] in the form of an increase in its thickness by 20 % and collagen density per unit area up to 60 %, which continues to increase during immobilization. The changes increased during the immobilization of the joint, and by the 4th week, the thickness of the capsule increased by 50 %, and the density of collagen increased by 78 %. According to Y. Zhou et al. [49] the activity of joint capsule remodeling slows down after 6 weeks of immobilization. It has been established that the stretching of the capsule depends on its thickness [51, 52], and it can be assumed that hypertrophy of the capsule affects the development of arthrogenic contracture.

In the first week of immobilization, the cartilage surface loses its shine [52], in the second week it becomes rough, and in the fourth week signs of degeneration appear [53]. On the 32nd week in an immobilized joint without load, cartilage was shown to be replaced by bone [54]. The process begins from the second week of immobilization of the knee joints and progresses to 14, 75, 95, 100 % within 2, 4, 8, 16 weeks of immobilization, respectively [55]. The authors emphasize that such changes are irreversible [54].

Immobilization affects not only the structure of the joint and muscles, but also the blood vessels. According to R. D. Hyldahl et al. [56], 10 days after its onset, the diameter of resistant arteries significantly decreased and vascular functions were suppressed, which, in turn, negatively affected the nutrition of the joint and, accordingly, its structural and functional features.

A conceptual model of the formation of contractures has been proposed based on the created temporal sequence of changes in joint components (Fig. 5). It is based on the presence of three main elements, namely: the control system — the movement control center; movement mechanism — joint; life support systems.

The created conceptual model of the development of contractures suggests that the immobilization of the joint of the injured limb blocks the execution of the signal of motor impulses, that is, the mobility of the joint becomes impossible or significantly limited. After a short period of time, the lack of movement in the joint leads to a decrease in muscle strength and a slowing of blood circulation, which causes the narrowing of blood vessels in the near future. These processes are interconnected, i. e. hypotonia of the muscle is simultaneously triggered by the limitation of nutrition resources through the blood supply, at the same time, the lack of contractile activity of the muscles results in the reorganization of the blood vessels.

Despite the fact that cartilage does not have blood vessels, its nutrition is carried out through the subchondral bone and thanks to osmosis from the synovial fluid, the synthesis of which, in turn, requires the nutrition of the capillary-rich synovial membrane. All this happens under conditions of joint mobility. The lack of movement limits the supply of nutrition, the synthesis of relevant proteins is disrupted, the surface of the cartilage, synovial membrane and fluid begins to be rebuilt, the joint capsule, ligaments, and tendons thicken, and their density increases. As a result of the distortion of biochemical processes with the cessation of a full supply of nutrition, the amount of connective tissue in the muscles increases, they become shorter and denser.

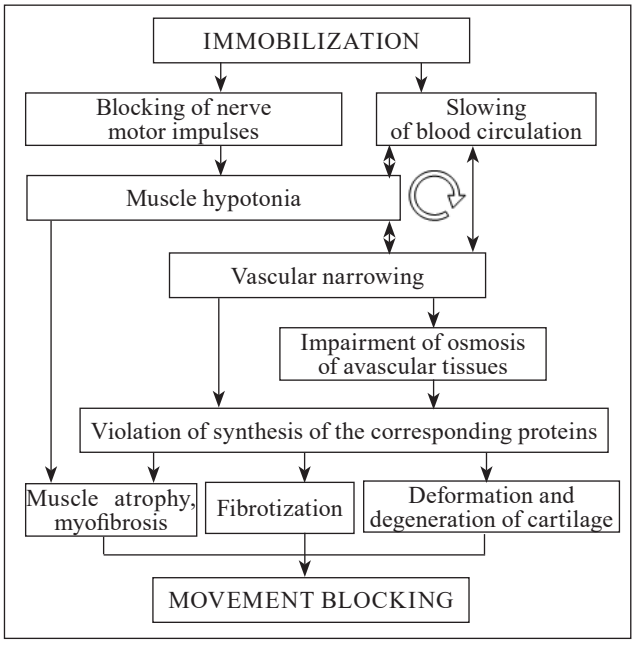

Fig. 5. Conceptual model of contracture development

In long-term immobilization, degenerative processes in the tissues of the joint lead to deterioration of its general condition, which may later cause its complete immobilization.

Conclusions

A conceptual model of the formation of immobilization contractures of joints is proposed, which takes into account structural and functional changes in them under conditions of immobilization. Considering the cumulative effect of destructive disorders, it is possible to predict at what time of immobilization irreversible changes in the joint occur. Immobilization affects all components of the joint and adjacent tissues from the first days, the changes progress over time. The model can be used to develop a system of treatment measures to prevent the development of contractures.

Conflict of interest. The authors declare no conflict of interest.

References

1. https://compendium.com.ua/uk/clinical-guidelines-uk/osteoartroz-praktichna-nastanova/glava-3-budova-sinovialnih-suglobiv/
2. Spuzyak M. I. X-ray diagnostics of endocrine osteopathies [Rentgenodiagnostika endokrinnykh osteopatiy] / M. I. Spuzyak. — Kyiv: Zdorov'ya, 1988. — 160 p.
3. Composition and structure of articular cartilage: a template for tissue repair / A. R. Poole, T. Kojima, T. Yasuda [et al.] // Clinical Orthopaedics and Related Research. — 2001. — No. 391 (Suppl). — P. S26–33. — DOI: 10.1097/00003086-200110001-00004.
4. Stockwell R. A. The lipid and glycogen content of rabbit articular hyaline and non-articular hyaline cartilage / R. A. Stockwell // Journal of Anatomy. — 1967. — Vol. 102 (Pt 1). — P. 87–94.
5. Huber M. Anatomy, biochemistry, and physiology of articular cartilage / M. Huber, S. Trattnig, F. Lintner // Investigative Radiology. — 2000. — Vol. 35 (10). — P. 573–80. — DOI: 10.1097/00004424-200010000-00003.
6. Alford J. W. Cartilage restoration, part 1: basic science, historical perspective, patient evaluation, and treatment options / J. W. Alford, B. J. Cole // The American Journal of Sports Medicine. — 2005. — Vol. 3 (2). — P. 295–306. — DOI: 10.1177/0363546504273510.
7. Iannotti J. P. Physiology / J. P. Iannotti, R. D. Parker // Netter Collection of Medical Illustrations: Musculoskeletal System, Part III — Biology and Systemic Diseases. — 1991. — P. 25–66.
8. Boos M. A. Multiscale strain transfer in cartilage / M. A. Boos, S. R. Lamande, K. S. Stok // Frontiers in Cell and Developmental Biology. — 2022. — Vol. 10. — Article ID: 795522. — DOI: 10.3389/fcell.2022.795522.
9. Diurnal variations in articular cartilage thickness and strain in the human knee / J. L. Coleman, M. R. Widmyer, H. A. Leddy [et al.] // The Journal of Biomechanics. — 2013. — Vol. 46 (3). — P. 541–547. — DOI: 10.1016/j.jbiomech.2012.09.013.
10. Functional analysis of articular cartilage deformation, recovery, and fluid flow following dynamic exercise *in vivo* / F. Eckstein, M. Tieschky, S. Faber [et al.] // Anatomy and Embryology. — 1999. — Vol. 200 (4). — P. 419–424. — DOI: 10.1007/s004290050291.
11. Lu X. L. Proteoglycans and mechanical behavior of condylar cartilage / X. L. Lu, V. C. Mow, X. E. Guo // Journal of Dental Research. — 2009. — Vol. 88 (3). — P. 244–248. — DOI: 10.1177/0022034508330432.
12. Wong M. Articular cartilage functional histomorphology and mechanobiology: a research perspective / M. Wong, D. R. Carter // Bone. — 2003. — Vol. 33 (1). — P. 1–13. — DOI: 10.1016/s8756-3282(03)00083-8.
13. Basic science of articular cartilage / C. B. Carballo, Y. Nakagawa, I. Sekiya, S. A. Rodeo // Clinics in Sports Medicine. — 2017. — Vol. 36 (3). — P. 413–425. — DOI: 10.1016/j.csm.2017.02.001.
14. The effect of mechanical stress on cartilage energy metabolism / R. B. Lee, R. J. Wilkins, S. Razaq, J. P. Urban // Biorheology. — 2002. — Vol. 39 (1–2). — P. 133–143.
15. Kuettner K. E. Cartilage integrity and homeostasis / K. E. Kuettner, E. J.–M. A. Thonar // Rheumatology / P. Dieppe, J. Klippel (eds). — 2nd edition. — London: Mosby–Wolfe, 1998. — P. 8.6.1–8.6.13.
16. Gubsky Yu. I. Biological chemistry: Textbook [Biolohichna khimiya: Pidruchnyk] / Yu. I. Gubsky. — Kyiv–Ternopil : Ukrmedknyga, 2000. — 508 p. (in Ukrainian)
17. Behrens F, Kraft EL, Oegema TR Jr. Biochemical changes in articular cartilage after joint immobilization by casting or external fixation // Journal of Orthopaedic Research. — 1989. — Vol. 7 (3). — P. 335–343. — DOI: 10.1002/jor.1100070305.
18. Thinning of articular cartilage after joint unloading or immobilization. An experimental investigation of the pathogenesis in mice / M. Nomura, N. Sakitani, H. Iwasawa [et al.] // Osteoarthritis & Cartilage. — 2017. — Vol. 25 (5). — P. 727–736. — DOI: 10.1016/j.joca.2016.11.013.
19. Proteoglycan alterations following immobilization and remobilization in the articular cartilage of young canine knee (stifle) joint / A. M. Säämänen, M. Tammi, J. Jurvelin [et al.] // Journal of Orthopaedic Research. — 1990. — Vol. 8 (6). — P. 863–873. — DOI: 10.1002/jor.1100080612.
20. Vincent TL, Wann AKT. Mechanoadaptation: articular cartilage through thick and thin / T. L. Vincent, A. K. T. Wann // Journal of Physiology. — 2019. — Vol. 597 (5). — P. 1271–1281. — DOI: 10.1113/JP275451.
21. Effect of bed rest immobilization on metabolic turnover of bone and bone mineral density / H. Fukuoka, Y. Nishimura, M. Haruna [et al.] // Journal of Gravitational Physiology. — 1997. — Vol. 4 (1). — P. S75–S81.
22. Ohshima H. [Bone metabolism in human space flight and bed rest study] / H. Ohshima, C. Mukai // Clin Calcium. — 2008. — Vol. 18 (9). — P. 1245–1253. (in Japanese).
23. Kovalenko V. M. Osteoarthrosis. Practical instruction / V. M. Kovalenko, O. P. Bortkevich. — 3rd edition. — Kyiv : MORION, 2010.
24. An anatomic study on the attachment of the joint capsule to the tibia in the lateral side of the knee / H. Nasu, A. Nimura, S. Sugiura [et al.] // Surgical and Radiologic Anatomy. — 2018. — Vol. 40 (5). — P. 499–506. — DOI: 10.1007/s00276-017-1942-8.
25. Evans B. Experimental immobilization and remobilization of rat knee joints / B. Evans, G. Eggers, J. Butler // Journal of Bone and Joint Surgery. Amarican volume. — 1960. — Vol. 42. — P. 737–758.
26. Thaxter T. H. Degeneration of immobilized knee joints in rats; histological and autoradiographic study / T. H. Thaxter, R. A. Mann, C. E. Anderson // Journal of Bone and Joint Surgery. Amarican volume. — 1965. — Vol. 47. — P. 567–585.
27. Effects of joint immobilization on changes in myofibroblasts and collagen in the rat knee contracture model / R. Sasabe, J. Sakamoto, K. Goto [et al.] // Journal of Orthopaedic Research — 2017. — Vol. 35 (9). — P. 1998–2006. — DOI: 10.1002/jor.23498.
28. Therapeutic effect of intra-articular injection of ribbon-type decoy oligonucleotides for hypoxia inducible factor-1 on joint contracture in an immobilized knee animal model / D. Sotobayashi, H. Kawahata, N. Anada [et al.] // Journal of Gene

Medicine. — 2016. — Vol. 18 (8). — P. 180–192. — DOI: 10.1002/jgm.2891.
29. The effect of immobilization on the types of collagen synthesized in periarticular connective tissue / D. Amiel, W. H. Akeson, F. L. Harwood, G. L. Mechanic // Connective Tissue Research. — 1980. — Vol. 8 (1). — P. 27–32. — DOI: 10.3109/03008208009152118.
30. Kelley's textbook of rheumatology / Eds. G. S. Firestein, R. C. Budd, S. E. Gabrie [et al.]. — 11th edition. — Elsevier, 2021. — 2400 p.
31. Morphological and immunocytochemical characterization of cultured fibroblast-like cells derived from adult human synovial membrane / F. Vandenabeele, C. De Bari, M. Moreels [et al.] // Archives of Histology and Cytology. — 2003. — Vol. 66 (2). — P. 145–153. — DOI: 10.1679/aohc.66.145.
32. Development and maintenance of tendons and ligaments / L. Bobzin, R. R. Roberts, H. J. Chen [et al.] // Development. — 2021. — Vol. 148 (8). — Article ID : dev186916. — DOI: 10.1242/dev.186916.
33. Benjamin M. Structure-function relationships in tendons: a review / M. Benjamin, E. Kaiser, S. Milz // Journal of Anatomy. — 2008. — Vol. 212 (3). — P. 211–228. — DOI: 10.1111/j.1469-7580.2008.00864.x.
34. Connizzo B. K. Structure-function relationships of postnatal tendon development: a parallel to healing / B. K. Connizzo, S. M. Yannascoli, L. J. Soslowsky // Matrix Biology. — 2013. — Vol. 32 (2). — P. 106–116. — DOI: 10.1016/j.matbio.2013.01.007.
35. Regulation of tendon differentiation by scleraxis distinguishes force-transmitting tendons from muscle-anchoring tendons / N. D. Murchison, B. A. Price, D. A. Conner [et al.] // Development. — 2007. — Vol. 134 (14). — P. 2697–2708. — DOI: 10.1242/dev.001933.
36. Functional morphology of the supraspinatus tendon / J. Fallon, F. T. Blevins, K. Vogel, J. Trotter // Journal of Orthopaedic Research. — 2002. — Vol. 20 (5). — P. 920–926. — DOI: 10.1016/S0736-0266(02)00023-2.
37. An investigation into the effects of the hierarchical structure of tendon fascicles on micromechanical properties / H. R. Screen, D. A. Lee, D. L. Bader, J. C. Shelton // Proceedings of the Institution of Mechanical Engineers, Part H. — 2004. — Vol. 218 (2). — P. 109–119. — DOI: 10.1243/095441104322984004.
38. Tozer S. Tendon and ligament: development, repair and disease / S. Tozer, D. Duprez // Birth Defects Research Part C: Embryo Today: Reviews. — 2005. — Vol. 75 (3). — P. 226–236. — DOI: 10.1002/bdrc.20049.
39. The effects of immobilization on the mechanical properties of the patellar tendon in younger and older men / C. Couppe, C. Suetta, M. Kongsgaard [et al.] // Clinical Biomechanics (Bristol, Avon). — 2012. — Vol. 27 (9). — P. 949–954. — DOI: 10.1016/j.clinbiomech.2012.06.003.
40. Nonuniform loss of muscle strength and atrophy during bed rest: a systematic review / U. Marusic, M. Narici, B. Simunic [et al.] // Journal of Applied Physiology. — 2021. — Vol. 131 (1). — P. 194–206. — DOI: 10.1152/japplphysiol.00363.2020.
41. Quantitative alterations in intramuscular connective tissue following immobilization: an experimental study in the rat calf muscles / L. Jozsa, J. Thoring, M. Jarvinen [et al.] // Experimental and Molecular Pathology. — 1988. — Vol. 49 (2). — P. 267–278. — DOI: 10.1016/0014-4800(88)90039-1.
42. Suetta C. Plasticity and function of human skeletal muscle in relation to disuse and rehabilitation: Influence of ageing and surgery / C. Suetta // Danish Medical Journal. — 2017. — Vol. 64 (8). — Article ID: B5377.
43. Four weeks of mobility after 8 weeks of immobility fails to restore normal motion: a preliminary study / J. Zhou, H. K. Uhthoff, O. Laneuville // Clinical orthopaedics and related research. — 2008. — Vol. 466 (5). — P. 1239–1244. — DOI: 10.1007/s11999-008-0181-z.
44. Trudel G. Differentiating the myogenic and arthrogenic components of joint contractures. An experimental study on the rat knee joint/ G. Trudel // International Journal of Rehabilitation Research. — 1997. — Vol. 20 (4). — P. 397–404. — DOI: 10.1097/00004356-199712000-00006.
45. Lindboe C. F. Effect of immobilization of short duration on the muscle fibre size / C. F. Lindboe, C. S. Platou // Clin Physiol. — 1984. — Vol. 4 (2). — P. 183–188. — DOI: 10.1111/j.1475-097x.1984.tb00234.x.
46. Effects of reduced joint mobility on sarcomere length, collagen fibril arrangement in the endomysium, and hyaluronan in rat soleus muscle / M. Okita, T. Yoshimura, J. Nakano [et al.] / Journal of Muscle Research and Cell Motility. — 2004. — Vol. 25 (2). — P. 159–166. — DOI: 10.1023/b:jure.0000035851.12800.39.
47. Metformin reduces myogenic contracture and myofibrosis induced by rat knee joint immobilization via AMPK-mediated inhibition of TGF-β1/Smad signaling pathway / F. Wang, C. X. Zhou, Z. Zheng [et al.] // Connective Tissue Research. — 2022. — Vol. 20. — P. 1–14. — DOI: 10.1080/03008207.2022.2088365.
48. Consequences of ankle joint immobilisation: insights from a morphometric analysis about fibre typification, intramuscular connective tissue, and muscle spindle in rats / W. P. Mayer, J. Baptista, F. De Oliveira [et al.] // Histochemistry and Cell Biology. — 2021. — Vol. 156 (6). — P. 583–594. — DOI: 10.1007/s00418-021-02027-3.
49. Rabbit model of extending knee joint contracture: progression of joint motion restriction and subsequent joint capsule changes after immobilization / Y. Zhou, Q. B. Zhang, H. Z. Zhong [et al.] // Journal of Knee Surgery. — 2020. — Vol. 33 (1). — P. 15–21. — DOI: 10.1055/s-0038-1676502.
50. Structural and mechanical properties of the glenohumeral joint posterior capsule / M. J. Bey, S. A. Hunter, N. Kilambi [et al.] // Journal of Shoulder and Elbow Surgery. — 2005. — Vol. 14 (2). — P. 201–206. — DOI: 10.1016/j.jse.2004.06.016.
51. Spatial distribution of hip capsule structural and material properties / K. J. Stewart, R. H. Edmonds-Wilson, R. A. Brand, T. D. Brown // J Biomech. — 2002. — Vol. 35 (11). — P. 1491–1498. — DOI: 10.1016/s0021-9290(02)00091-x.
52. Remobilization causes site-specific cyst formation in immobilization-induced knee cartilage degeneration in an immobilized rat model / M. Nagai, A. Ito, J. Tajino [et al.] // Journal of Anatomy. — 2016. — Vol. 228 (6). — P. 929–939. — DOI: 10.1111/joa.12453.
53. Cartilage matrix changes in contralateral mobile knees in a rabbit model of osteoarthritis induced by immobilization / Q. Zhou, B. Wei, S. Liu [et al.] // BMC Musculoskeletal Disorders. — 2015. — Vol. 16. — Article ID: 224. — DOI: 10.1186/s12891-015-0679-y.
54. Bone replaces articular cartilage in the rat knee joint after prolonged immobilization / T. M. Campbell, K. Reilly, O. Laneuville [et al.] // Bone. — 2018. — Vol. 106. — P. 42–51. — DOI: 10.1016/j.bone.2017.09.018.
55. Bone replaces unloaded articular cartilage during knee immobilization. A longitudinal study in the rat / M. Watanabe, T. M. Campbell, K. Reilly [et al.] // Bone. — 2021. — Vol. 142. — Article ID: 115694. — DOI: 10.1016/j.bone.2020.115694.
56. Passive muscle heating attenuates the decline in vascular function caused by limb disuse / R. D. Hyldahl, P. S. Hafen, W. B. Nelson [et al.] // The Journal of Physiology. — 2021. — Vol. 599 (20). — P. 4581–4596. — DOI: 10.1113/JP281900.

The article has been sent to the editors 22.08.2022

ISSN 0030-5987. Orthopaedics, traumatology and prosthetics. 2022. № 3–4

CONCEPTUAL MODEL OF THE PROCESS OF FORMATION OF IMMOBILIZATION CONTRACTURES

O. A. Tyazhelov [1], A. M. Khasawneh Ayham [2], O. D. Karpinska [1], M. Yu. Karpinsky [1], M. Z. Bitsadze [1]

[1] Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv
[2] National Pirogov Memorial Medical University, Vinnytsya. Ukraine

✉ Olexiy Tyazhelov, MD, Prof. in Orthopaedics and Traumatology: alzhar3001@gmail.com
✉ Ayham Adli Mohammad Khasawneh, MD: dr.aiham.k@gmail.com
✉ Olena Karpinska: helen.karpinska@gmail.com
✉ Mykhaylo Karpinsky: korab.karpinsky9@gmail.com
✉ Marianna Bitsadze, MD, PhD in Orthopaedics and Traumatology: bitsadze.marianna@gmail.com