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BONE TISSUE

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Annotation. This article describes a review of the literature on bone tissue, its composition, anatomical and physiological structure of bone tissue, bone tissue as an organ. Details are given about the cellular composition of bone tissue, as well as the intercellular matrix, its organic and inorganic composition. As well as the mechanisms of bone tissue restructuring in physiological and pathological conditions.

Keywords: bone, bone tissue, osteoblasts, osteoclasts, osteocytes, modeling, remodeling, bone resorption, collagen.

Bone tissue is a specialized mineralized type of connective tissue. Being the basis of the musculoskeletal system, it performs the function of mechanical protection of internal organs from external influences [3,8]. Bone tissue stores up to 95% of inorganic substances, including 99% of calcium reserves, 87% of phosphorus and 58% of magnesium [1]. In addition, one of the most important functions of bone tissue is its participation in hematopoiesis. Studying bone tissue, Omelianenko, N.P., distinguishes between the concepts of "bone as an organ" and the concept of "bone tissue"[6]. Bone tissue, first of all, is a highly specialized type of connective tissue. Like any tissue, it consists of cells and intercellular matter. A distinctive feature of connective tissue is its high hardness, mechanical strength, and the presence of a large amount of intercellular matter with a relatively small number of bone cells. Bone tissue contains 4 types of cells: osteoblasts, osteocytes, osteoclasts and stem cells [4].

Bone as an organ is a complex structure, its concept includes, in addition to the bone tissue itself, the periosteum, bone marrow, blood and lymph vessels, nerves, and may also include cartilage. Osteoblasts are polygonal cells, of medium size up to 15-40 microns, with developed organelles such as the Golgi complex, plasma network, ribosomes, and high actin content. Mature and immature osteoblasts are distinguished, active and inactive. Active osteoblasts secrete alkaline phosphatase, synthesize proteins, and form an osteoid. Alkaline phosphatase is a histochemical marker of osteoblasts, and the biochemical marker of these cells is osteocalcin. The main function of osteoblasts is to produce bone matrix, which includes protein synthesis, formation of collagen network, matrix vesicles, cytokines, growth factors, collagenase, glycoproteins, osteonectin, bone sialoprotein, etc. Among other things, osteoblasts have

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receptors on themselves and produce substances that regulate the remodeling process [8]. Osteocytes are differentiated osteoblasts. Due to the presence of long processes that form numerous anastomoses, they form a three-dimensional network through which various substances are transported [5]. In addition, osteocytes have receptors for PTH [10], synthesize osteocalcin, FF-23, thereby participate in the regulation of calcium-phosphorus metabolism, synthesize matrix proteins and sclerostin, an inhibitor of the Wnt signal in osteoblasts Osteocytes play the role of phagocytes in the process of bone resorption, so their activity in this process is great [11]. However, according to a number of authors, the main function of osteocytes is to transmit chemical and mechanical signals to osteoblasts, integumentary cells and osteoclasts, since signal transmission to these cells is necessary to start the remodeling process, both in physiological and pathological conditions.

Osteoclasts are giant multinucleated cells of hematopoietic origin. They perform mainly a resorbing function. This function is determined primarily by their ability to attach tightly to the surface of the bone, while forming a subcellular space completely isolated from extracellular fluid; secondly, by cell polarization, as a result of which the part of the cell membrane facing the bone acquires a corrugated structure, while increasing the area of contact with the bone and thereby facilitates the entry of cellular products into the resorption region; thirdly, they have a unique ability to secrete hydrogen ions and proteolytic enzymes into the resorbing region, and the products bone matrix disintegration is transcellularly removed into the surrounding space. Stem cells are the precursors of osteoblasts, which perform an important role in the process of bone tissue regeneration in case of damage [12]. Depending on the structure and function, bone tissue is divided into 2 types: trabecular (spongy) and cortical (compact) bone tissue [15].

The human skeleton consists of 80% compact tissue and 20% spongy bone tissue. The ratio of spongy and compact tissue varies in different bones. For example, spongy tissue prevails in the vertebrae (75:25), and in the heads of the femur the ratio of these types of tissues is equal (50:50), and in the diaphysis of the radius the compact tissue is 95% [11]. Bone tissue undergoes changes in both internal and external structure under the influence of factors of the external and internal environment (age, nutritional conditions, muscle work, the state of the nervous and endocrine system, the presence of pathology of internal organs). In addition, bone tissue has the ability to adapt to external influences. All this happens due to 2 processes, modeling and remodeling processes occurring in the bone, as a result of which the destruction of the old and the creation of a new bone occurs [2].

Modeling is the process of formation of new bone, determining the microstructure of bone

during growth or recovery after injury. Modeling is the process of coordinating resorption and osteogenesis occurring simultaneously in different areas of the bone. This process is regulated by a variety of metabolic and mechanical factors [7,14]. Thus, thanks to modeling, the bone adapts to increased loads, and also restores its shape in case of various injuries.

Remodeling is a process of coordinated interaction between osteoblasts and osteoclasts, which results in the destruction of old bone and the replacement of its newly formed tissue. As a result of remodeling, bone tissue does not change the shape and size of the organ, but is the process that provides bone strength and mineral homeostasis [13]. Remodeling processes occur at all, regardless of age. In children and the fetus, the remodeling and modeling processes run in parallel. The basis of connective tissue is the intercellular substance. It provides transport of various nutrients, as well as mechanical support to cells. The intercellular substance consists of glycoproteins, proteoglycans and hyaluronic acid. Collagen content prevails among glycoproteins. Collagen is a fibrillar structural protein of the extracellular substance of connective tissue, containing several domains and consisting of 3 polypeptide chains arranged in a triple helix. The primary structure of the polypeptide chains of collagen can be represented in the form of a formula (Gli-X-Y), where X and Y can be any amino acids, but most often the amino acid proline is in place of X, and hydroxyproline or hydroxylysine is in place of Y. In the formation of a specific spatial configuration of the collagen molecule, the presence of these amino acids plays a key role.

Collagen is a polymorphic protein, and has 28 different types, differing from each other in the primary structure of the polypeptide chain, in function and location. A special formula is used to designate each type of collagen, which uses Roman numerals indicating the type of collagen and Arabic numerals indicating the collagen chain. For example, type 1 collagen is written with the formula [α1(I)2 α2(I)]. The index in parentheses indicates the number of identical chains in the collagen molecule. Due to the polymorphism of the collagen molecule, there are different classifications of collagen proteins. According to the most common classification, there are 5 groups of collagen proteins.

1. Fibrillating collagens. This includes collagen types I II III V XI XXIV XXVII. 2. Collagens associated with fibrils: IX XII XIV XVI XIX XXI XXII

3. Collagens forming reticular structures: IV VI VIII X XXVIII

4. Transmembrane collagens: XIII XVII XXIII XXV

5. Collagens with multiple interrupting domains of the triple helix: XV XVIII.

90-95% of the organic matrix of bone tissue is type I collagen, which ensures the strength of

bone tissue. Each type I collagen molecule consists of 2 α1 chains and 1 α2 chains. Each of these chains consists of a helical domain, with C- (carboxytherminal) and N- (aminotherminal) terminal propeptides at the end necessary for the formation of a triple helix of a tropocollagen molecule. In the process of collagen biosynthesis, during the formation of the tropocollagen molecule, the N-terminal (amino terminal) and C-terminal (carboxytherminal) propeptide are cleaved off with the help of specific proteases. These propeptides are necessary for the formation of the triple helix of the collagen molecule and for the further formation of collagen fibrils. When the terminal propeptides are cleaved from the procollagen molecule, they are released into the blood. The detection of these terminal propeptides (C- and N-terminal propeptides) are of important clinical and diagnostic importance, since they reflect the exchange of collagen molecules, i.e. functional activity of osteoblasts. PINP (aminotherminal propeptide of procollagen type I) and PICP (carboxytherminal propeptide of procollagen type I) serve as biochemical markers of bone formation. These markers have proven themselves well in monitoring the effectiveness of anti-osteoporotic treatment. In addition, they are of great value in the diagnosis of diseases such as osteoporosis, Penjet's disease, renal osteodystrophy, as well as in some oncological and rheumatic diseases.

Type II collagen is an important component for the normal development of bones and teeth. It is most present in cartilage, intervertebral discs, as well as in the vitreous body. Its molecule consists of three identical α chains, each of which consists of 1060 amino acid residues with an extended continuous domain and short non-spiral fragments. Collagen fibrils are relatively thinner than type I collagen fibrils. Type III collagen is a homotrimer (α1(III). Each of the α chains contains up to 1029 amino acid residues. It is the predominant protein in the skin and interstitial blood vessels. It is present in bone tissue only in trace amounts. Collagen IV is a key structural component of the basement membranes. Its molecules form hexameric structures formed by the "butt-to-butt" connection of the N-ends of collagen trimers. These hexamers are additionally stabilized by transverse covalent crosslinking between lysine and meteonin residues. The spirals of type IV collagen, connecting with each other, form a "web" characteristic of this type of collagen, which plays an important role in regulating the permeability of the basement membranes. Type V collagen is present in the skin, in fetal bone tissue, in the mature cornea and interstitial kidneys. It is considered as a factor in the initiation of the assembly of type I collagen molecules.

The main component of descemet membranes of the corneal endothelium is type VIII collagen. It is also present in large quantities in the subendothelial layer of blood vessels. Type VIII

collagen chains (α1 and α2) are structurally similar to type X collagen chains. Type X collagen is secreted by hypertrophied chondrocytes during endochondrial ossification. It is represented by a homotrimer in which each of the α chains contains short spiralized sections of 154 amino acid residues, limited by non-collagen domains from the N- and C-terminus, with a length of 37 and 161 amino acid residues, respectively. Unlike fibrillar collagens, terminal fragments are not cleaved off during posttranslational modification. And the presence of non-collagen domains provides a characteristic structure for collagens of types IV, VIII and X. There are transmembrane collagens, which belong to the class of transmembrane proteins. These collagens have a short cytoplasmic terminal fragment (N-terminus) and, connected to a hydrophobic membrane site, an extracellular long interrupted spiralized domain. The presence of extracellular domains in the molecules of transmembrane collagens ensures their cellular adhesion. Type VIII collagen is mainly found in focal contacts, type XVII collagen in hemidesmosomes, type XXV collagen in neurons, type XXIII collagen is expressed by prostate carcinoma cells.

Collagens XV and XVIII are classified as chondroitin sulfate and heparan sulfate proteinoglycans, respectively. They are mainly localized in the area of the basement membranes. Type XV collagen is most common in skeletal muscles, heart and placenta. They are expressed by the adrenal glands, kidneys and pancreas. Type XVIII collagen pre-mRNA in humans undergoes 2 types of splicing. During translation, 2 isoforms of this protein are formed: short and long.The short chain is expressed in various organs and tissues, but the synthesis of the long isoform is characteristic only of the liver.The biological role of these types of collagen has not been fully studied. But it is assumed that they are involved in the regulation of the functions of specialized basement membranes. Thus, in most diseases of the skeleton, the metabolism of bone tissue is disrupted, remodeling processes with predominant bone resorption occur intensively, as a result of which type I collagen degradation products are released into the blood in large quantities, which are widely used in the diagnosis of many diseases of bone tissue, and are also widely used to control treatment.

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