The production and reabsorption of bone tissue and

The human skeleton system is a rigid structure formed of 206 bones that support the human body. It consists of bones, muscles and all elements of mesodermal derivation. The bone is a hard, resistant and specialised form of connective tissue.

Bone tissue is characterised by a particular hardness and resentence to the mechanical stresses, so they can support during the movement and remodelling cycle (Bone Tissue, 2017). The poster will discuss further about bone tissue, how hormones and physical stress regulate bone remodelling and Paget's disease. The organic part of bone tissue is composed of: osteoprogenitor cells, osteoblasts, osteocytes and osteoclasts that provide for the growth, production and reabsorption of bone tissue and extracellular matrix. Microscopic observation of the bone structure allows us to recognise: a fibrous and a lamellar bone tissue. Fibrous bone is an immature bone and found in the embryo, metaphyseal area, infants and during the fracture healing.

Once deposited, it is reabsorbed and replaced with lamellar bone tissue. Under the microscope, the fibrous bone tissue is presented as a series of fibres intertwined in the three dimensions of the space in an almost random manner. The meshes of this " three-dimensional spider web" are made up of large collagen fibres of considerable thickness. The fibrous bone tissue is more elastic and less consistent than the lamellar one, due to the lower quantity of minerals and the lack of a preferential orientation of the collagen fibres.

On the other hand, lamellar bone tissue forms the mature bone that results from the remodelling of the fibrous bone or pre-existing bone. It is an organised tissue, with an ordered and parallel orientation of the collagen fibres, which are arranged in overlapping layers, called bony lamellae (Figure 1). Between one lamella and the other, small spaces communicate with each other through a system of canaliculi and contact with the areas of the bone from which they can receive nutritive materials. The lamellar bone tissue is divided into cancellous bone and compact bone (Palastanga & Soames, 2012). The cancellous (trabecular) bone is located in the innermost part of the bones.

It looks like a sponge and inside there are many spaces between the trabeculae. The trabeculae are variously oriented and intersected to each other (Figure 1). The red marrow (haematopoietic) and yellow (fat) found in medullary cavity (Bone Tissue, 2017).

On the contrary, the compact bone forms the outer portion of the bones and the diaphysis of the latter. It presents itself with the lamella structure organised in osteons. Inside them, the bone cells (osteocytes) are distributed in cavities in the form of a biconvex lens called bone lacunae (Figure 2). The most evident characteristic of the osteon is given by the presence of concentric lamella columns that delimit a central channel. Together, lamellae and canal form the Hadrian system (synonym of osteon).

The various systems of human body communicate with each other (anastomosis), with the medullary cavity and with the free surface of the bone through the channels arranged transversely and obliquely, known as

channels of Volkmann (Horvai & Link, 2012). As shown in (Figure 2), in the periosteum, there are two types of channels: longitudinal (of Havers) in which the blood capillary flows and transversals (of Volkmann), which come from the periosteum and form the endostea and flow into the longitudinal ones (Horvai & Link, 2012). Bone is a tissue in continuous remodelling due to the dynamic balance between processes of biosynthesis and resorption processes. The osteoblasts are to synthesise the organic bone matrix and to favour its mineralisation; the main role of osteoclasts consists in the formation of the reabsorption cavities and in the dissolution of both the organic and mineral matrix. Most of the osteoblasts after having terminated the deposition of the matrix, differentiate into osteocytes; others remain on the surface of the new bone lining cell. The process of bone remodelling is regulated by several hormonal factors.

Vitamin D stimulates osteoblast activity with a consequent increase in extracellular matrix mineralisation and the differentiation of osteoclast precursors into mature osteoclasts (Raisz, 2017). Oestrogens maintains the bone growth and influence bone remodelling by regulating the release of cytokines and growth factors by the cells of the bone microenvironment. Hyperthyroidism increases the frequency of activation of BMUs and, on the contrary, reduces the duration of the reabsorption and neo apposition phases, determining the loss of bone mass. Secrete cytokines and growth factors produce the sclerostin protein which, by blocking the WNT pathway. It inhibits osteoblastic differentiation, therefore, occurs the deposition of the bone matrix (Figure 3). The substances that regulate the balance (homeostasis) of calcium are parathyroid hormone (PTH), calcitriol (the

hydroxylated form of vitamin D) and, locally in the bone tissue, calcitonin. PTH increases calcium reabsorption from bone and kidney and increases the production of calcitriol (Figure 4).

The latter increases the functions of the osteoblasts and contrasts the excretion of calcium by the kidney; calcitonin inhibits calcium renal reabsorption, bone resorption and increases the production of calcitriol, operated by osteoclasts. Also, daily physical exercise, practising rhythmic gymnastics and AMP–activated protein kinases increase high circulating levels of sclerostin deacetylase, also led to inhibition of the proapoptotic effect of sclerostin in association with activation of autophagy which can affect bone osteogenesis and remodelling. However, a rapid bone remodelling is very risky and can cause disease such as Paget’s disease of bone (Raisz, 2017). It is a metabolic bone disease, also known as deforming osteitis, caused by osteoclasts and osteoblasts. Osteoblasts are responsible for the construction of bone mass through a deposition process, while osteoclasts are responsible for the demolition of the bone tissue through a defined resorption process. The disease most frequently affects the bones of pelvis, skull, spine and legs (Figure 5). In patients with Paget’s bone disease, the normal process of bone turnover is weak.

The dynamic balance between osteoblasts and osteoclasts is in fact missing – the demolition of the bone tissue occurs very quickly (Reddy, 2016). It is followed by an abnormal neoformation, where the bone structure is disorganised and deformed. Initially, there is a marked increase in bone resorption in localised areas, due to the activity of numerous osteoclasts. Osteolysis is followed by a compensatory increase in bone formation,

induced by osteoblasts recruited in the area. The intense and accelerated osteoblastic activity produces a coarse tissue, consisting of thick lamellae and trabeculae that are arranged in a chaotic way (mosaic model), rather than respecting the normal lamellar model, as shown in tibia (Figure 5). The resorbed bone tissue is replaced and the medullary spaces are filled with an excess of fibrous connective tissue, with a marked increase in new blood vessels (hypervascularization of the newly formed bone).

Hypercellularity of the bone can, therefore, cause malignant degeneration (pagetic bone). The pathological alteration of the cycle of reabsorption and neoformation of the bones makes the new bone bigger and softer. The risk of Paget’s disease is related to an increase in age. Although, there is no specific cure – some medications can help reduce pain (Reddy, 2016).

However, bone is a living tissue and metabolically very active, thanks to the continuous renewal in progress. The correct quantities of nutrients, calcium and physical effort in our daily life will help to avoid major bone diseases and keeping skeleton system healthy.