The skeletal system is composed of bones and cartilage, which are connected by ligaments to form a framework for the remainder of the body tissues. There are two parts to the skeleton:

- **Axial skeleton** – bones along the axis of the body, including the skull, vertebral column and ribcage;
- **Appendicular skeleton** – appendages, such as the upper and lower limbs, pelvic girdle and shoulder girdle.

**Function**

As well as contributing to the body's overall shape, the skeletal system has several key functions, including:

- Support and movement;
- Protection;
- Mineral homeostasis;
- Blood-cell formation;
- Triglyceride storage.

**Support and movement**

Bones are a site of attachment for ligaments and tendons, providing a skeletal framework that can produce movement through the coordinated use of levers, muscles, tendons and ligaments. The bones act as levers, while the muscles generate the forces responsible for moving the bones.

**Protection**

Bones provide protective boundaries for soft organs: the cranium around the brain, the vertebral column surrounding the spinal cord, the ribcage containing the heart and lungs, and the pelvis protecting the urogenital organs.

**Mineral homeostasis**

As the main reservoirs for minerals in the body, bones contain approximately 99% of the body's calcium, 85% of its phosphate and 50% of its magnesium (Bartl and Bartl, 2017). They are essential in maintaining homeostasis of minerals in the blood with minerals stored in the bone are released in response to the body's demands, with levels maintained and regulated by hormones, such as parathyroid hormone.

**Blood-cell formation (haemopoiesis)**

Blood cells are formed from haemopoietic stem cells present in red bone marrow. Babies are born with only red bone marrow; over time this is replaced by yellow marrow due to a decrease in erythropoietin, the hormone responsible for stimulating the production of erythrocytes (red blood cells) in the bone marrow. By adulthood, the amount of red marrow...
has halved, and this reduces further to around 30% in older age (Robson and Syndercombe Court, 2018).

**Triglyceride storage**
Yellow bone marrow (Fig 1) acts as a potential energy reserve for the body; it consists largely of adipose cells, which store triglycerides (a type of lipid that occurs naturally in the blood) (Tortora and Derrickson, 2009).

**Bone composition**
Bone matrix has three main components:
- 25% organic matrix (osteoid);
- 50% inorganic mineral content (mineral salts);
- 25% water (Robson and Syndercombe Court, 2018).

Organic matrix (osteoid) is made up of approximately 90% type-I collagen fibres and 10% other proteins, such as glycoprotein, osteocalcin, and proteoglycans (Bartl and Bartl, 2017). It forms the framework for bones, which are hardened through the deposit of the calcium and other minerals around the fibres (Robson and Syndercombe Court, 2018).

Mineral salts are first deposited between the gaps in the collagen layers with once these spaces are filled, minerals accumulate around the collagen fibres, crystallising and causing the tissue to harden; this process is called ossification (Tortora and Derrickson, 2009). The hardness of the bone depends on the type and quantity of the minerals available for the body to use; hydroxyapatite is one of the main minerals present in bones. While bones need sufficient minerals to strengthen them, they also need to prevent being broken by maintaining sufficient flexibility to withstand the daily forces exerted on them. This flexibility and tensile strength of bone is derived from the collagen fibres. Over-mineralisation of the fibres or impaired collagen production can increase the brittleness of bones – as with the genetic disorder osteogenesis imperfecta – and increase bone fragility (Ralston and McInnes, 2014).

**Structure**
Bone architecture is made up of two types of bone tissue:
- Cortical bone;
- Cancellous bone.

**Cortical bone**
Also known as compact bone, this dense outer layer provides support and protection for the inner cancellous structure. Cortical bone comprises three elements:
- Periosteum (Fig 1);
- Intracortical area;
- Endosteum (Bartl and Bartl, 2017).

The periosteum is a tough, fibrous outer membrane. It is highly vascular and almost completely covers the bone, except for the surfaces that form joints; these are covered by hyaline cartilage. Tendons and ligaments attach to the outer layer of the periosteum, whereas the inner layer contains osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells) responsible for bone remodelling.

The function of the periosteum is to:
- Protect the bone;
- Help with fracture repair;
- Nourish bone tissue (Robson and Syndercombe Court, 2018).

It also contains Volkmann’s canals, small channels running perpendicular to the diaphysis of the bone (Fig 1); these convey blood vessels, lymph vessels and nerves from the periosteal surface through to the intracortical layer. The periosteum has numerous sensory fibres, so bone injuries (such as fractures or tumours) can be extremely painful (Drake et al, 2019).

The intracortical bone is organised into structural units, referred to as osteons or Haversian systems (Fig 2). These are cylindrical structures, composed of concentric layers of bone called lamellae, whose structure contributes to the strength of the cortical bone. Osteocytes (mature bone cells) sit in the small spaces between the concentric layers of lamellae, which are known as lacunae. Canaliculi are microscopic canals between the lacunae, in which the osteocytes are networked to each other by filamentous extensions. In the centre of each osteon is a central (Haversian) canal.
Bone is found in the outer cortical layer. It is a hard, calcified connective tissue that lines the inside of the bone canals with the periosteum.

Volkmann’s canals connect adjacent osteons and the blood vessels of the central canal through which the blood vessels, lymph vessels and nerves pass. These central canals tend to run parallel to the axis of the bone; Volkmann’s canals connect adjacent osteons and the blood vessels of the central canals with the periosteum.

The endosteum consists of a thin layer of connective tissue that lines the inside of the cortical surface (Bartl and Bartl, 2017) (Fig 1).

Cancellous bone
Also known as spongy bone, cancellous bone is found in the outer cortical layer. It is formed of lamellae arranged in an irregular lattice structure of trabeculae, which gives a honeycomb appearance. The large gaps between the trabeculae help make the bones lighter, and so easier to mobilise.

Trabeculae are characteristically oriented along the lines of stress to help resist forces and reduce the risk of fracture (Tortora and Derrickson, 2009). The closer the trabecular structures are spaced, the greater the stability and structure of the bone (Bartl and Bartl, 2017). Red or yellow bone marrow exists in these spaces (Robson and Syndercombe Court, 2018). Red bone marrow in adults is found in the ribs, sternum, vertebrae and ends of long bones (Tortora and Derrickson, 2009); it is haemopoietic tissue, which produces erythrocytes, leucocytes (white blood cells) and platelets.

Blood supply
Bone and marrow are highly vascularised and account for approximately 10-20% of cardiac output (Bartl and Bartl, 2017). Blood vessels in bone are necessary for nearly all skeletal functions, including the delivery of oxygen and nutrients, homoeostasis and repair (Tomlinson and Silva, 2013). The blood supply in long bones is derived from the nutrient artery and the periosteal, epiphyseal and metaphyseal arteries (Iyer, 2019).

Each artery is also accompanied by nerve fibres, which branch into the marrow cavities. Arteries are the main source of blood and nutrients for long bones, entering through the nutrient foramen, then dividing into ascending and descending branches. The ends of long bones are supplied by the metaphyseal and epiphyseal arteries, which arise from the arteries from the associated joint (Bartl and Bartl, 2017).

If the blood supply to bone is disrupted, it can result in the death of bone tissue (osteonecrosis). A common example is following a fracture to the femoral neck, which disrupts the blood supply to the femoral head and causes the bone tissue to become necrotic. The femoral head structure then collapses, causing pain and dysfunction.

Growth
Bones begin to form in utero in the first eight weeks following fertilisation (Moini, 2019). The embryonic skeleton is first formed of mesenchyme (connective tissue) structures; this primitive skeleton is referred to as the skeletal template. These structures are then developed into bone, either through intramembranous ossification or endochondral ossification (replacing cartilage with bone).

Bones are classified according to their shape (Box 1). Flat bones develop from membrane (membrane models) and sesamoid bones from tendon (tendon models) (Waugh and Grant, 2018). The term intramembranous ossification describes the direct conversion of mesenchyme structures to bone, in which the fibrous tissues become ossified as the mesenchymal stem cells differentiate into osteoblasts. The osteoblasts then start to lay down bone matrix, which becomes ossified to form new bone.

Long, short and irregular bones develop from an initial model of hyaline cartilage (cartilage models). Once the cartilage model has been formed, the osteoblasts gradually replace the cartilage with bone matrix through endochondral ossification (Robson and Syndercombe Court, 2018). Mineralisation starts at the centre of the
cartilage structure, which is known as the primary ossification centre. Secondary ossification centres also form at the epiphyses (epiphyseal growth plates) (Danner, 2019). The epiphyseal growth plate is composed of hyaline cartilage and has four regions (Fig 3):

- **Resting or quiescent zone** - situated closest to the epiphysis, this is composed of small scattered chondrocytes with a low proliferation rate and anchors the growth plate to the epiphysis;
- **Growth or proliferation zone** - this area has larger chondrocytes, arranged like stacks of coins, which divide and are responsible for the longitudinal growth of the bone;
- **Hypertrophic zone** - this consists of large maturing chondrocytes, which migrate towards the metaphysis.
- **Calcification zone** - this final zone of the growth plate is only a few cells thick. Through the process of endochondral ossification, the cells in this zone become ossified and form part of the ‘new diaphysis’ (Tortora and Derrickson, 2009).

Bones are not fully developed at birth, and continue to form until skeletal maturity is reached. By the end of adolescence around 90% of adult bone is formed and skeletal maturity occurs at around 20-25 years, although this can vary depending on geographical location and socio-economic conditions; for example, malnutrition may delay bone maturity (Drake et al, 2019; Bartl and Bartl, 2017). In rare cases, a genetic mutation can disrupt cartilage development, and therefore the development of bone. This can result in reduced growth and short stature and is known as achondroplasia. The human growth hormone (somatotropin) is the main stimulus for growth at the epiphyseal growth plates. During puberty, levels of sex hormones (oestrogen and testosterone) increase, which stops cell division within the growth plate. As the chondrocytes in the proliferation zone stop dividing, the growth plate thins and eventually calcifies, and longitudinal bone growth stops (Ralston and McInnes, 2014). Males are on average taller than females because male puberty tends to occur later, so male bones have more time to grow (Waugh and Grant, 2018). Over-secretion of human growth hormone during childhood can produce gigantism, whereby the person is taller and heavier than usually expected, while over-secretion in adults results in a condition called acromegaly.

If there is a fracture in the epiphyseal growth plate while bones are still growing, this can subsequently inhibit bone growth, resulting in reduced bone formation and the bone being shorter. It may also cause misalignment of the joint surfaces and cause a predisposition to developing secondary arthritis later in life. A discrepancy in leg length can lead to pelvic obliquity, with subsequent scoliosis caused by trying to compensate for the difference.

**Remodelling**

Once bone has formed and matured, it undergoes constant remodelling by osteoclasts and osteoblasts, whereby old bone tissue is replaced by new bone tissue (Fig 4). Bone remodelling has several functions, including mobilisation of calcium and other minerals from the skeletal tissue to maintain serum homeostasis, replacing old tissue and repairing damaged bone, as well as helping the body adapt to different forces, loads and stress applied to the skeleton.

Calcium plays a significant role in the body and is required for muscle contraction, nerve conduction, cell division and blood coagulation. As only 1% of the body’s calcium is in the blood, the skeleton acts as a storage facility, releasing calcium in response to the body’s demands. Serum calcium levels are tightly regulated by two hormones, which work antagonistically to maintain homeostasis. Calcitonin facilitates the deposition of calcium to bone, lowering the serum levels, whereas the parathyroid hormone stimulates the release of calcium from bone, raising the serum calcium levels.

Osteoclasts are large multinucleated cells typically found at sites where there is active bone growth, repair or remodelling, such as around the periosteum, within the endosteum and in the removal of calluses formed during fracture healing (Waugh and Grant, 2018). The osteoclast cell membrane has numerous folds that face the surface of the bone and osteoclasts break down bone tissue by secreting lysosomal enzymes and acids into the space between the ruffled membrane (Robson and Syndercombe Court, 2018). These enzymes
dissolve the minerals and some of the bone matrix. The minerals are released from the bone matrix into the extracellular space and the rest of the matrix is phagocytosed and metabolised in the cytoplasm of the osteoclasts (Bartl and Bartl, 2017). Once the area of bone has been resorbed, the osteoclasts move on, while the osteoblasts move in to rebuild the bone matrix.

Osteoblasts synthesise collagen fibres and other organic components that make up the bone matrix. They also secrete alkaline phosphatase, which initiates calcification through the deposit of calcium and other minerals around the matrix (Robson and Syndercombe Court, 2018). As the osteoclasts deposit new bone tissue around themselves, they become trapped in pockets of bone called lacunae. Once this happens, the cells differentiate into osteocytes, which are mature bone cells that no longer secrete bone matrix.

The remodelling process is achieved through the balanced activity of osteoclasts and osteoblasts. If bone is built without the appropriate balance of osteocytes, it results in abnormally thick bone or bony spurs. Conversely, too much tissue loss or calcium depletion can lead to fragile bone that is more susceptible to fracture. This is due to the loss of mineral in the matrix and a reduction in the flexibility of the collagen.

Diet and lifestyle factors

Adequate intake of vitamins and minerals is essential for optimum bone formation and ongoing bone health. Two of the most important are calcium and vitamin D, but many others are needed to keep bones strong and healthy (Box 2).

Box 2. Vitamins and minerals needed for bone health

Key nutritional requirements for bone health include minerals such as calcium and phosphorus, as well as smaller qualities of fluoride, manganese, and iron (Robson and Syndercombe Court, 2018). Calcium, phosphorus and vitamin D are essential for effective bone mineralisation. Vitamin D promotes calcium absorption in the intestines, and deficiency in calcium or vitamin D can predispose an individual to ineffective mineralisation and increased risk of developing conditions such as osteoporosis and osteomalacia.

Other key vitamins for healthy bones include vitamin A for osteoblast function and vitamin C for collagen synthesis (Waugh and Grant, 2018).

Physical exercise, in particular weight-bearing exercise, is important in maintaining or increasing bone mineral density and the overall quality and strength of the bone. This is because osteoblasts are stimulated by load-bearing exercise and so bones subjected to mechanical stresses undergo a higher rate of bone remodelling. Reduced skeletal loading is associated with an increased risk of developing osteoporosis (Robson and Syndercombe Court, 2018).

Conclusion

Bones are an important part of the musculoskeletal system and serve many core functions, as well as supporting the body’s structure and facilitating movement. Bone is a dynamic structure, which is continually remodelled in response to stresses placed on the body. Changes to this remodelling process, or inadequate intake of nutrients, can result in changes to bone structure that may predispose the body to increased risk of fracture. Part 2 of this series will review the structure and function of the skeletal system.