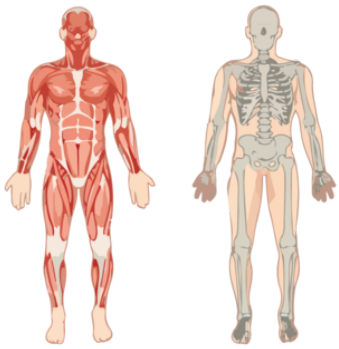

UNIT 12

MUSCULOSKELETAL SYSTEM

Structure

12.1 INTRODUCTION

This unit deals with the structure and functions of human skeleton and muscular system. You know that the human body has intricately interconnected musculoskeletal network. This intricate nature of musculoskeletal interconnection provides the body with a proper form, stability, voluntary movement, and robustness. The musculoskeletal organization is made up of many different structural elements such as bones, joints, ligaments, tendons and the voluntary muscle tissue of the body that support the organism with the day-to-day activities. The ‘contraction force’ is then transferred to the skeletal elements resulting in the movement of body parts. Our body has specialized contractile cells; the muscle cells; which generate motile forces *via* contraction, which is the direct manifestation of the

interaction of the 'contractile proteins' ***actin*** and ***myosin***. The contractile proteins, in association with other components of myofilaments and affiliated proteins, work in unison to generate the motor forces necessary for cellular contraction.

In this unit, you will study about structure and function of bone and muscle cells. You will also learn about the structural components of skeletal muscle, smooth muscle and cardiac muscles. The role of sarcomere, actin, myosin and troponin and calcium in muscular contraction is also described.

Expected Learning Outcomes

After studying this unit, you should be able to:

- explain gross anatomy of bones;
- identify of bone tissue and cells and their functions;
- explain structure of osteon;
- discuss the osteogenesis and distinguish between intramembranous ossification and endochondral ossification;
- describe structure of the smooth, skeletal muscle and cardiac cells and differentiate between them;
- highlight the role of calcium in Excitation–contraction coupling ; and
- enlist the steps of muscle contraction.

12.2 BIOLOGICAL SIGNIFICANCE OF MUSCULOSKELETAL SYSTEM

Musculoskeletal system consists of muscles, bones, cartilage, ligaments, joints, and other connective tissues. Its primary function is the movement of body and it also keeps organs in place and, gives support and protection to the body. The skeleton system is a complex structure consisting of bones and cartilage. Human body has a total of 206 bones with two distinct divisions. The bones vary in shape and are classified as long, short, flat and irregular based on their shape.

Our body has three types of muscle cells; skeletal muscles, cardiac muscles and smooth muscles; among which the skeletal muscles and smooth muscles are part of musculoskeletal system. Skeletal muscles are **'striated muscles'** associated with the bones and are the only **'voluntary muscles'.** The cardiac muscles are present only in the heart and are striated and involuntary in nature. Smooth muscles are present in the lumen of the hollow organs of GIT, blood vessels, urinary bladder etc. Their primary function is the contraction; and help in the movement of food material and substances such as bile and enzymes through the gastrointestinal tract. The smooth muscles adjust blood vessel's diameter and thus regulate the rate of blood flow.

The musculoskeletal system performs several basic functions:

- **Support**: The skeleton serves as the structural framework for the body by supporting soft tissues and providing attachment points for the tendons of most skeletal muscles.
- **Protection:** The skeleton protects the most important internal organs from injury. For example, cranial bones protect the brain, vertebrae (backbones) protect the spinal cord, and the rib cage protects the heart and lungs.
- **Assistance in body movement:** Most skeletal muscles are attached to the bones. Their contraction pull bones to produce movement. Movements of the whole body, such as walking and running, and localized movements such as grasping a pencil or nodding the head as a result of muscular contractions, rely on the integrated functioning of skeletal muscles, bones, and joints.
- **Mineral homeostasis**: Bone tissue stores several minerals, especially calcium (about 99%) and phosphorus, which contribute to the strength of bone. On demand, bone releases minerals into the blood to maintain critical mineral balances (homeostasis) and to distribute the minerals to other parts of the body.
- **Blood cell production:** The developing bones of the fetus and some adult bones, such as the hip bones, ribs, breastbone, vertebrae (backbones), skull, and ends of the bones of the arm and thigh have a connective tissue called red bone marrow. It consists of developing blood cells, adipocytes, fibroblasts, and macrophages within a network of reticular fibers; and produces red blood cells, white blood cells, and platelets by a process, called **hemopoiesis**.
- **Stabilizing body positions:** Skeletal muscle contractions stabilize joints and help maintain body positions, such as standing or sitting. Postural muscles contract continuously when you are awake; for example, sustained contractions of your neck muscles hold your head upright.
- **Storing and moving substances within the body:** Storage is accomplished by sustained contractions of ring-like bands of smooth muscle called sphincters, which prevent outflow of the contents of a hollow organ. Temporary storage of food in the stomach or urine in the urinary bladder is possible because smooth muscle sphincters close off the outlets of these organs.
- **Generating heat:** As muscular tissue contracts, it produces heat, a process known as **thermogenesis**. Much of the heat generated by muscles is used to maintain normal body temperature. Involuntary contractions of skeletal muscles, known as shivering, can increase the rate of heat production.

SAQ 1

Fill in the blanks:

i) The skeletal system consists of .....

ii) The rigid framework of the body is called.....

iii) Calcium is stored mainly in .....

iv) ..... are the voluntary and striated muscles cells.

v) Cardiac muscles are present only in .....

12.3 ANATOMY OF BONE

The bone is a crucial living tissue that makes skeletal system of the body. A bone has two main parts (Fig. 12.3):

1. **Diaphysis** is hollow and cylindrical main portion of the bone.
2. **Epiphyses** (-is, sing.) form the bulbous proximal and distal ends of the bone.

In addition, there are **metaphyses** - special regions present amid the diaphysis and the epiphyses which contain the epiphyseal growth plates in growing bones.

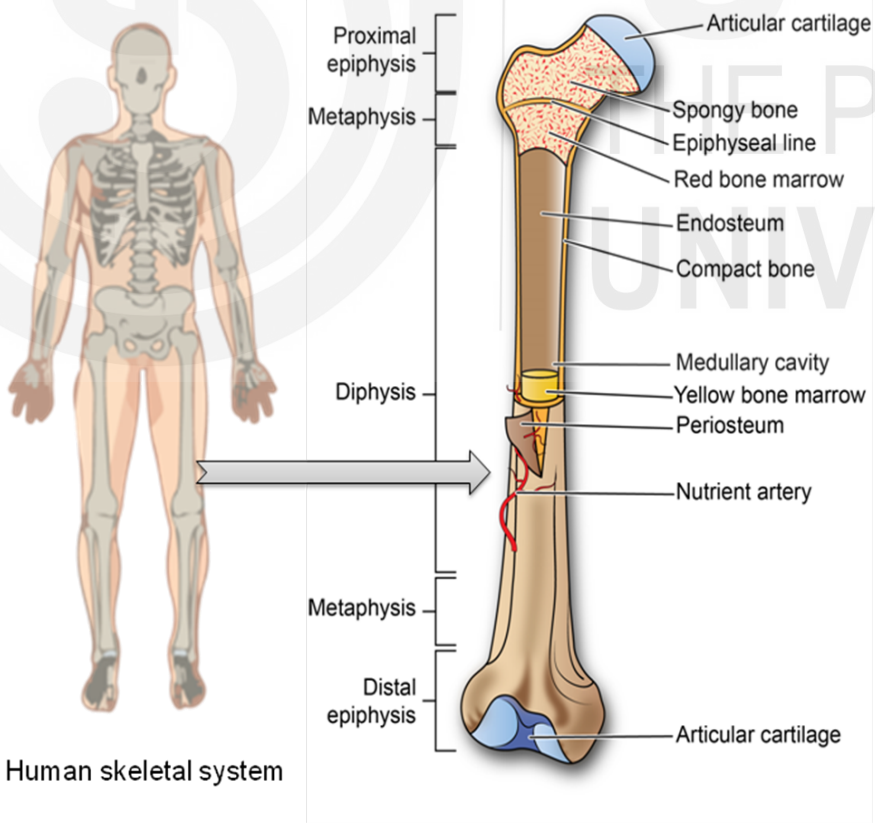

Fig. 12.1: Parts of a long bone. (Image source: http://cnx.org/contents/14fb4ad7-39a1-4eee-ab6e-3ef2482e3e22@7.1@7.1).OpenStax College.

The epiphyseal growth plates are layers of specialized hyaline cartilage which allows the bone to grow in length till 18–21 years of age. Once the bones cease to grow, the hyaline cartilage of the epiphyseal plate gets replaced by osseous material resulting in the formation of a bony structure called the '**epiphyseal line**'. The articular facets/tips of epiphyses are covered and protected by is a thin layer of hyaline cartilage called '**articular cartilage'** (Fig. 12.3). It forms the 'articulation' (joint) with another bone, reduces friction and absorbs shock.

The long cylindrical shaft of diaphysis encloses a '**medullary cavity**' or '**marrow cavity**', which is filled with the **red bone marrow** or **fatty yellow bone marrow** in adults. The walls of the diaphysis are composed of dense and hard compact bone.

Almost the entire external surface of the bone is covered by a tough dense fibrous sheath called '**periosteum**' except the articular cartilage. The muscles, tendons, and ligaments are inserted into the periosteum. The internal surface of the medullary cavity of bone is lined by a thin cellular membrane, **endosteum**. The inner surface of the bone (in the marrow cavity) is spongy. Bones also have **subchondral smooth tissue** present at their ends which is covered with cartilage (Fig. 12.2).

Thus, based on the presence of compact and spongy tissues, bones are categorized into compact and spongy bones.

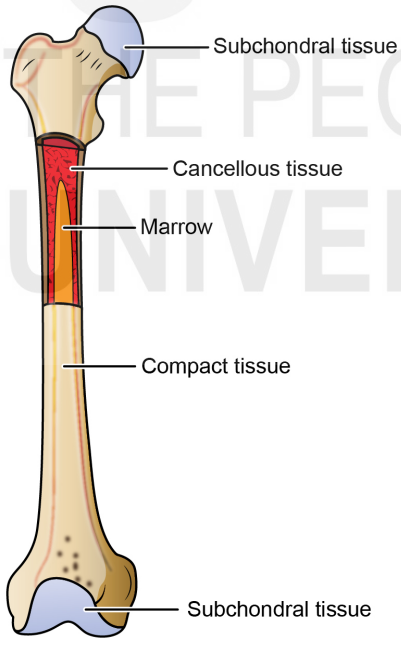

Fig. 12.2: Anatomical structure of bone.

12.3.1 Compact Bone

In the wall of the long bones, the bony material is compressed and compacted making it a very hard structure, hence such bones are also known as

'**compact bones**'. The hard wall of compact bones is made of numerous hollow, long, multi-layered bony columns referred to as '**osteons**'.

The osteon is made of 'osseous tissue'- a tough organic material (mostly collagen fibers and some homogeneous gelatinous substance- the ground substance), which later gets mineralized and hardened. The osteons run parallel to the long axis of the bone, in the line of stress exerted on them. Each multilayered osteon column is made up of concentric layers of lamellae arranged around a 'central channel' called '**Haversian canal**' (or 'canals of Havers'). The central canal contains blood vessels, lymphatics and nerves (neurovascular bundles). These neurovascular channels of Havers along with their concentric bony lamellae form the '**Haversian system**' or 'osteon'. The canals, with their neurovascular bundles, remain connected with one another, and with the endosteum and periosteum *via* 'Volkmann's canals' or 'perforating canals' which pierce the columns horizontally (at right angles to the long axis of the bone) or obliquely to the Haversian canals (Fig. 12.3a&b).

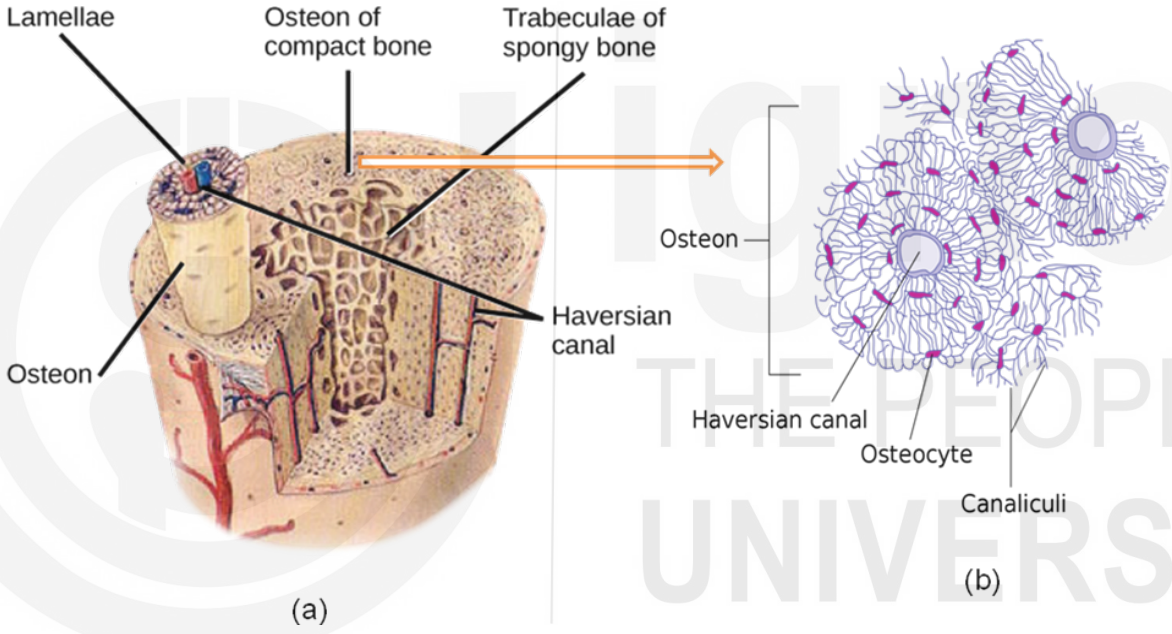

Fig. 12.3(a) Structure of an osteon showing both compact and spongy bone. The arrangement of osteocytes forming the lamellae around a single Haversian canal (b) Transverse section of a compact bone's cortex. (a-Image attribution:http://cnx.org/contents/GFy_h8cu@10.53:rZudN6XP@2/Introduction) (b) https://commons.wikimedia.org/wiki/File:Transverse_section_of_bone_en.sg under licensed: Creative Commons Attribution-Share Alike 4.0 International

12.3.2 Spongy Bone

The spongy bone tissue is always located in the medullary cavities or diploë of a bone, protected by a covering of compact bone. It is strategically located where bones are not heavily stressed or where stresses are applied from many different directions. The spongy bone tissue makes the bulk of the epiphyses of long bones, where it is present beneath a paper-thin protective layer of compact bone; whereas, it lines the medullary cavities of long bones

and makes the interiors of most of the short, flat, sesamoid, and irregularly-shaped bones.

Unlike the hard, compact bone tissue, the **spongy bone,** known as '**trabecular'** or '**cancellous'** bone, does not contain discrete osteons (Fig. 12.4). It consists of an irregular pattern of thin columns called **trabeculae**. The individual trabeculae are made of '**concentric lamellae**', wherein the osteocytes lie in lacunae and extend their cytoplasmic processes through the fine minute canaliculi that radiate outward from the lacunae. The wide gaps/interstitial spaces between the trabeculae are filled with the red bone marrow in hematopoietically active bones, and with yellow bone marrow (adipose tissue) in others. Both contain numerous small blood vessels that supply nutrients to the osteocytes.

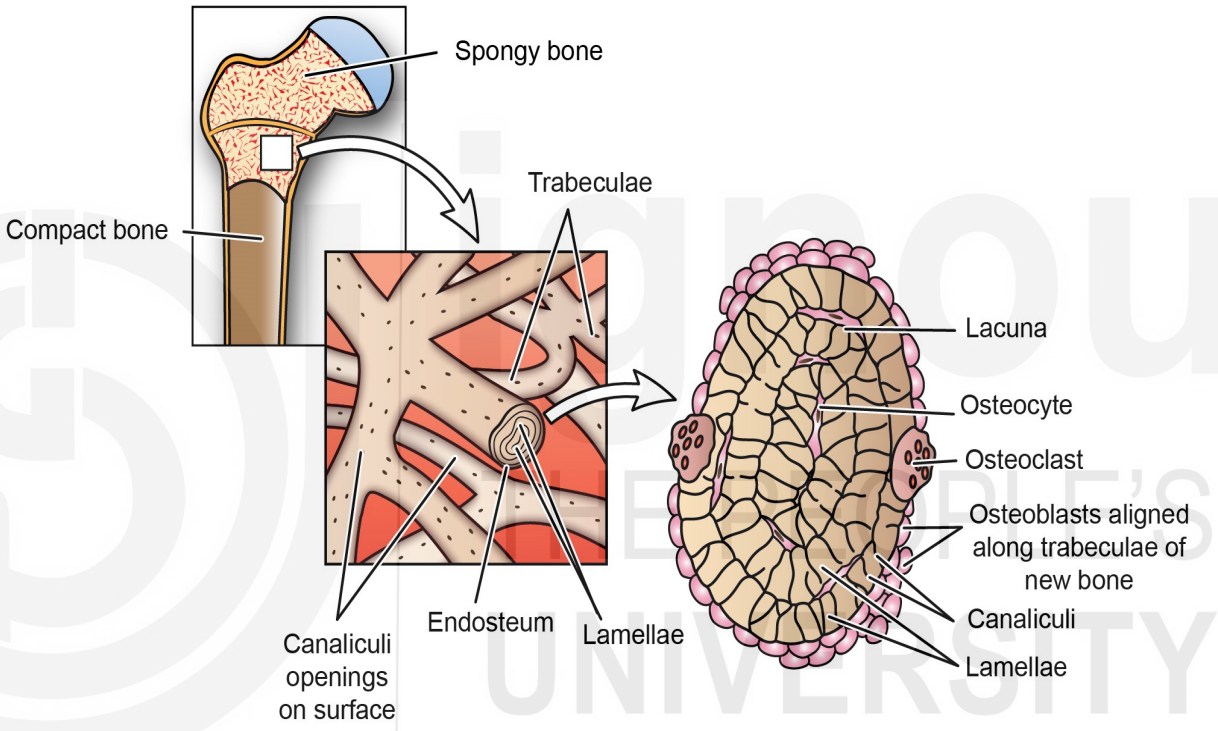

Fig. 12.4: Structure of spongy bone.

12.3.3 Bone Cells

The bone tissue contains four types of cells: (a) osteogenic cells, (b) osteoblasts, (c) osteocytes, and (d) osteoclasts.

(a) **Osteogenic cells or Osteoprogenitor cells** are the uncommitted, unspecialized stem cells of bone which give rise to the bone-forming osteoblasts. They are derived from mesenchymal tissue and are the only cells that undergo mitotic cell division in a bone. These stem cells are found in the lining along the inner portion of the periosteum, in the endosteum, and in the central canals of osteons (Fig.12.5).

(b) **Osteoblasts** are the bone-forming cells. They secrete, around themselves, the organic osseous material, mainly containing collagen fibers, and other organic components needed to build the extracellular matrix (ECM) of bone tissue. Following the secretion of bone ECM, they

initiate bone hardening process called '**calcification / mineralization**', and the individual osteoblasts transform into 'osteocytes'.

(c) **Osteocytes** are the mature bone cells and cannot divide. They are the main cells in bone tissue which maintain and monitor the tissue of its daily metabolism, such as the exchange of nutrients and wastes with the blood. The osteocytes are surrounded with and embedded into ECM of bone; trapped/enclosed singly within lacunae. These cells are involved in maintaining the bone matrix and their death is followed by resorption of the matrix.

(d) **Osteoclasts** are giant, multi-nucleated motile cells of the bone, derived from the fusion of as many as **50 bone marrow-derived blood monocytes**. They are mostly present concentrated in the endosteum. One side of the cell that faces the bone surface, has its plasma membrane deeply folded into a ruffled border from where they release lysosomal lytic enzymes and acids that digest the protein and mineral components of the underlying bone matrix. This process of breaking-down of bone matrix is known as '**bone resorption**'. In these areas, the osteoclasts lie within enzymatically engraved depressions in the matrix known as **resorption bays** (or **Howship lacunae**). The resorption is part of the normal development, maintenance, and repair of bone, which is under the control of hormones such as parathormone, calcitonin etc. Osteoclasts help in regulating the blood calcium level.

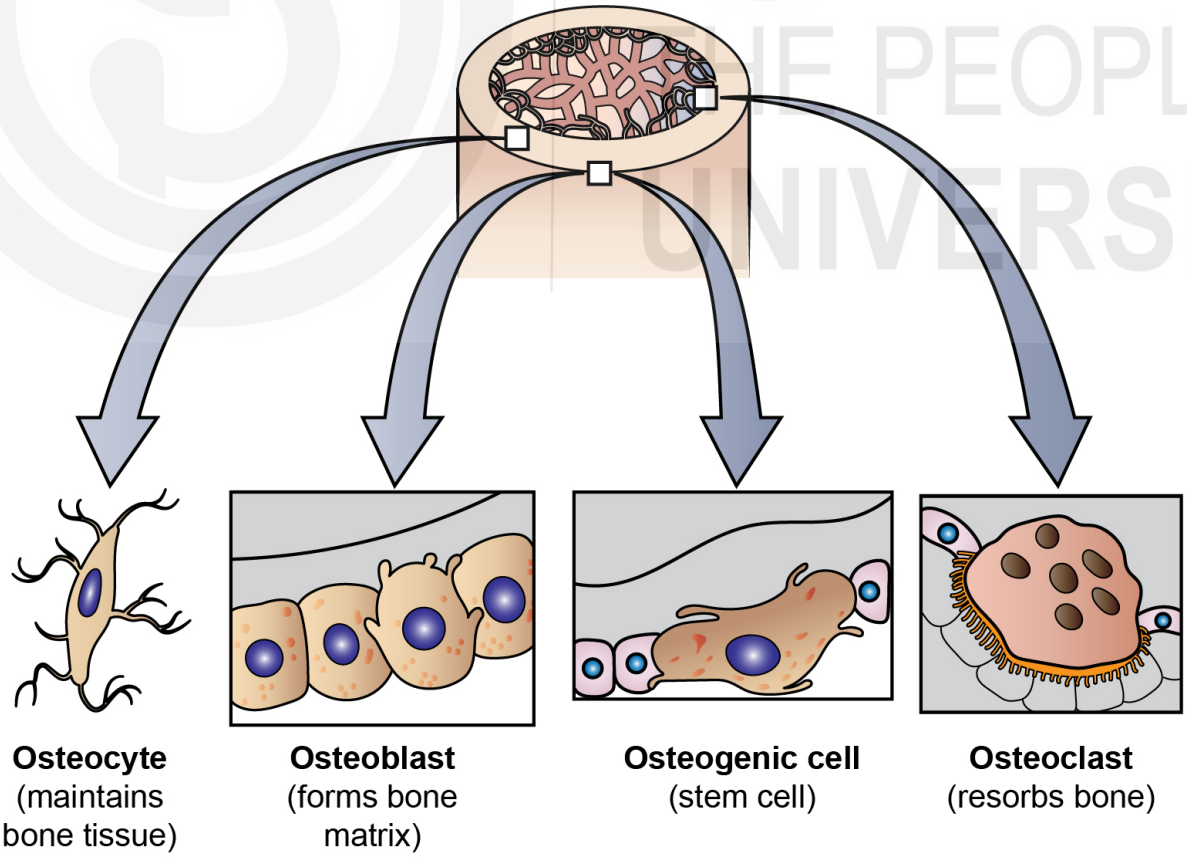

Fig. 12.5: Types of cells in bone tissue.

SAQ 2

(a) Fill in the blanks:

i) The membrane that covers the bone is known as .....

ii) Microscopic unit of a bone is .....

iii) A circular and tubular structure within bone is called.....

iv) The irregular pattern of trabeculae form the .....

v) A specific region between diaphysis and the epiphyses is called .....

vi) The cells of bone are.....

(b) The bone is among the hardest parts of the body. Is bone live or lifeless?

(c) Enlist the basic parts of the bones.

(d) Name the tissues of bones.

12.4 FORMATION OF BONES

You studied in the earlier section that the basic structural and functional unit of a bone is the osteon. It is made of 'osseous tissue'- a tough organic material (mostly collagen fibers and some homogeneous gelatinous substance- the ground substance), which later gets mineralized and hardened. Bone (osseous) tissue is generally dense and hard connective tissue.

Osteogenesis or **Ossification** is the process of bone formation. During early embryonic development, the initiation of bone formation can happen in two different ways:

i) Intramembranous ossification: The osteoblasts differentiate directly from the undifferentiated embryonic mesenchymal stem cells and secrete new bone matrix material, osteoid, which gets calcified later.

ii) Endochondral ossification: The matrix of the preexisting 'hyaline cartilage templates' gets eroded and replaced by osteoblasts, which then produce the osteoid.

Following both these processes, the bone that is formed first is called **primary** or **woven** bone, which is a temporary bone. The temporary bones are soon replaced by the definitive **secondary** or **lamellar bones**.

In addition, bone formation also occurs in various other situations such as during the -

(a) infancy, early childhood, and adolescence until bones reach the adult sizes,

(b) remodeling of bones that occur throughout life, wherein the older bones are replaced with new ones, and

(c) process of repairing bone fractures and breaks.

i) Intramembranous Ossification:

- It is a process of bone formation, by which most **flat bones** are formed; e.g., *frontal* and *parietal* bones of the skull, some parts of the *occipital* and *temporal* bones, and the lower and upper jaw bones- the *mandibles* and the *maxillae*, respectively (Fig. 12.6).
- In this process, the bone formation is initiated within a "condensation layer or membrane" of embryonic mesenchymal tissue.
- Within this cellular membrane, the 'starting point' for bone formation is called an '**ossification center**', where groups of mesenchymal cells differentiate into **osteoblasts**.

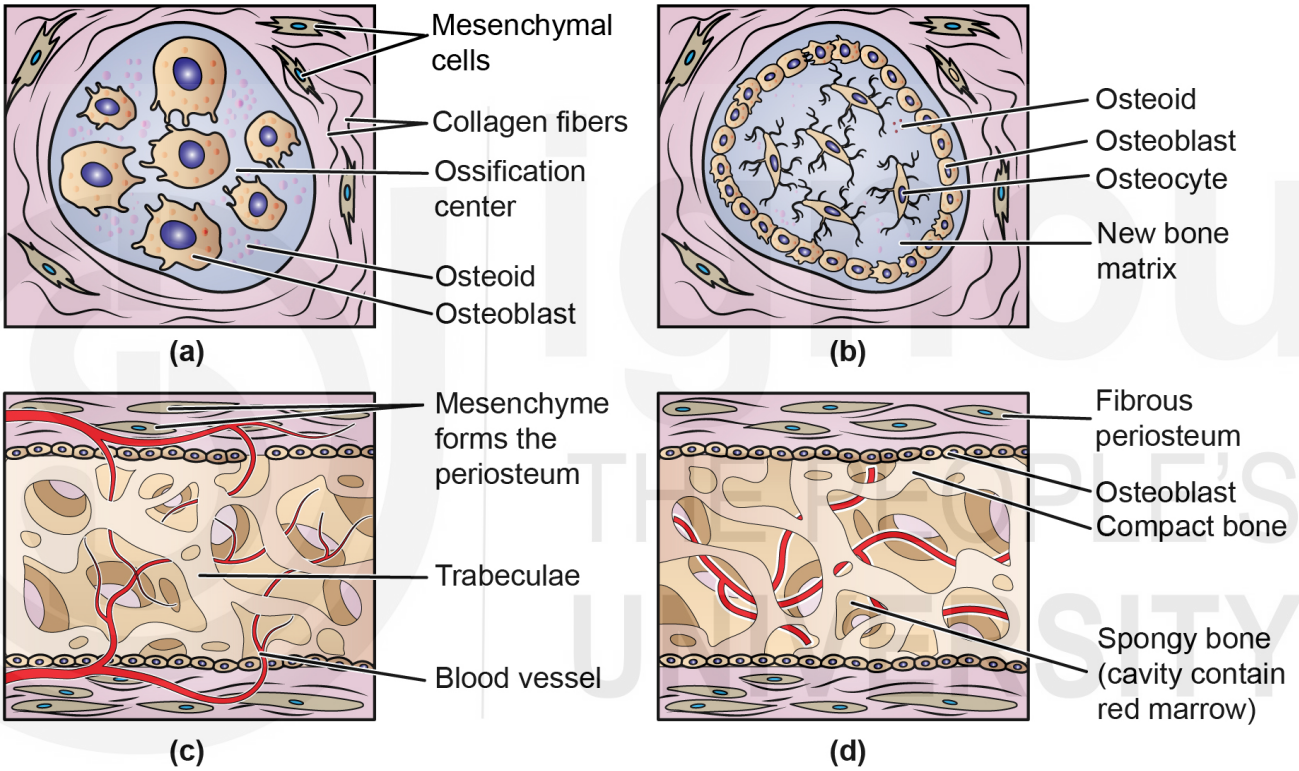

Fig. 12.6: The basic steps of Intramembranous Ossification. (a) Development of the ossification center, (b) calcification, (c) fusion of ossification centers and formation of trabeculae, and (d) development of the periosteum. In the end, the primary woven bone is replaced by the compact lamellar bone.

- Osteoblasts clusters then synthesize and secrete the new bone matrix, called the **osteoid,** at many spots called '**Ossification Centers'**.
- These centers undergo mineralization/ calcification converting the bone ECM into a hard, bony material.
- During the process of hardening of the matrix, some osteoblasts get encapsulated and transform into **osteocytes**.
- All these individual islands of developing bone, form walls that delineate elongated cavities containing capillaries, bone marrow cells, and undifferentiated cells.

- Many such osteoblast clusters arise almost simultaneously at the ossification center, and their fusion between the walls gives the bone a spongy appearance.
- Now, the connective tissue that remains among the bone walls is penetrated by the newly formed blood vessels (angiogenesis) and additional undifferentiated mesenchymal cells, giving rise to the bone marrow.
- The ossification centers of a bone grow radially and finally fuse together, replacing the original connective tissue with a hard mechanically supporting structure.

ii) Endochondral Ossification:

- This is the other method of the bone formation wherein the ossification takes place within a preexisting 'hyaline cartilage template' whose shape resembles a miniature version/model of the future bone, to be formed (Fig. 12.7).
- The cylindrical bones (*long* as well as *short* bones) of the body are formed by this type of ossification.
- The chondroblasts start to secrete cartilage matrix and produce a hyaline cartilage model.
- Periosteal capillaries start to grow into the disintegrating calcified cartilage and induce growth of a '**primary ossification center**', a region deep in the matrix where bone tissue will replace most of the cartilage.
- Osteoblasts then actively deposit bone matrix over the remnants of mineralized cartilage, resulting in the formation of 'spongy bone trabeculae'. Then the process of ossification spreads from this location toward both ends of the cartilage model.
- Secondary ossification centers develop in the epiphyses usually around the time of birth, when the branches of the epiphyseal artery penetrate the epiphyses.
- However, no medullary cavities are formed in epiphyses, and spongy bone remains intact in the interior of the epiphyses.
- A thin layer of hyaline cartilage covers the spongy bone of epiphyses.

In the last stage of prenatal bone development,

- The thin layer of hyaline cartilage that covers the spongy bone of epiphyses forms the **'articular cartilage'** where two adjacent bones articulate at joints.
- The articular cartilage persists throughout adult life and doesn't contribute to bone growth.
- The two ossification centers do not merge, some hyaline cartilage is left unossified in between the two, which forms the **epiphyseal (growth) plate**.

- The growth plate connects each epiphysis to the diaphysis. This is the '*area of growth*' in a long bone until the age of 18-21 years.
- Thereafter, the epiphyseal plate disappears ("**epiphyseal closure**") at different times with different bones, and for all bones by about age twenty-one.
- So, as the individual bones mature, the epiphyseal plate gradually progresses to become an epiphyseal line, where no growth in length can occur anymore.

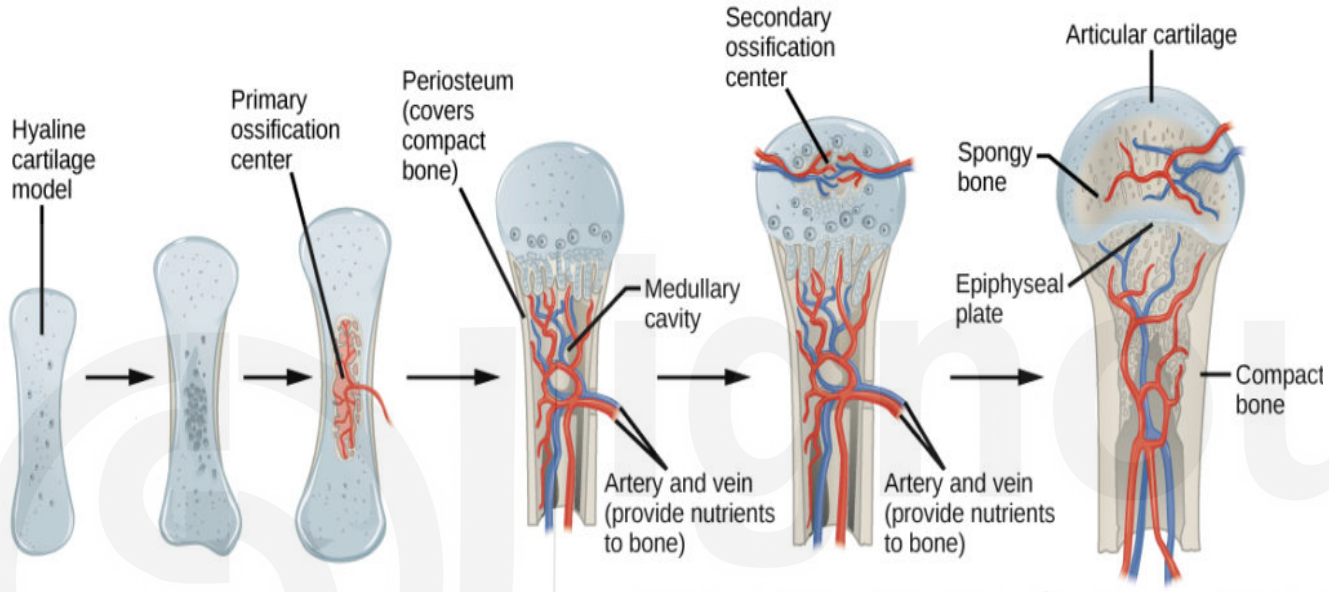

Fig. 12.7: Basic steps of endochondral ossification. (Image credit: http://cnx.org/contents/GFy_h8cu@10.53:rZudN6XP@2/Introduction)

Matrix of Mature Bone

A mature compact bone is composed of inorganic salts (~70%) and organic bone matrix (30%).

- The organic matrix is made of 90 - 95% *collagen protein fibers* (almost exclusively *type I fibers*) in a homogeneous gelatinous *ground substance*, which makes up the rest.
- The ground substance is made of extracellular fluid, proteoglycans such as '***chondroitin sulfate*** & ***hyaluronic acid***', and a group of non-collagen molecules such as ***osteocalcin, osteonectin, sialoproteins*** *etc.*, believed to regulate the process of bone mineralization.

✓ ***Osteocalcin*** is involved in calcium binding and transportation during the calcification process,

✓ ***osteonectin*** acts as a bridge between collagen and the mineral component,

✓ ***sialoproteins*** are rich in sialic acid and are thought to be responsible for nucleation of hydroxyapatite crystals and deposition of calcium salts.

Vitamins A, C, D, and minerals such as calcium, phosphorous, and magnesium are essential for normal growth of bone. Hormones such as parathyroid hormone, growth hormone, and calcitonin helps in formation of bone.

We must include balanced diet rich food in our diet to meet the daily requirement of vitamins and minerals required for the proper growth of the body.

SAQ 3

(a) Fill in the blanks:

i) Bone (osseous) tissue can be described as .....

ii) What is the template for the formation of long bones?.....

iii) Vertical growth (length) of a person stops once .....

(b) Differentiate between intramembranous and endochondral ossification

Now let us understand the structure and function of muscle cells.

12.5 STRUCTURE OF MUSCLE CELLS

All body cells have a universal property of 'contractility', but only muscle tissue has undergone the required modification for optimal use of this attribute. These specialized contractile cells -muscle cells- generate motile forces *via* contraction, which is the direct manifestation of the interaction of the 'contractile proteins' **actin** and **myosin**. These contractile proteins, in association with other components of myofilaments and affiliated proteins, work in unison to generate the motor forces necessary for cellular contraction.

These muscular forces generate momentum in different organs, move different body parts, and the body as a whole. Some of the cytoplasmic organelles of muscle cell have acquired highly specialized functionality, and thus special terminology is used for them; ***sarcolemma*** for plasma membrane, ***sarcoplasm*** for cytoplasm, and ***sarcoplasmic reticulum*** for smooth endoplasmic reticulum.

Muscles are of three kinds (Fig. 12.8):

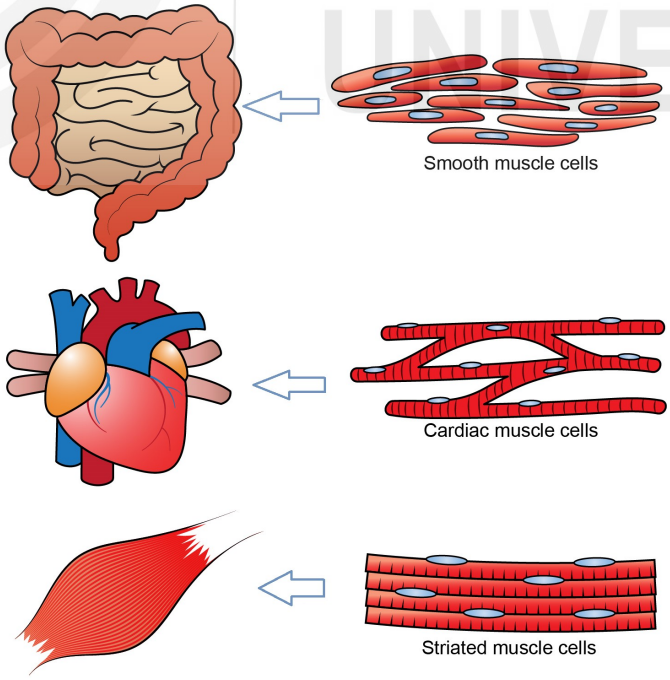

Fig. 12.8: Types of Muscles cells.

1. **Skeletal muscles:** These muscles are connected to the skeletal elements and help to move the skeleton and different body parts/organs such as limbs, the eye ball, the tongue etc. They are under one's own voluntary control hence referred to as **'*voluntary muscles*'**. The arrangement of the contractile protein filaments in the sarcoplasm (cytoplasm) gives them a peculiar appearance of prominent wavy cross-striations in under microscope, hence also referred to as **'*striated muscle*'**.

2. **Smooth muscles:** On the other hand, are so named as, unlike skeletal muscles, there is no wavy, striated appearance when observed under microscope. The smooth muscles can be seen restricted mainly to visceral organs, blood vessels etc. hence the name **'*visceral muscle*'.** They are **'*involuntary muscles'*** as they are not under voluntary control but under inherent autonomic and hormonal control.

3. **Cardiac muscles:** Though, like those of skeletal muscle cells, they appear striated, they are ***not*** under voluntary control. However, they have many structural and functional attributes that are intermediate to those of skeletal and smooth muscles. The most important feature of cardiac muscles is the continuous, rhythmic contractility, because of which the heart beats continuously.

Let us understand structure of body's muscles cells one by one:

12.5.1 Skeletal Muscle Cells

- The skeletal muscles are made of extremely elongated contractile cells, which are cylindrical and multinucleated; and are with diameter in the range of 10–100 μm (Fig. 12.9).
- The multinucleated feature tells about their syncytial nature, i.e., the individual giant muscle cell is formed by the fusion of embryonic mesenchymal cells called **'myoblasts'**. The cytoplasm of cells fuses but all the individual nuclei remain intact resulting in their giant size.
- Because of their elongated nature, they are often called **'muscle fibers'**.
- The nuclei are long and oval, and found at the periphery of the cell just beneath the cell sarcolemma. This feature helps in discriminating skeletal muscles from cardiac and smooth muscles, where, often a single nucleus is present located centrally.
- Each muscle is externally surrounded by a connective tissue sheath called the '**epimysium'**, whereas, the sarcolemma of individual muscle fibers (myocytes or muscle cells) is overlaid by a delicate areolar connective tissue layer called the **'endomysium'.**
- A cluster of 100-150 muscle fibers is ensheathed by a collagenous supporting tissue sheath called **'perimysium'** and form a **muscle fascicle**.

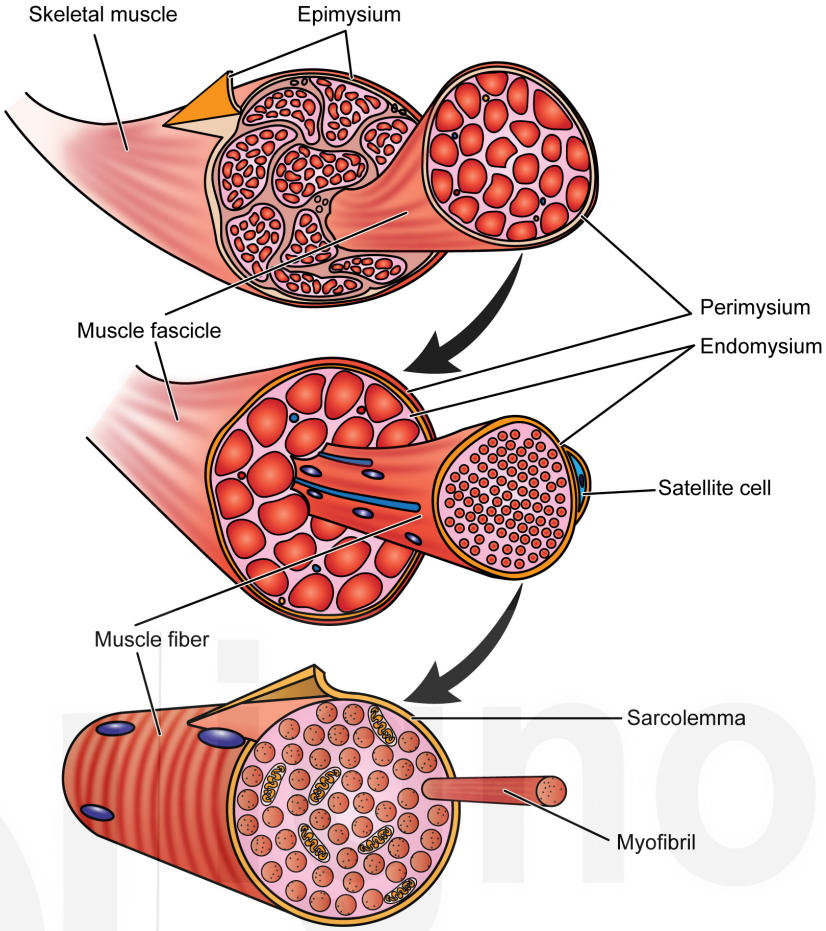

Fig. 12.9: Structure of skeletal muscle cells.

Microscopic organization of a skeletal muscle fiber:

- The sarcoplasm (cytoplasm) of a muscle fiber is filled with bundles of long contractile protein fibrils called the **myofibrils** (Fig. 12.10). The fibrils run along the entire length of a muscle cell.
- The sarcoplasm has large amounts of **glycerol** (source of energy for muscle cells), a protein called **myoglobin** (stores oxygen for metabolism), **mitochondria**, **nuclei** in the periphery and the highly specialized smooth endoplasmic reticulum, the **sarcoplasmic reticulum**.
- The sarcoplasmic reticulum forms a network around every single myofibril.
- The terminal sacs of it, called the **terminal cisternae,** store calcium ions, which play a very important role in muscle contraction.
- Each myofibril is made of several repeating units, referred to as '**sarcomere**', the functional units of the muscle.
- The striated appearance is due to the repeating bands of the actin (form light I bands) and myosin (form dark A bands) proteins present along the length of myofibrils.

- Each I band has a dense line running vertically through the middle called a Z disc or Z line. The Z discs mark the border of **sarcomeres**. Thus, one sarcomere is the span between two consecutive Z discs and contains one entire A band and two halves of an I band.
- The thick filaments interspersed between the thin filaments at the center of the sarcomere span the entire ***A band.*** The thick filaments are bound to proteins of the M line and to the Z disc across the **I bands** by a *massive protein* called **'titin',** which has *spring-like domains*.
- Projections from the thick filaments called **cross-bridges** extend toward the thin filaments. Cross-bridges play a fundamental role in muscle contraction.

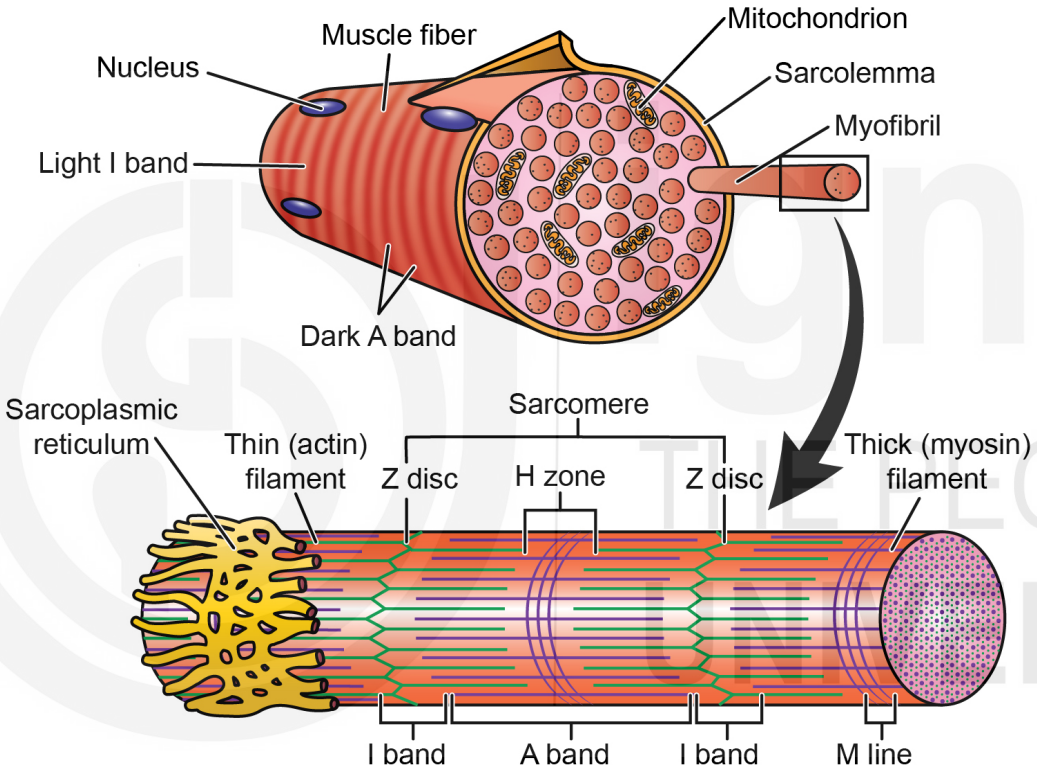

Fig. 12.10: Structural organization of a muscle fiber.

The sarcomere itself is bundled within the myofibril that runs the entire length of the muscle fiber and attaches to the sarcolemma at its end. A sarcomere is a highly organized structure of contractile thick (myosin) and thin filaments (actin) along with other regulatory proteins, troponin and tropomyosin (Fig. 12.11). When observed under electron microscope (TEM), an oblique section of myofibrils shows both **A** and **I** bands, and arrangement of **thin** and **thick** myofilament in a ***hexagonal*** pattern. They are arranged in such a manner that each **myosin** filament contacts with **six actin filaments**. Large mitochondria in cross-section and SER cisternae are also present between the myofibrils.

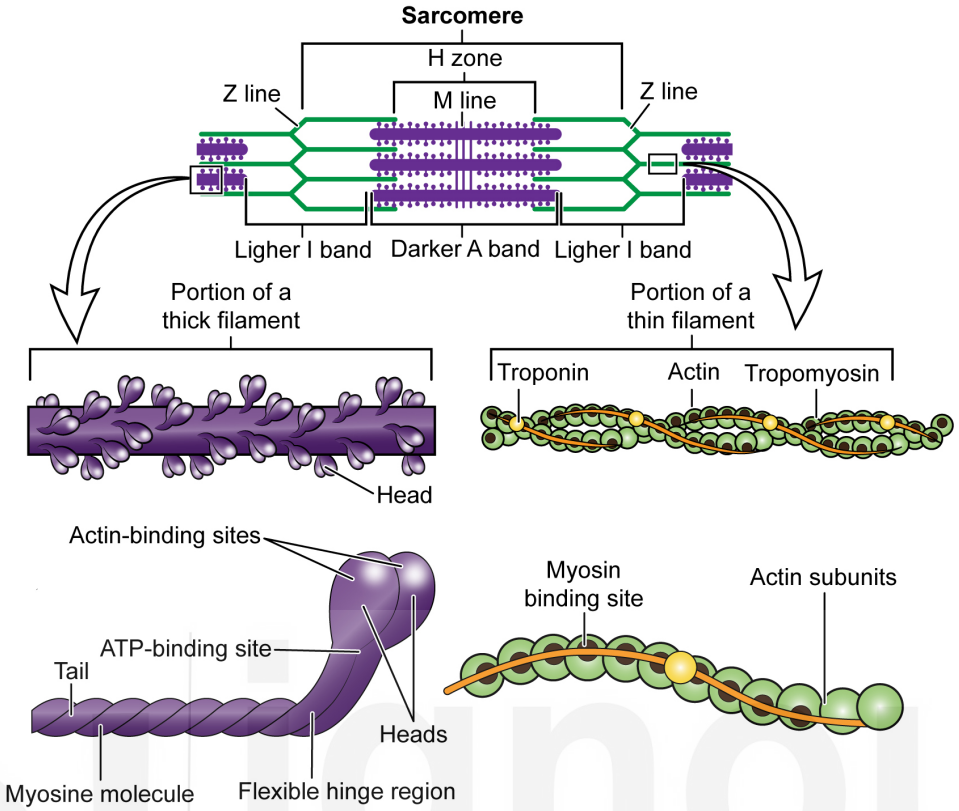

Fig. 12.11: Structure of a sarcomere.

12.5.2 Smooth Muscle Cells

- Smooth muscles are '*involuntary*' in nature, and devoid of wavy striations (that found in skeletal muscles) as they do not have sarcomeres; hence the name "**smooth**" muscles.
- Smooth muscles have **two** distinct muscle types - the **'visceral (single-unit) smooth muscle tissues'** and **'multi-unit smooth muscle tissues'**.
- The former is abundant in skin, small blood vessels/capillaries, GI tract, bladder, uterus etc.; whereas the latter is found in the walls of large arteries, bronchioles, arrector pili of hair follicles, iris and the ciliary body of eye etc.
- These fibers are covered by endomysium, are spindle-shaped, i.e., wide at the middle and tapering towards the tips, and have a single nucleus.
- Their size, in a relaxed condition, ranges from 30 to 200 μm (thousands of times shorter than skeletal muscle fibers).
- Sarcomeres are absent in smooth muscle fibers though the cell's sarcoplasm do have actin and myosin contractile proteins, which are organized into 'thick' and 'thin filaments'.
- The thin filaments are anchored firmly to special structures called ***'dense bodies'***, which are invested in the inner membrane of the sarcolemma and functionally *analogous* to the ***'Z-discs'*** of skeletal muscle fibers (Fig. 12.12).

- Some of these dense bodies can also be found dispersed throughout the sarcoplasm. All the dense bodies of a single muscle fiber are interconnected in a reticular fashion with the help of bundles of stretched **'*intermediate filaments*'**.

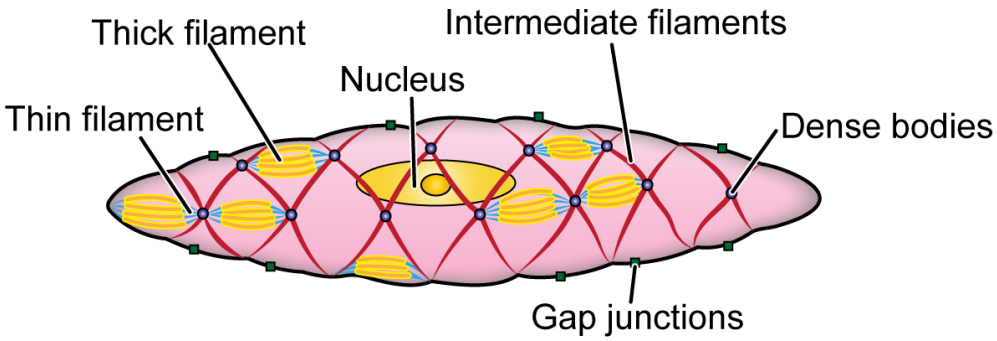

Fig. 12.12: Structure of smooth muscle cells.

12.5.3 Cardiac Muscle Cells

The 'cardiac muscle tissue' is a one of its kind, found only in the wall of heart (Fig.12.13).

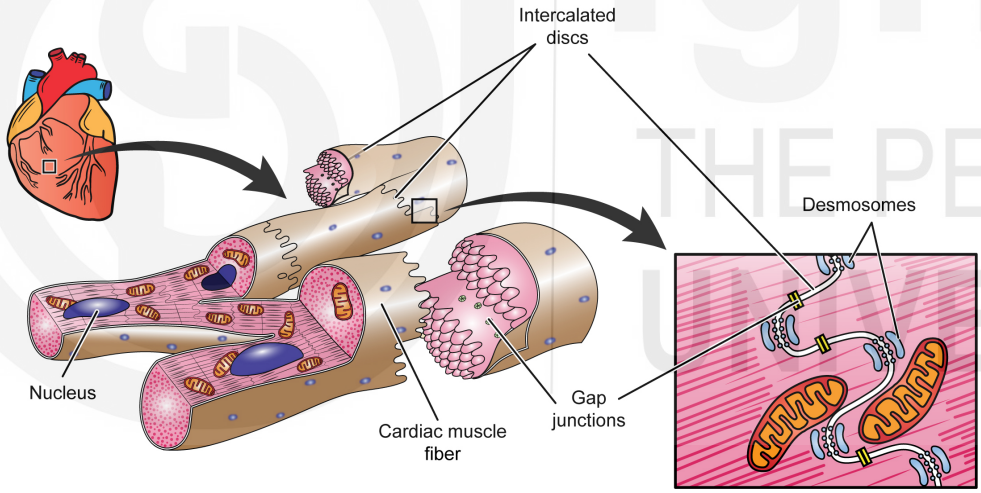

Fig. 12.13: Structure of cardiac muscles.

- They are 50–100 μm long and 14 μm in diameter.
- The uniqueness of this tissue is its 'highly coordinated contractions' in order to pump blood into the vessels of the circulatory system.
- Another unique feature is, the cardiac muscle cells are extensively branched.
- The branched cells are connected to one another at their ends by specialized wavy structures called the **'intercalated discs'**, which enable the heart to work as a pump.

- These discs are formed by the sarcolemma and contain two very important structures: **'gap junctions'** and **'desmosomes'**.
- The gap junctions between adjacent cardiac muscle fibers form a sort of 'electric couplings' thus creating a '**functional syncytium'**.
- This arrangement of electrically connected cardiac muscle cells allows quick transmission of action potentials between adjacent fibers, thereby leading to coordinated contraction of the entire heart.

SAQ 4

(a) Fill in the blanks:

i) ..... form most of the heart wall.

ii) .....is the outermost layer which encloses the entire muscle

iii) The plasma membrane of muscle fiber is known as .....

iv) The thread like structures of muscles cells called ..... known as myofibrils.

v) The functional unit of myofibril is .....

vi) The highly specialized smooth endoplasmic reticulum in skeletal muscle cells is called .....

vii) ..... is the source of energy for muscle cells.

viii) Why the muscle cells are that long and multinucleated? ..... .

ix) What are the long multinuclear cells of muscular tissue called: … .....

x) Myofibrils of muscle fibers are made of: .....

xi) The branched cardiac muscle cells are connected to one another by: … ….

xii) The physical contact point between the muscle and nerve: .....… .

xiii) The process of interlinking the nerve impulse and muscle contraction.....

(b) Match the column I with that column II.

Column I	Column II
A. Z disc	1. has all thin filaments
B. A-band	2. consists of thick filaments but no thin filaments
C. I-band	3. Entire length of thick filaments
D. H-line	4. present in the center of H-zone
E. M-line	5. Separates two sarcomere

12.6 PHYSIOLOGY OF MUSCLE CONTRACTION

All eukaryotic cells have membrane potential or electrical gradient across the membrane based on movement of positive and negative electrolytes. The movement of electrical potential is selectively controlled by membrane ion channels which forms the basis of muscle contraction and relaxation. A muscle contracts when its fibers receive an input through a somatic motor neuron.

- The motor neurons innervate the skeletal muscle fibers where the axon terminal of each motor axon divides into a cluster (> 2000) of synaptic end bulbs/boutons, each of which forms a junction/synapse with a muscle fiber called **Neuromuscular Junction (NMJ)**.
- Each synaptic end bulb contains hundreds of membrane-enclosed **'synaptic vesicles'**, each of which contains neurotransmitter **'acetylcholine'** (**Ach**) molecules.
- Thus, NMJ is the physical site where the information in the form of an electrical current (action potential/excitation) gets transformed into mechanical action which, in turn, gets translates into muscle contraction.
- All the biochemical-mechanical sequence of events leading to contraction of muscle are collectively called **'excitation-contraction coupling'**.

12.6.1 Excitation-Contraction (EC) Coupling

Excitation–contraction coupling is the physiological process that converts an electrical stimulus into a mechanical response. It is the link of action potential between nerve action and muscle contraction.

The process of EC coupling involves four steps (Fig. 12.14)**:**

- propagation of the action potential into the transverse (T) tubules and release of Ca^{2+} from the terminal cisternae (TC) of sarcoplasmic reticulum,
  - activation of the muscle proteins by Ca^{2+},
  - generation of tension by the muscle proteins, and
  - relaxation of the muscle.

(a) Release of Ca^{2+}: The action potential reaches NMJ through the motor neuron, polarizes the motor end plate (MEP), resulting in generation of graded potential called **End Plate Potential** (**EPP**).

- The EPP, in turn, causes an *action potential* in the post-synaptic sarcolemma due to the release of Na^{+}, which depolarizes it.
- The depolarization (action potential) spreads across and deeper into the muscle fiber *via* the T tubules.

- Depolarization of the T tubule by the action potential causes the opening of **voltage-gated Ca^{2+} channels**.
- Ca^{2+} flows out of the TC and into the cytoplasm, thereby raising the relaxed-state concentration of Ca^{2+} from 0.1 micromole per litre to several hundreds of times higher.

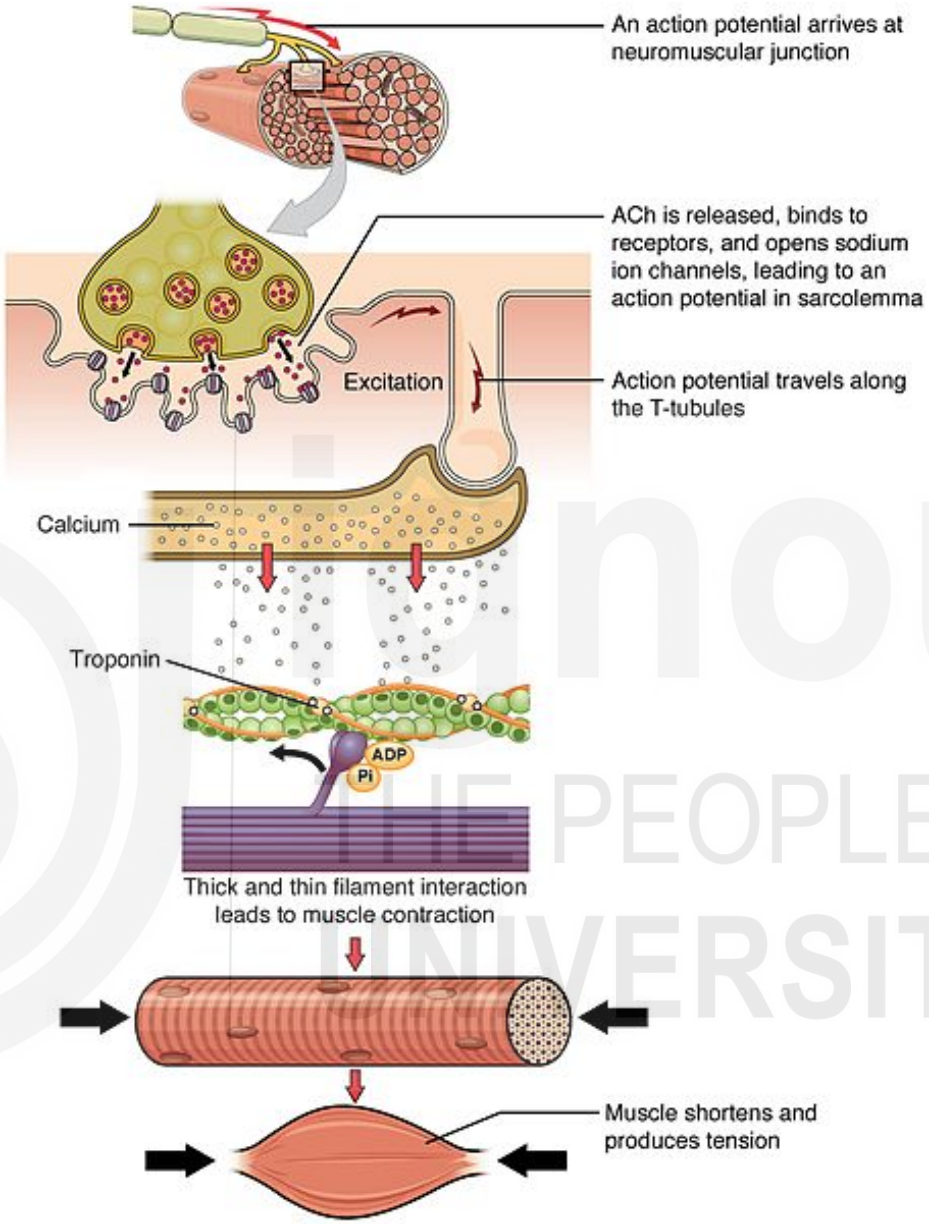

Fig. 12.14: Excitation-contraction coupling in a skeletal muscle contraction.
(Image source: https://cnx.org/contents/FPtK1zmh@8.25:fEI3C8Ot@10/Preface & https://commons.wikimedia.org/)

(b) Activation of muscle proteins: For a muscle to contract, the **thick** and **thin** filaments must *interact*.

- When the cell is at rest, this interaction is inhibited by troponin I (**TnI**) of thin filament.
- Ca^{2+} *removes* this inhibition by binding to troponin C (**TnC**) on the thin filament.

- In the myosin molecule, r**otation** can occur at two points. First site is located in the tail region to rotate the molecule outward when the spacing between the thick and thin filaments changes. The other site is located at the junction of the head and tail where the cross-bridge bends generating tension.

- The cross-bridge has **myosin-ATPase** enzyme which hydrolyzes **ATP** and provides the energy for muscle contraction.

(c) Generation of tension: Tension is generated by the *cycling* of the cross-bridges, which occurs after they bind to the thin filament.

(d) Relaxation occurs when the Ca^{2+} ions are removed from the cytoplasm by **Ca^{2+} active transport pumps** (**Ca^{2+}-ATPase**) located on the membrane of sarcoplasmic reticulum.

12.6.2 Contraction of Skeletal Muscles

During the contraction of striated muscles (skeletal & cardiac muscles), neither the thick nor thin filaments change their original length. Rather, the thick and thin filaments overlap each other and ***slide past one another***. The myosin heads attach and walk along the thin filaments, a mechanism known as '**Sliding filament Mechanism**'. Contraction is induced when an action potential arrives at the *neuromuscular junction* (**NMJ**), and is transmitted along the ***T tubules*** to the *sarcoplasmic reticulum* to trigger ***Ca^{2+} release***. In a resting muscle, the myosin heads cannot bind to the actin filaments because the myosin binding sites are concealed by the troponin-tropomyosin complex on the actin filaments. Calcium ions released, upon neural stimulation, bind to troponin, changing its shape and moving tropomyosin on the F-actin to reveal the myosin-binding active sites. **Following this**, a repeating sequence of biochemico-mechanical events sets off, leading to a cycle of muscle contraction (Fig. 12.15). The sequence of events is as follows—

a) ***ATP hydrolysis and formation of cross bridges*:** The myosin heads, which contain an ATP binding site and ATPase activity, hydrolyze ATP (ATP → ADP + Pi). The energy thus released energizes the myosin heads, which then interact with their binding sites on the actin filament, forming characteristic biomechanical structures called the ***'cross bridges'***.

b) ***Cross bridge cycling and power stroke*:** Binding of myosin heads to actin produce a conformational change and pivot (swivel) the myosin thus generating force, which pulls the thin filaments farther into the A band, toward the Z disc.

c) The 'power stroke' which leads to gradual shortening of sarcomeres. The cross bridges cycle continuously, generate force and shorten the sarcomere. A single muscle contraction results from hundreds of these cycles.

d) ***Detachment of myosin heads from actin*:** When the neural impulse stops (acetylcholine at the NMJ is broken down by acetylcholinesterase, this stops the stream of action potentials along the muscle fiber) and levels of free calcium diminish, the myosin heads detach from their binding sites. Tropomyosin again covers the myosin-binding sites on actin and the filaments passively slide back and sarcomeres return to their relaxed length.

- In the continued presence of Ca^{2+} and ATP, these ***attach-pivot-detach*** events occur in a repeating cycle, each lasting about ***50 milliseconds***, which shortens the sarcomere and contracts the entire muscle. However, in the absence of ATP, the *actin-myosin cross-bridges* become stable, which accounts for the rigidity of skeletal muscles **(rigor mortis)** that occurs as mitochondrial activity stops after death.

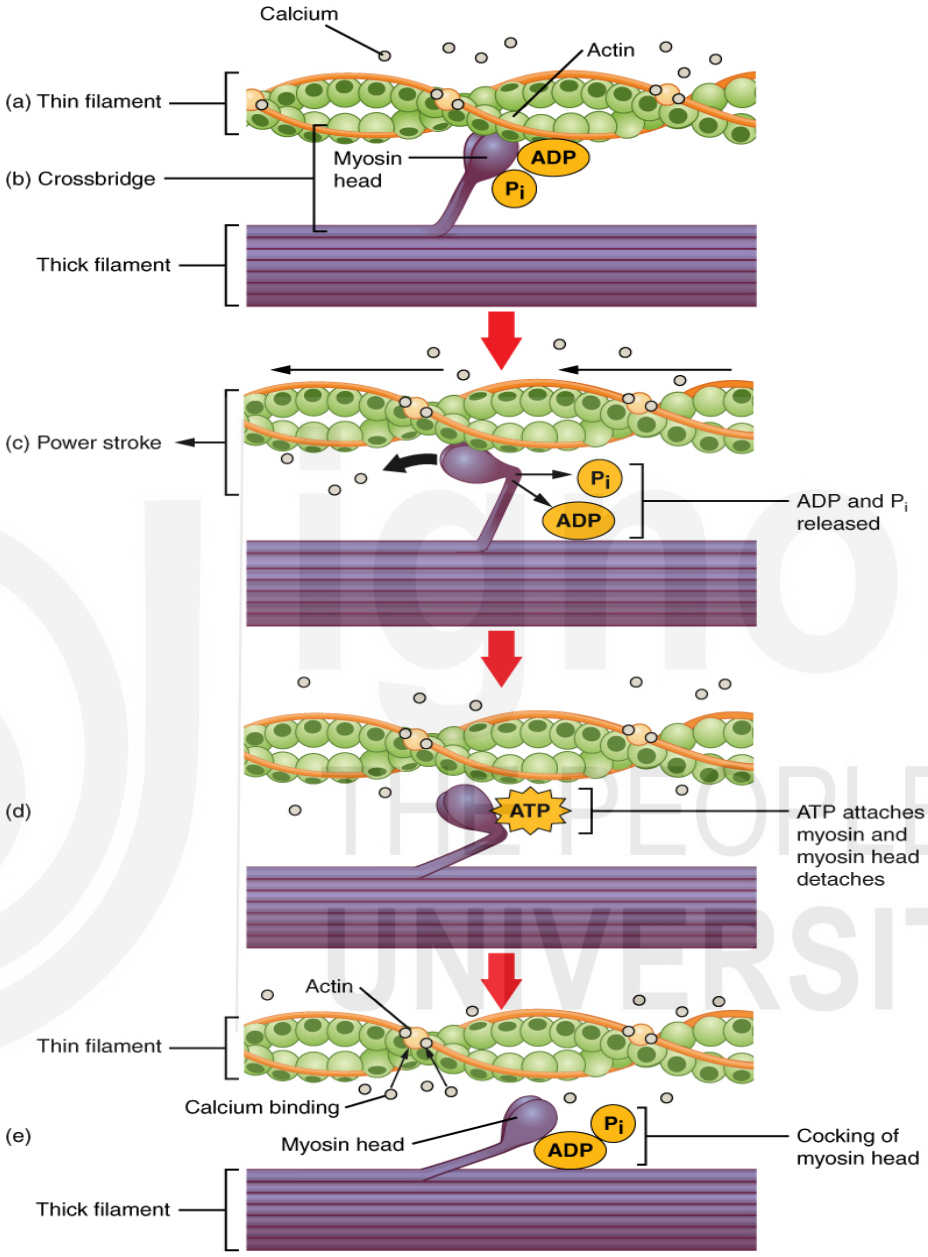

Fig. 12.15: Sequence of events of Excitation-Contraction (EC) Coupling in skeletal muscle.

(Image attribution: https://cnx.org/contents/FPtK1zmh@8.25:fEI3C8Ot@10/Preface by OpenStax)

12.6.3 Contraction of Smooth Muscles

The mechanism that controls smooth muscle contraction is different from that of striated muscles.

- The reason being, though the smooth muscle contains actin and myosin filaments, it doesn't possess the normal *troponin-tropomyosin complex* that is required for the control of contraction, instead, regulated by calcium binding protein **calmodulin** (Fig. 12.16).

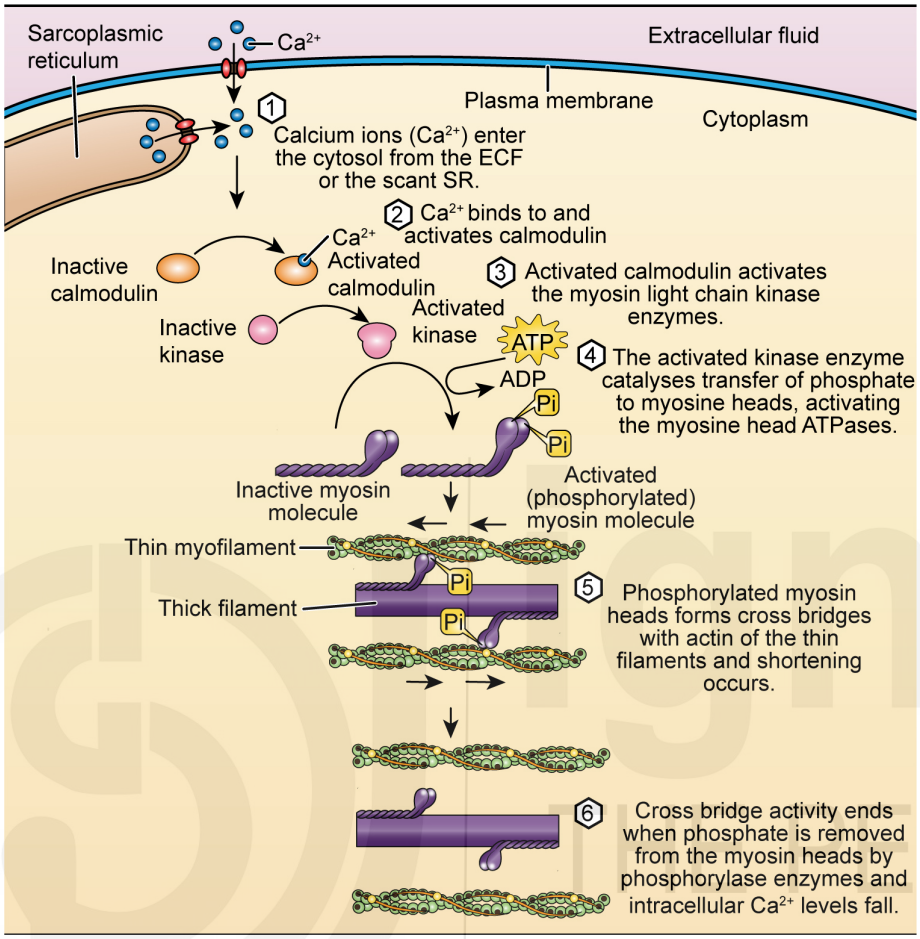

Fig. 12.16: Sequence of events of Excitation-Contraction (EC) Coupling in a smooth muscle.

- Because of their much smaller diameter than skeletal muscle cells, even the T-tubules are not required to spread the action potential to the deep interiors of the cell.

- Moreover, the contractile thick and thin filaments of the smooth muscles are not organized into sarcomeres like that seen in striated muscles.

- Instead, as explained earlier, bundles of large number of actin thin filaments bind to dense bodies, and the myosin thick filaments can be seen interspersed among the actin filaments.

- Because of the limited calcium storing capacity of sarcoplasmic reticulum, the calcium ions required for contraction are pulled in from two sources- ***(i)*** external Ca^{2+} ions brought in through the 'slow' calcium channels of sarcolemma indentations called 'calveoli', and **(ii)** additional Ca^{2+} ions supplied by the sarcoplasmic reticulum of the muscle fibers.

- These Ca^{2+} ions bind to calcium binding protein **calmodulin**, forming **'Ca^{2+}-calmodulin complexes'**.

- The complexes then activate an enzyme called **'myosin light chain kinase'**, which, in turn, activates the myosin heads by hydrolyzing ATP to ADP and Pi, with the Pi remain attached to the myosin heads.
- The energized (phosphorylated) myosin heads attach to the binding sites on the actin filament and pull them towards the center.
- In this manner, the force thus developed pull on the bundles of thin filaments, and in turn, the dense bodies close together, with some additional help from the cord-like intermediate filament network attached to them.
- This arrangement causes the entire muscle fiber to contract in a manner whereby the pointed ends are pulled toward the center, causing the midsection to bulge and overall shortening of the muscle.
- In this manner, the muscle continues to contract until the Ca^{2+} ions are transported back into the SR and out of the cell by active transport with the help of 'ATP-dependent calcium pumps'.
- However, a minimal concentration of calcium (basal levels) remains in the sarcoplasm, maintains the muscle tone, and keeps the muscle slightly contracted, which is important especially around blood vessels to maintain blood flow at a particular pressure.
- As the smooth muscles of viscera and other organs have to function for long periods without rest, their power output is relatively low, but constant. Thus, the smooth muscle contractions can continue without using large amounts of energy.
- They can remain in a state of contraction even after Ca^{2+} is removed and myosin kinase is dephosphorylated by the formation of **latch-bridges**, which are a type subset of cross-bridges formed between myosin heads and actin.
  - The latch-bridges keep the thick and thin filaments linked together for a prolonged period, without a need to hydrolyze ATP.

SAQ 5

(a) Fill in the blanks:

i) Calcium, binds with... .....during skeletal muscle contraction

ii) The binding sites for the cross-bridges are located on .....

iii) The ion ..... is necessary in the chemical events for muscular contraction.

iv) Thick and thin filament interaction leads to .....

v) ..... is the contractile protein of muscles cells.

vi) Calcium associates with ..... during smooth muscle contraction

(b) Enlist the four steps of EC coupling.

12.7 SUMMARY

- Musculoskeletal system is made up of bones (the skeleton), muscles, cartilage, ligaments, joints, and other connective tissue. It gives shape and support and; helps in the movement of the body.
- Bone is the main elements of the human skeleton system. Our body has 206 bones which can be long, flat, short, sesamoid and irregular based on their shape.
- A long bone is longer bone of the body. It has two parts: the **diaphysis** and the **epiphysis.** The diaphysis is the hollow, tubular shaft that is present between the proximal and distal ends of the bone. Inside the long bone is the **medullary cavity**, an inner cavity filled with yellow bone marrow in an adult. The outer wall of the diaphysis is hard that made up of osseous tissue (connective tissues).
- Bone tissue consists of four types of cells; osteoblasts, osteocytes, osteogenic cells, and osteoclasts. These cells form less than 2% of the bone mass. Osteogenic cells develop into osteoblasts, the mononucleate cells from which bones develop. Osteoclasts are responsible for bone resorption and osteocytes are star-shaped bone cells found in the cells of mature bone and maintain mineral concentration of matrix.
- Most bones have varying amount of compact and spongy osseous tissue based on their overall function. Compact bone is more dense and hard so that they can hold the compressive forces while spongy bone is a cancellous and soft bone with lightweight that can readily accommodate as per changing needs of the body.
- Osteon (or Haversian system) is the structural unit of bone. It is roughly cylindrical structure that is arranged into a lamellar bone. It is about 0.2 mm in diameter. Each ring of osteon is composed of collagen fiber and calcified matrix called lamella. The collagen fibers and lamella run parallel twisting each other in multiple directions. The lamellae run at perpendicular angles to each other, allowing osteons to resist twisting forces. Inside the osteon, a central canal, or Haversian canal contains blood vessels, nerves, and lymphatic vessels that supply the nutrient and electrolytes-rich blood.
- Osteogenesis is the process of development of bone. It is of two types: intramembranous ossification process form bone from fibrous membranes while endochondral ossification develops bone from the hyaline cartilage.
- The structure and function of bones are supported and coordinated by muscle cells. There are three types of body's muscle cells: Skeletal muscle, cardiac muscle and smooth muscle. Skeletal muscles are associated with skeletal structures (bone), cardiac muscle are restricted to heart and smooth muscle form the lumen of GIT, blood vessels etc.

- Muscle cells have a universal property of ‘contractility’ which can do modification for optimal use of this attribute. The muscle cells are often known as called ‘muscle fibers’.
- Skeletal muscles are generally extremely elongated, cylindrical and multinucleated contractile cells. They are closely associated with bones and help to move the skeleton and different body parts/organs. They are voluntary and striated muscles. The sarcoplasm (cytoplasm) of a muscle fiber is bound with long bundles of contractile protein fibrils called the ‘myofibrils’.
- Sarcomere is the functional units of the muscle. The thick filaments and thin filaments are connected with the sarcomere and are inter-dispersed and coordinated with the A band, M line and Z disc across the I bands by a massive protein called ‘titin’. The dark areas in the center of the sarcomere are called A bands. The light areas on either side of the Z disc are called I bands which contain only thin filaments. Each I band is bisected by a Z line. Thus, each sarcomere has 2 half I bands, one each on either end of it.
- Smooth muscles are ‘involuntary’ in nature, and devoid of wavy striations as they do not have sarcomeres; hence the name “smooth” muscles. They form two distinct muscle types; the ‘visceral (single-unit) smooth muscle tissues’ and ‘multiunit smooth muscle tissues’. Smooth muscles rich in contractile proteins, actin and myosin, are organized into ‘thick’ and ‘thin filaments’. They have dense bodies that are interconnected in a reticular fashion with the help of bundles of stretched ‘*intermediate filaments*’.
- Cardiac muscles are striated like skeletal muscle cells and present in only in heart. They constantly perform rhythmic contractility, because of which the heart beats continuously.
- Excitation–contraction coupling is process of skeletal muscle contraction in which an electrical potential converts to a mechanical response. The sarcoplasmic reticulum is a specialized endoplasmic reticulum that release calcium ion which causes muscle to contract. This process is mediated by the neurotransmitter Acetylcholine (ACh) that binds to receptors in the motor end plate.
- During the contraction of striated muscles, the length of thick or thin filaments does not change. Instead, these filaments overlap and slide past one another. The myosin heads attach and walk along the thin filaments, a mechanism known as ‘Sliding filament Mechanism’.

12.8 TERMINAL QUESTIONS

1. Discuss in detail the gross anatomy of a long bone.
2. Discuss the structural organization of spongy bone.
3. Explain the process of bone formation.
4. Discuss the histology of bone.

5. Give an account of the structure and function of skeletal, cardiac and smooth muscle.
6. Draw the labeled diagram of sarcomere.
7. Describe and contrast the process of contraction of skeletal muscles and smooth muscles.
8. Explain what is excitation contraction coupling.
9. Differentiate between skeletal muscles and smooth muscles.

12.9 ANSWERS

Self assessment Questions

1. i) bones and cartilage
   ii) Skeletal system
   iii) Axial and appendicular
   iv) teeth and bone
   v) Skeletal muscles
   vi) heart.

2. a) i) compact bone
   ii) Spongy bone
   iii) osteon
   iv) Haversian canals.
   v) Spongy bone
   vi) metaphyses –
   vii) osteogenic cells, osteoblasts, osteocytes, and osteoclasts

   b) Epiphysis, metaphysis and diaphysis.

   c) The bone is very much live. It contains blood vessels and nervous supply as well.

   d) Compact and spongy tissues.

4. a) i) dense, hard connective tissue
   ii) Hyaline cartilage templates.
   iii) the epiphysis fuses with the diaphysis and epiphyseal closure occurs.

b)

Intramembranous ossification	Indochondral ossification
It forms flat bone of the skull, temporal bones, jaw bones	Forms most skeletal (long bones) of the body.
Chondroblasts form the osteoid	Chondroblasts produce a hyaline cartilage.
A bone is directly formed from a mesenchymal connective tissue	A cartilage is first formed and then is replaced with bone for form skeletal.
Intermediate cartilage does not form	Intermediate cartilage is formed

5. a) i) Cardiac muscle cells
   ii) Epimysium
   iii) Plasmalemma
   iv) Myofibrils.
   v) Sarcomere
   v) Sarcoplasmic reticulum
   vi) The glycerol
   vii) They are syncytial cells, formed by the fusion of embryonic myoblasts.
   viii) muscle fibers.
   ix) Contractile proteins organized into sarcomeres.
   x) intercalated discs.
   xi) neuromuscular junction.
   xii) Excitation-contraction (EC) coupling.

   b) A-5, B-3, C-1, D-2, E 4

6. i) Troponin
   ii) Actin.
   iii) Calcium
   iv) Muscle contraction
   v) Myosin.

vi) Calmodulin

Terminal Questions

1. Refer to Section: 12.3. Anatomy of Bone
2. Refer to section 12.3.2. Spongy bone
3. Refer to Section: 12.4. Formation of Bones
4. Refer to Section: 12.3.3 Bone Cells
5. Refer to Sections: 12.5. Structure of Muscle Cells, 12.5.1. Skeletal muscle cells, 12.5.2. Smooth muscle cells, and 12.5.3. Cardiac muscle cells
6. Refer to Section: 12.5.1. Skeletal muscle cells and Fig. 12.13 Structure of a sarcomere.
7. Refer to Sections: 12.6. Physiology of Muscle Contraction. 12.6.1 Excitation-contraction (EC) coupling, 12.6.2 Contraction of skeletal muscles and 12.6.3. Contraction of smooth muscles
8. Refer to Section: 12.6.1 Excitation-contraction (EC) coupling
9. Refer to Sections: 12.5.1. Skeletal muscle cells and 12.5.2. Smooth muscle cells.