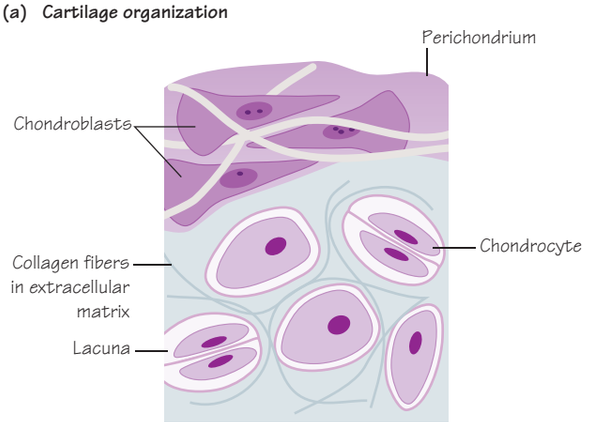
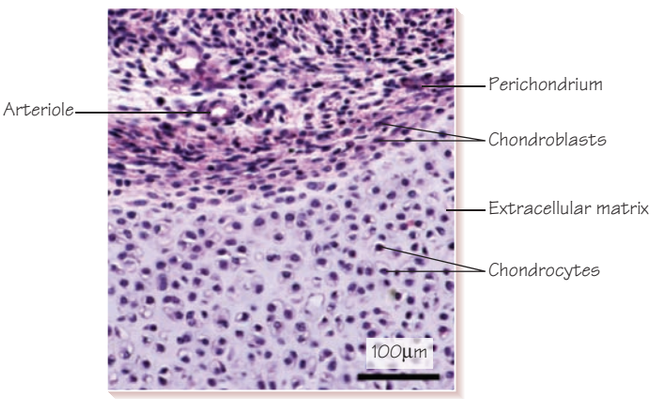
15 Cartilage

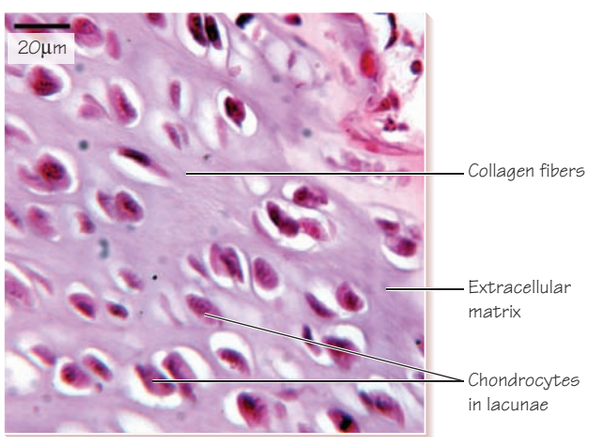
(a) Cartilage organization



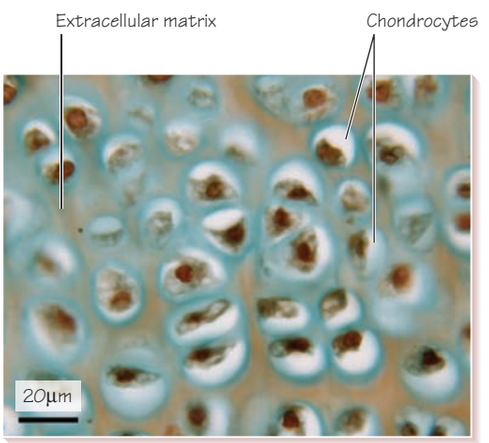
(b) Hyaline cartilage in fetal foot



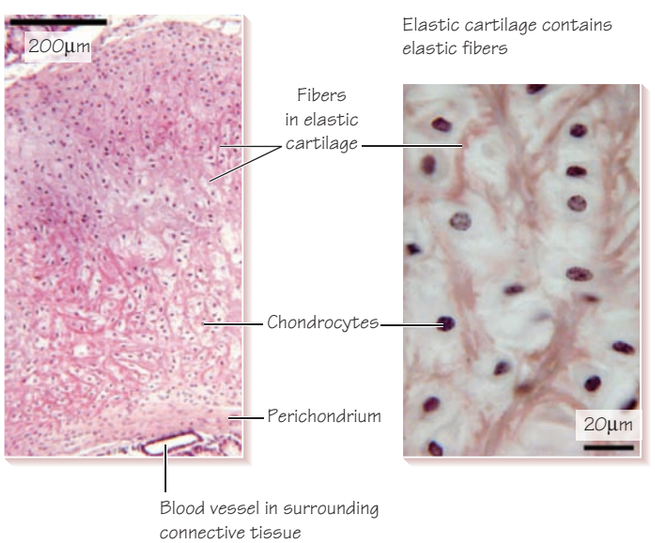
(c) Hyaline cartilage (epiphyseal plate)



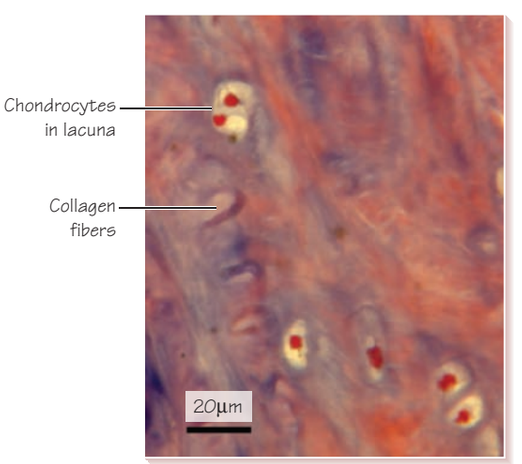
(d) Hyaline cartilage in the trachea (trichrome stain)



(e) Elastic cartilage (epiglottis)



(f) Fibrocartilage (invertebral disc)



Fibrocartilage does not have a perichondrium. It is very rich in collagen fibers, and there is less matrix material around the chondrocytes than in hyaline cartilage

Cartilage is a rigid form of connective tissue. It consists of cells embedded in an extracellular matrix, the content of which defines their property. The extracellular matrix is a mixture of glycosaminoglycans (GAGs), fibers and structural glycoproteins (see Chapter 12).

Cartilage is thin, does not have a blood supply (avascular), is flexible, resistant to compressive forces, and yet can bend.

Functions of cartilage

1 A supporting framework for the walls of airways in the nose, trachea, larynx and bronchi, preventing airway collapse.
2 Forms the articulating surfaces of bones.
3 Forms the template for the growth and development of most of the fetal skeleton including long bones. In children, the cartilaginous epiphyseal growth plates at the ends of long bones show up on X-rays. They disappear when adults reach their full height.

Constituents of cartilage

Cells

The cells in cartilage are **chondroblasts** and **chondrocytes** (*chondro* means 'cartilage'). Chondroblasts are found in the outer covering layer of cartilage (Fig. 15a). They secrete the extracellular matrix and fibers and, as they do so, they become trapped inside it and mature into chondrocytes.

In **growing cartilage**, the chondrocytes can divide, and the daughter cells remain close together in groups, forming a 'nest' of 2–4 cells. These trapped cells sit together in clear areas called **lacunae** (*lacunae* means 'little lakes').

Active chondrocytes are large secretory cells with a basophilic (purple staining) cytoplasm, which arises from a high content of rough endoplasmic reticulum (ER).

Older chondrocytes contain fat droplets.

Fixation of cartilage usually causes some shrinkage between the cell border and the lacunar wall, so that the lacunae look more prominent in fixed tissue.

Extracellular matrix

The extracellular matrix (ECM) of cartilage is made up of **aggrecan** (10%), water (75%) and fibers. **Aggrecan** is formed of aggregates of up to 100 molecules of the GAG, chondroitin sulfate, bound to hyaluronic acid. Chondroitin sulfate is rubbery, provides cartilage with resilience, and this type of GAG is only found in cartilage.

Fibers in cartilage are either collagen, or a mixture of collagen and elastin fibers. A network of collagen fibers generates a very high tensile strength. Elastic fibers provide elasticity.

A layer of dense irregular connective tissue called the **perichondrium** (*peri* means 'around') surrounds hyaline and elastic cartilage. The outer layer of the perichondrium contains collagen-producing fibroblasts, and the inner layer contains chondroblasts.

Unlike other connective tissue, cartilage is **avascular** (like epithelium). Cartilage is nourished by long-range diffusion from nearby capillaries in the perichondrium. Therefore, cartilage can never become very thick, as diffusion would not be sufficient to supply the cartilage with nutrients and oxygen.

Two ways that cartilage grows

- **Interstitial growth:** chondrocytes grow and divide and lay down more matrix inside the existing cartilage. This mainly occurs during childhood and adolescence.
- **Appositional growth:** new surface layers of matrix are added to the pre-existing matrix by new chondroblasts from the perichondrium.

Types of cartilage

There are three types of cartilage: hyaline, elastic, and fibro-cartilage.

Hyaline cartilage

This is the most common, and the weakest type of cartilage. Its name comes from the glassy appearance of living cartilage (*hyalos* is Greek for 'glass').

- It stains light purple (basophilic) in H&E.
- It contains dispersed fine type II collagen fibers, which provide strength. (These are difficult to see in sections.)
- It has an outer layer called the perichondrium.
- Hyaline cartilage is a precursor of bone (Fig. 15b).
- Hyaline cartilage is found in epiphyseal growth plates (Fig. 15c), ribs, nose, larynx,and trachea (Fig. 15d).

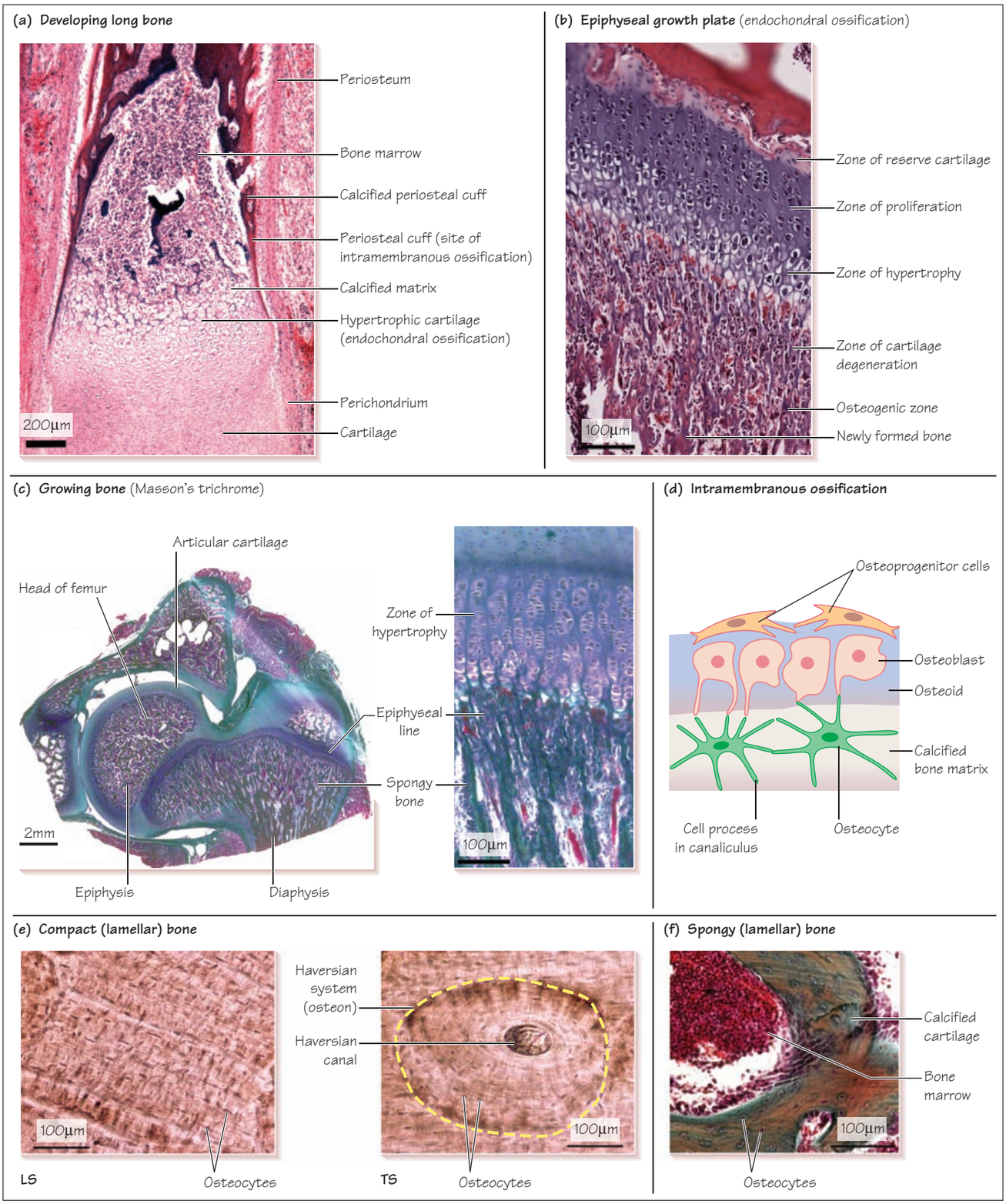
Elastic cartilage

- It is found in the external ear, larynx, and epiglottis (Fig. 15e), where it helps to maintain their shapes.
- It is flexible and resilient and contains elastic as well as collagen fibers.
- The chondrocytes are found in a threadlike network of **elastic fibers** within the matrix.
- It has a perichondrium.

Fibro-cartilage

- Fibro-cartilage is found in joint capsules, ligaments, tendon insertions, and intervertebral discs (Fig. 15f).
- It is made up of alternating layers of hyaline cartilage matrix and thick layers of dense parallel bundles of collagen fibers, oriented in the direction of applied stresses, to reinforce this cartilage.
- This is strongest kind of cartilage.
- It does not have a perichondrium as it is usually sandwiched between hyaline cartilage and tendons or ligaments.

16 Bone


(a) Developing long bone
Periosteum
Bone marrow
Calcified periosteal cuff
Periosteal cuff (site of intramembranous ossification)
Calcified matrix
Hypertrophic cartilage (endochondral ossification)
Perichondrium
Cartilage
200µm
(b) Epiphyseal growth plate (endochondral ossification)
Zone of reserve cartilage
Zone of proliferation
Zone of hypertrophy
Zone of cartilage degeneration
Osteogenic zone
Newly formed bone
100µm
(c) Growing bone (Masson's trichrome)
Articular cartilage
Head of femur
Epiphyseal line
Spongy bone
2mm
Epiphysis
Diaphysis
Zone of hypertrophy
100µm
(d) Intramembranous ossification
Osteoprogenitor cells
Osteoblast
Osteoid
Calcified bone matrix
Cell process in canaliculus
Osteocyte
(e) Compact (lamellar) bone
100µm
LS
Osteocytes
Haversian system (osteon)
Haversian canal
100µm
TS
Osteocytes
(f) Spongy (lamellar) bone
Calcified cartilage
Bone marrow
100µm
Osteocytes

Bone, like cartilage, is a strong, flexible and semi-rigid form of connective tissue. It can withstand compression forces, and resists bending, twisting, compression and stretch.

It contains cells embedded in an extracellular calcified collagen rich matrix, which makes bone very strong.

Unlike cartilage, it is highly vascularized.

Functions of bone

1 **Support:** Bones provide a structural framework for the body.
2 **Protection:** Bones in the skull and the ribs protect internal organs such as the brain, and the heart and lungs, respectively.
3 **Assisting movement:** Bones provide the major attachment sites for muscles, and joints between bones allow movement to take place.
4 **Mineral homeostasis:** Bone stores calcium and phosphorus.
5 **Blood cell production:** Cells are produced in the bone marrow.

Types of bone formation

1 **Endochondral** (most common): bone forms on a temporary cartilage model (Fig. 16a–c).
- Cartilage grows (zone of proliferation), the chondrocytes mature (zone of maturation) and start to hypertrophy (zone of hypertrophy).
- The matrix starts to calcify, and the chondrocytes die (zone of cartilage degeneration).
- The fragmented calcified matrix left behind acts as structural framework for bony material. Osteoprogenitor cells and blood vessels from the periosteum invade this area, proliferate, and differentiate into osteoblasts, which start to lay down bone matrix (osteogenic zone).

2 **Intramembranous** (rarer): bone forms directly onto fibrous connective tissue (the periosteal cuff) without an intermediate cartilage stage (Fig. 16a,d). Intramembranous ossification occurs in a few specialized places such as the flat bones of skull (i.e. parietal bone), mandible, maxilla, and clavicles.

Bone formation in the fetus

The primary ossification center forms first in the **diaphysis** (shaft) of long bones. Later on a secondary ossification center forms in the **epiphysis** (rounded end of long bones).

Bone replaces cartilage in the epiphysis and diaphysis, except in the epiphyseal plate region (Fig. 16b,c). Here the bone continues to grow, until maturity (around 18 years old). The growth plate can be seen in X-rays.

The long shafts of bone are made up of a thick walled cylinder that encloses a central bone marrow cavity.

Content of bone

Cells

Osteoprogenitor cells, osteoblasts, osteocytes, and osteoclasts are all found in bone.

Osteoprogenitor cells are the 'stem' cells of bone, and are the source of new **osteoblasts**.

Osteoblasts line the surface of bone, and secrete collagen and the organic matrix of bone (osteoid), which then becomes calcified.

Osteoblasts become trapped in the organic matrix, and differentiate into **osteocytes.**

Osteocytes maintain bone tissue. They sit in the calcified matrix, in small spaces called lacunae (singular, lacuna). They project fine processes out through small channels (canaliculi), which transport nutrients and waste. The tips of these processes contact those from other osteocytes, and are connected by communicating gap junctions.

Osteoclasts are large, multinucleated (4–6 nuclei) cells with a 'ruffled border', that resorb bone matrix, and are important for bone remodeling, growth, and repair. They secrete enzymes (e.g., carbonic anhydrase), to acidify and decalcify the matrix, and hydrolases, to break down the matrix once it is decalcified.

They are **not** derived from osteoprogenitor cells, but are derived from monocytes/macrophages (see Chapter 13).

Bone is remodeled in response to mechanical stress and hormones (parathyroid hormone stimulates resorption and calcitonin inhibits resorption).

Extracellular matrix

The extracellular matrix (ECM) (30%) contains proteoglycans: glycosaminoglycans, osteonectin (anchors bone mineral to collagen), glycoproteins, and osteocalcin (calcium-binding protein).

Fibers

Bone contains collagen fibers (90% are type I fibers), which help to resist tensile stresses.

Bone also contains **water** (25%) and **hydroxyapatite**, a bone mineral (~70% of bone).

Bone is hard because the ECM is calcified. Calcium salts crystallize in the spaces between collagen fibers.

The **periosteum** is a dense fibrous layer, found on the outside of bone where muscles insert, but not in regions of bone covered by articular cartilage. It contains bone-forming (osteoprogenitor) cells.

The **endosteum** lines the inner surfaces of bones.

Types of bone

Woven (primary) bone is the first type of bone to be formed at any site, and contains randomly arranged collagen fibers. This is quickly replaced by **lamellar** bone, in which collagen fibers become remodeled into parallel layers.

There are two types of **mature bone**, compact (80% of all bone) and spongy (20%).

Compact bone

Compact bone is found in the shafts (diaphyses) of long bones (Fig. 16e). Older compact bone is organized into **Haversian systems** (or **osteons**). The osteocytes are arranged in concentric rings of bone matrix called lamellae (little plates), around a central Haversian canal (which runs longitudinally), and their processes run in interconnecting canaliculi. The central Haversian canal, and horizontal canals (perforating or Volkmann's canals) contain blood vessels and nerves from the periosteum.

Spongy (cancellous) bone

Cancellous bone is found at the **ends of long bones** (in the epiphysis, Fig. 16c,f). It contains red bone marrow in large open spaces (marrow spaces) between a network of bony plates (trabeculae).

Growth and nourishment of bone

Bone is well vascularized. The central cavity contains blood vessels and stores bone marrow. All osteocytes in bone are within 0.2 mm of a capillary.